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IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Main report

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

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1. WHAT IS THE PROBLEM AND WHY IS IT A PROBLEM?

1.1. Introduction

In this impact assessment the potential impacts of secondary legislation *(implementing and delegated acts)*, required by Regulations (EC) No 1107/2009[1] and Regulation (EU) No 528/2012[2], are evaluated. Under these regulations, there is a legal obligation for the European Commission to set specific scientific criteria to identify substances which have endocrine disrupting properties, hereafter called "endocrine disruptors" (EDs). In particular under the Biocidal Products (BP) Regulation the Commission should adopt a delegated act as regards the criteria by December 2013. The Court judgement on the Case T-521/14 (December 2015) states that the European Commission breached EU law by failing to set criteria to identify endocrine disruptors under the BP Regulation within the legal deadline.

The impact assessment is considered important to take a sound decision based on science and evidence, in particular because the EU legislation was the first worldwide to introduce regulatory consequences on EDs and there is also no precedent of setting scientific criteria to identify EDs in a regulatory context. Recent developments have taken place outside of a regulatory context (e.g. World Health Organization[3;4;5;6] (WHO), and Organisation for Economic Co-Operation and Development[7] (OECD)), or in a context of substance prioritisation for further assessment and risk management (e.g. US EPA Endocrine Disruptor Screening Programme[8]).

The regulatory consequences for the substances identified as EDs are already defined in the regulations mentioned above with respect to plant protection or biocidal products. Active substances which are identified as ED shall not be approved (they are not allowed on the EU market) unless specific "derogations" could be applied. These derogations have a wider scope under the BP Regulation in comparison to the PPP Regulation, adding a layer of complexity to the analysis of the evidence regarding potential impacts.

Because of the regulatory consequences mentioned above (the non-approval of active substances or restricted approval if derogations apply), impacts are expected once the criteria are applied. These impacts may be on human health, environment, sectorial competiveness including agriculture, and trade. They are expected to be higher under the PPP Regulation than under the BP Regulation because of the different scope of the derogations. This was confirmed in the public consultation where respondents expressed diverging views on the expected impacts and on their different preferred options (see more details in Annex 2 and Section 5.2 of this main report).

[1] Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309.

[2] Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products. Official Journal of the European Union, L 167, 27 June 2012. doi:10.3000/19770677.L_2012.167.eng

[3] WHO/UNEP. 2012. State of the science of endocrine disrupting chemical. An assessment of the state of the science of endocrine disruptors prepared by a group of experts for the United Nations Environment Programme (UNEP).

[4] WHO 2014. Identification of risks from exposure to EDCs at the country level. Retrieved from: http://www.euro.who.int/en/publications/abstracts/identification-of-risks-from-exposure-to-endocrine-disrupting-chemicals-at-the-country-level

[5] WHO. 2015. Identification of risks of EDCs: overview of existing practices and steps ahead. Report of a meeting in Bonn, Germany 7-8 July 2014

[6] WHO/UNEP 2015 Strategic Approach to International Chemicals Management (SAICM). International Conference on Chemicals Management fourth Session. SAICM/ICCM.4/9. Emerging policy issues and other issues of concern.

[7] OECD Work Related to Endocrine Disrupters. Retrieved from: http://www.oecd.org/env/ehs/testing/oecdworkrelatedtoendocrinedisrupters.htm

[8] United States Environmental Protection Agency (EPA). Endocrine Disruptor Screening Program (EDSP) Overview. Retrieved from: http://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-edsp-overview

This impact assessment is not concluding on any preferred option for setting scientific criteria to identify endocrine disruptors, but aims at providing additional information to decision makers on the potential implications of these different options under the PPP and BP Regulations. The impact assessment is focused on PPP and BP and not directly related to other EU legislative acts, because only the PPP and BP require by law to set criteria to identify EDs. However, setting the criteria to identify EDs may have potential implications on other legislations which contain specific provisions on EDs (REACH, Cosmetics, and Water Framework Directive)[9].

1.2. Endocrine disruptors, background and general regulatory context

EDs are chemicals which can interfere with the endocrine (hormone) systems[10] in animals and humans. Both synthetic as well as naturally-occurring chemicals are known to have endocrine disrupting properties. For instance, it has been found that bisphenol F forms during mustard production from a natural ingredient of mustard grains[11,12] at high concentrations which may pose a risk to specific groups of the human population.[13] Exposure to synthetic chemicals can occur from different sources, e.g. from residues of plant protection products or biocidal products, but also from consumer products or articles used in daily life.

Knowledge about the potential toxicity of chemicals, including which chemicals may induce certain adverse effects, is available since long time and is already reflected in the EU legislation on chemicals (since the 90'ies for PPP and BP). Compared to this, endocrine disruption is a relatively recent way of looking at the toxicity of chemicals, where first scientific discussions started in the 1990s.[14] Endocrine disruption aims to understand the mode of action, i.e. *how* exposure to chemicals leads to the adverse effects observed.

Although the focus on EDs is recent in a regulatory context, many of the adverse effects which may be caused by EDs (e.g. carcinogenicity or reproductive effects) have already been studied and regulated for many years in the EU chemical's legislation, without detailed knowledge of the potential endocrine mode of action. This resulted in a reduction in general terms of the exposure of humans and the environment to the number of chemicals and to an increase of protection of humans and the environment. In Section 1.3 more details on the regulatory context are given.

Focusing on the EU, in 1999 the European Commission's Scientific Committee for Toxicity, Ecotoxicity and the Environment (CSTEE) stated that EDs posed a 'potential global problem

[9] REACH (Regulation (EC) 1907/2006), Cosmetics (Regulation (EC) 1223/2009), Water Framework Directive (Directive 2000/60/EC),

[10] The endocrine system is the system in the body which produces hormones to provide an internal communication system between cells located in distant parts of the body. Retrieved from: http://www.yourhormones.info/, Society of Endocrinology, UK

[11] Swiss Federal Department of Home Affairs FDHA. Federal Food Safety and Veterinary Office FSVO. Risk Assessment. Bisphenol F in mustard. Retrieved from: http://www.efsa.europa.eu/sites/default/files/assets/af150611a-ax11.6.pdf

[12] Zoller, O. et al. 2016. Natural occurrence of bisphenol F in mustard, Food Additives & Contaminants: Part A, 33:1, 137-146, DOI: 10.1080/19440049.2015.1110623

[13] Higashihara N, et al. 2007. Subacute oral toxicity study of bisphenol F based on the draft protocol for the "Enhanced OECD Test Guideline no. 407". Arch Toxicol. Dec;81(12):825-32. Epub 2007 Jul 13. Retrieved from: http://www.ncbi.nlm.nih.gov/pubmed/17628788

[14] "The Impact of Endocrine Disruptors on Human Health and Wildlife" workshop, Weybridge (UK), 2 to 4 December 1996. The workshop was supported by European Commission, European Environment Agency, WHO European Centre for Environment and Health, OECD, national authorities and agencies of the UK, Germany, Sweden and The Netherlands, CEFIC and ECETOC.

for wildlife'[15] and subsequently the Community Strategy for EDs[16] was adopted. Since then, different *specific* provisions on EDs have been included in various pieces of EU legislation[17] with the aim of being able to take regulatory decisions based on more detailed knowledge.

Although these provisions on EDs are in force, agreed scientific criteria for identifying EDs *in a regulatory context* are so far lacking, internationally or at EU level. In the context of the PPP and BP Regulations the European Commission has the legal obligation to establish scientific criteria to identify substances with endocrine disrupting properties by December 2013. Further, both the Council of the European Union and the European Parliament have addressed EDs at several occasions during the last years. In particular, in 2000[18] and 2013[19] the European Parliament adopted Resolutions on EDs. In 2000, the Environment Council adopted Conclusions[20] on EDs.

1.2.1. Scientific developments which are relevant in the EU regulatory context

In 2002 the WHO/International Programme for Chemical Safety (WHO/IPCS) defined an ED as: "*an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations"*. This definition serves as a basis for the options developed for this impact assessment because it reached wide consensus among scientists.

Several relevant scientific reports relevant in the EU regulatory context have been published during the last years by EU agencies, EU Scientific Committees, or in the context of activities co-ordinated or commissioned by the European Commission, indicating the advancement of the scientific discussion on some concepts. In particular:

- In 2010 the European Food Safety Authority (EFSA) published a scientific report[21] which provides an overview of existing knowledge on endocrine active substances and of the challenges for risk assessment in relation to food and feed, as well as a summary of current initiatives at national, EU and international levels.[5]
- The report "State of the Art Assessment of Endocrine Disruptors"[22] commissioned by the European Commission summarises advances in the state of the science from 2002 to 2011

[15] European Commission's Scientific Committee for Toxicity, Ecotoxicity and the Environment (CSTEE) Opinion on Human and Wildlife Health Effects of Endocrine Disrupting Chemicals, with Emphasis on Wildlife and on Ecotoxicology Test Methods: March 1999. Available at: http://ec.europa.eu/health/ph_risk/committees/sct/documents/out37_en.pdf

[16] Communication from the Commission to the Council and the European Parliament - Community strategy for endocrine disruptors - A range of substances suspected of interfering with the hormone systems of humans and wildlife /* COM/99/0706 final */

[17] Provisions were added into the Water Framework Directive (Directive 2000/60/EC), the chemicals regulation REACH (Regulation (EC) 1907/2006), the Plant Protection Products Regulation (EC) 1107/2009, the Biocidal Products Regulation (EU) 528/2012, and the Regulations on Cosmetics (Regulation (EC) 1223/2009). Provisions were also included in the Proposal for a regulation on medical devices (amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009).

[18] European Parliament resolution on the Commission communication to the Council and the European Parliament on a Community strategy for endocrine disruptors - a range of substances suspected of interfering with the hormone systems of humans and wildlife (COM(1999) 706 - C5-0107/2000 - 2000/2071(COS))

[19] European Parliament resolution of 14 March 2013 on the protection of public health from endocrine disrupters (2012/2066(INI))

[20] Council conclusions (Environment) on endocrine disrupters. Brussels, 30 March 2000. Retrieved from: http://www.consilium.europa.eu/en/uedocs/cms_data/docs/pressdata/en/envir/07352.en0.html#_Toc480100459

[21] European Food Safety Authority; EFSA scientific report of the Endocrine Active Substances Task Force. EFSA Journal 2010; 8(11):1932. [59 pp.] doi:10.2903/j.efsa.2010.1932.

[22] Kortenkamp, Martin, Faust, Evans, McKinlay, Orton, Rosivatz. 2011. State of the art assessment of endocrine disruptors. Final Report, Project Contract Number 070307/2009/550687/SER/D3. Retrieved from: http://ec.europa.eu/environment/chemicals/endocrine/pdf/sota_edc_final_report.pdf

and maps ways of addressing EDs in important pieces of EU chemicals legislation (e.g. PPP Regulation, BP Regulation, REACH).

- In 2013, two reports published by the Joint Research Centre (JRC) summarise the work of the "Endocrine Disruptors Expert Advisory Group".[23,24] The reports indicate that the experts agreed that existing standardised assays are mainly available only for the estrogenic, androgenic, thyroid and steroidogenic modalities (EATS), and that test guidelines are lacking for birds and invertebrates. Agreement was not reached on some elements, e.g. the role of hazard characterisation (potency, severity, lead toxicity, irreversibility) when identifying EDs, whether a threshold approach should be followed in the evaluation of EDs, regarding the evidence for low-dose effects and the relevance of non-monotonic dose-response curves.
- Also in 2013, EFSA published a "Scientific Opinion on the Hazard Assessment of Endocrine Disruptors".[25] The EFSA opinion supports the WHO/IPCS definition for EDs and a case-by-case risk assessment approach to assess EDs for regulatory decision making. Further, EFSA clarifies that issues regarding mixtures, critical windows of susceptibility and non-monotonic dose-response curves were general issues applicable to all chemicals (and not specific to EDs).
- Further, the Scientific Committee on Consumer Safety (SCCS) issued a "Memorandum on EDs",[26] in 2014, in which it supports the EFSA Opinion with respect of the use of risk assessment to assess EDs for decision making.
- A recent external scientific report of EFSA [27] (2016) evaluated the evidence for the non-monotonic dose-response (NMDR) hypothesis for substances in the area of food safety. The plausibility of NMDRs was assessed based on a systematic review methodology, which identified over 10'000 potentially relevant scientific studies. From these studies, 142 studies could be selected for the evaluation (49 in-vivo, 91 in-vitro, and 2 epidemiological studies). The report indicates that the empirical evidence for NMDR was limited or weak for most in vivo datasets that were selected for substances in the area of food safety. The report also indicates that *evaluation regarding the biological meaning (e.g. dose range studies, adversity of the effects, and toxicity at high doses leading to NMDR) and relevance for risk assessment were not part of this data analysis*, thus questioning the relevance of the evidence for the adverse effects.

Further, at the occasion of an expert conference organised by the German Federal Institute for Risk Assessment (BfR), held in Berlin in April 2016, a consensus statement on "Scientific principles for the identification of endocrine disrupting chemicals"[28] was signed by 20 internationally renowned scientists present at the conference. This document has been made available via the website of BfR recently, however it has not yet been published in a scientific

[23] Munn S., Goumenou M-P., Key scientific issues relevant to the identification and characterisation of endocrine disrupting substances - Report of the Endocrine Disrupters Expert Advisory Group (ED EAG). JRC-IHCP 2013. [29 pp.]DOI: 10.2788/8659 (online). Retrieved from: http://publications.jrc.ec.europa.eu/repository/bitstream/JRC79981/lbna25919enn.pdf

[24] Munn S., Goumenou M-P., Thresholds for Endocrine Disrupters and Related Uncertainties Report of the Endocrine Disrupters Expert Advisory Group (ED EAG). JRC-IHCP 2013. [19 pp.]DOI: 10.2788/8659 (online). Retrieved from: http://publications.jrc.ec.europa.eu/repository/bitstream/JRC83204/lb-na-26-068-en-n.pdf

[25] EFSA Scientific Committee; Scientific Opinion on the hazard assessment of endocrine disruptors: scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing effects mediated by these substances on human health and the environment. EFSA Journal 2013;11(3):3132. [84 pp.] doi: 10.2903/j.efsa.2013.3132.

[26] Scientific Committee on Consumer Safety (SCCS) Memorandum on Endocrine Disruptors. 2014. SCCS/1544/14. Retrieved from: http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_009.pdf

[27] Beausoleil et al, 2016. Review of non-monotonic dose-responses of substances for human risk assessment. EFSA supporting publication 2016:EN-1027. 290pp.

[28] International Expert Meeting on Endocrine Disruptors (Berlin, April 2016). Available at: http://www.bfr.bund.de/en/international_expert_meeting_on_endocrine_disruptors-197246.html

peer reviewed journal. Among others, the document lists the criteria for identifying the hazard potential of harmful endocrine substances. It also indicates that the assessment of the corresponding risks from EDs on human health and wildlife would require consideration of dose-response relationships, including potency, exposure assessment, and risk characterization, including susceptible sub-populations, severity and reversibility of effects. See for more details Box 1, which quotes from the consensus paper.

Box 1. Scientific principles for the identification of endocrine disrupting chemicals – a consensus statement - Outcome of an international expert meeting organized by the German Federal Institute for Risk Assessment (BfR). (Solecki, R.; Kortenkamp, A.; Bergman, Å.; et al. 2016.; in press)

"…

Scientific foundations of regulatory decision-making

19. The various relevant pieces of EU chemicals regulation require both hazard and risk assessment approaches to enable decision making to be applied in different ways.*

20. The identification of a compound as an endocrine disruptor is a hazard identification procedure. Established principles governing disruption of the programming function of hormones mean that hazard identification for endocrine disruption has to take account of the timing of exposure relative to life stage and that transient indices or effects should not necessarily be considered adverse.

21. We recognize that certain adverse outcomes appearing to arise from endocrine disruption can also occur through non-endocrine modes of action. Moreover, adverse effects or modes of action consistent with endocrine disrupting characteristics but demonstrated to be non-specific effects secondary to another toxic effect are not considered appropriate for identification of endocrine disruption. The identification of a chemical as an endocrine disruptor therefore has to rely on weight-of-evidence evaluations of both adversity and mode of action together. We agree that endocrine activity on its own should not trigger a chemical's identification as an endocrine disruptor.

22. We agree that a chemical's potency to induce an adverse effect is an important factor for consideration during the characterization of the hazards of endocrine disruptors. However, potency is not relevant for identification of a compound as an endocrine disruptor. However, there may be high doses (e.g. the oral toxicity limit of 1000 mg/kg body weight/day) above which identification as an ED would not be warranted.

23. Criteria for identifying chemicals as endocrine disruptors would need be accompanied by the implementation of relevant test systems in EU regulations. We note that many relevant OECD guidelines exist which have not yet been consistently integrated into the regulatory frameworks. There is lack of validated tests for a number of modes of actions. We recommend that respective EU directives, regulations and other relevant guidance are updated to incorporate validated and internationally agreed test systems for endocrine disruptors. In this context, guidance and scientific advice need to be up-dated to indicate how the outcome of those tests should be evaluated in the regulatory context, and to include endocrine pathways and adverse health effects that are insufficiently explored by current toxicological testing.

24. This document has focused on the identification of endocrine disruptors. However, the assessment of the corresponding risks on human health and wildlife would further require consideration of dose-response relationships, including potency, exposure assessment, and risk characterization, including susceptible sub-populations, severity and reversibility of effects. This emphasizes the importance of the "One Substance – One Toxicological Assessment" philosophy, and has implications for data generation of both regulated and unregulated chemicals.

** The WHO IPCS definitions for the four steps in risk assessment: hazard identification, hazard characterization, exposure assessment and risk characterization, have been used throughout this document.*

…"

In summary, the available relevant reports indicate that:

- There is consensus on the WHO/IPCS definition (2002) for identifying ED
- There are different endocrine modes of actions. Four modalities (pathways) are relatively well known and internationally agreed tests exist (the estrogen, androgen, thyroid and steroidogen modalities). There are other modalities which are not yet well known and for which no internationally agreed tests exist. For these modalities, still under discussion, science is under development and there is no consensus on the extent of evidence (e.g. diabetes) available.
- There is no consensus on the relevance of some scientific aspects for regulatory decision making (e.g. non-monotonic dose response curve, low dose effects and existence of safety thresholds for EDs), but a recent EU review on the empirical evidence and the BfR consensus statement mentioned above indicate that the evidence for this kind of curves is weak for most in vivo data.
- There is consensus that the assessment of potential risks from ED on human health and the environment would require consideration of dose-response relationships, exposure assessment, and risk characterisation (risk assessment).

1.3. Regulatory context of Plant Protection Products (PPP) and Biocidal Products (BP)

A 'pesticide' prevents, destroys, or controls a harmful organism ('pest') or disease. This expression covers plant protection products and biocidal products.

Plant protection products (PPP) protect crops as well as desirable or useful plants. They are used in agriculture, forestry, horticulture, industrial areas (e.g. railways), amenity areas and in gardens.

Biocidal products (BP) control unwanted organisms that are harmful to human or animal health, or that cause damage to human activities. BP include products such as insecticides, insect repellents, disinfectants, preservatives for materials and anti-fouling paints for the protection of ship hulls.

Both PPP and BP are formulated products (e.g. liquid concentrates, wettable powder, granules) that contain at least one active substance that is responsible for the effect of the PPP or BP, which could be a chemical, a plant extract, a pheromone or a micro-organism (including viruses).

In the EU, both PPP and BP have been regulated since the 1990s via Regulation (EC) No 1107/2009 (replacing Directive 91/414/EC) and Regulation (EU) No 528/2012 (replacing Directive 98/8/EC) with the objective of ensuring a high level of protection of human health and the environment, strengthening the functioning of the internal market, and for the PPP Regulation improving agricultural production.

As a consequence of the strict legislation in place since the 1990s, a significant number (about 60%) of active substances used in PPP have been taken off the market or have had their use restricted. This resulted in a reduction in general terms of the exposure of humans and the environment to the number of chemicals used in PPP . A recent study on the "Calculation of the Benefits of Chemical Legislation on Human Health and the Environment", commissioned by the European Commission[29], concluded that, as a consequence of the EU legislative

[29] RPA et al (2015): Study on the Calculation of the Benefits of Chemical Legislation on Human Health and the Environment, Final report for DG Environment, March 2016, London, Norfolk, UK.

measures taken over the last years, the exposure to certain substances known to have adverse effects on human health and the environment was reduced.

Both the PPP and BP regulations are based on pre-market approval ("positive list") and shift the responsibility for producing scientific evidence (burden of proof) to the industry[30]. Only PPP and BP which contain active substances placed on a "positive list" (via an EU approval process) can be used in PPP or BP in the EU (via authorisation processes at national level), provided the respective uses have been considered not to cause adverse effects on human or animal health or unacceptable effects to the environment. In other words, under the PPP and BP Regulations, no use of a substance – whether the mode of action of the substance is known or not – is authorised in the EU if an unacceptable risk of causing adverse effects to human health or the environment is identified. Further, approvals of active substances and authorisations of PPP or BP are granted only for a limited number of years, after which the approvals need to be renewed following similar processes as for the 1st approvals.

The two-step pre-market approval system described above (active substances approval at EU level, product authorisation at national level) is considered as one of the strictest worldwide. The Regulations (and their preceding Directives) also specify comprehensive data requirements[31;32] which have to be addressed and fulfilled before any approval of active substance or authorisation of a product can be considered. The data requirements list the experimental studies according to international agreed guidelines which need to be performed, and which results need to be submitted as part of the application dossiers, and already cover studies relevant for EDs. This implies that both PPP and BP are among the most "data rich" regulated product groups in the EU.

Besides assessment of toxicological properties of the substance with respect to human health and environment, traces of residues of PPP which may be found on the crop are also considered in the assessment done before any approval or authorisation can be granted. The levels of residues are assessed and maximum residue levels[33] (MRL) are established under Regulation (EC) No 396/2005.[34] MRLs must be respected in commodities produced in the EU or imported into the EU, in order to ensure consumers' safety. In addition, Regulation (EC) No 396/2005 provides that the Community's trading partners should be consulted via the WTO about the MRLs proposed. MRLs set at the international level by the Codex Alimentarius Commission should also be considered when Community MRLs are being set, taking into account the corresponding good agricultural practices.

1.3.1. Provisions on endocrine active substances under the PPP and BP Regulation

Both Regulation (EC) No 1107/2009 and Regulation (EU) No 528/2012 have introduced, compared to the previous legislation, specific hazard-based provisions (often referred to as

[30] These are elements of the precautionary principle, see Communication from the Commission on the precautionary principle, COM(2000) 1 final. Retrieved from: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52000DC0001

[31] Regulations EU 283/2013 and EU 284/2013, setting data requirements for active substances and for PPP, respectively; Communications 2013/C 95/01 and 2013/C 95/02, detailing the list of test methods and guidance documents for active substances and for PPP, respectively.

[32] Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products. Official Journal of the European Union, L 167, 27 June 2012. doi:10.3000/19770677.L_2012.167.eng

[33] An MRL is the upper legally allowed concentration for a residue in food or feed, based on good agricultural practice and protection of vulnerable consumers.

[34] Regulation (EC) No 396/2005 of the European Parliament and of the Council on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC OJ L 70, 16.3.2005, p. 1

“cut-off criteria") for certain hazardous classes of substances (e.g. mutagens, carcinogens). These provisions include substances identified as EDs, under both pieces of legislation, EDs are not approved unless certain derogations apply. These derogations have a wider scope under the BP Regulation in comparison with the PPP Regulation: while under the PPP Regulation the derogations are mainly hazard based, under the BP Regulation the derogations have a stronger risk component and include also socio-economic provisions (see Figure 1 and a more detailed description under Section 1.5).

In cases of approval of active substances under application of these derogations, special conditions apply: the substances are approved as "candidates for substitution". This implies shorter approval periods and the obligation for Member States (MS) to consider safer alternatives when authorising PPP or BP (comparative assessment). In addition, under both Regulations, if a substance is not identified as ED, it will still undergo a full risk assessment. This risk assessment is similar to the one in place in the previous legislations which focused on potential adverse effects irrespectively of the mode of action which causes this adverse effect. In other words, the ED provisions in the PPP and BP Regulations currently act as a "switch (with respect to adverse effects potentially linked to EDs)" which either leads to a non-approval of the active substances identified as ED (subject to derogations), or to a "standard" risk assessment which would cover any potential adverse effect and if appropriate lead to non-approval or restrictions of use of the active substance (this "standard" risk assessment is carried out in any case as all potential adverse effects are assessed). Most of the adverse effects which may be caused by EDs (e.g. carcinogenicity or reproductive effects) are already regulated since many years, without detailed knowledge of their mode of action. For instance, many of the PPP and BP often cited as EDs (atrazine, DDT, lindane, dieldrin, triphenyltin, tributyltin, etc.) have already been banned since years in the EU, as a consequence of the EU regulatory system (see more details in Annex 9 on human health – hormone related diseases).

As the difference between hazard and risk plays an important role in this impact assessment, it needs to be briefly explained: hazard is anything that can cause harm, whereas risk is the potential that a hazard will cause harm. In other words a hazard will not pose any risk unless exposure to that hazard is high enough so that it may cause harm. Risks associated with hazards can be zero, or at least greatly reduced, by reducing exposure. For instance, a knife – a hazardous object per se - would be banned completely if the decision is taken based on hazard, while it would be allowed for certain uses or restricted (e.g. not allowed for small children) if the decision is taken based on risk. Similarly, a substance (e.g. a drug or a pesticide active substance) is banned if the regulatory decision is based on its hazard, while it is allowed for certain uses, under certain (restricted) conditions and doses, if the decision is taken based on risk.

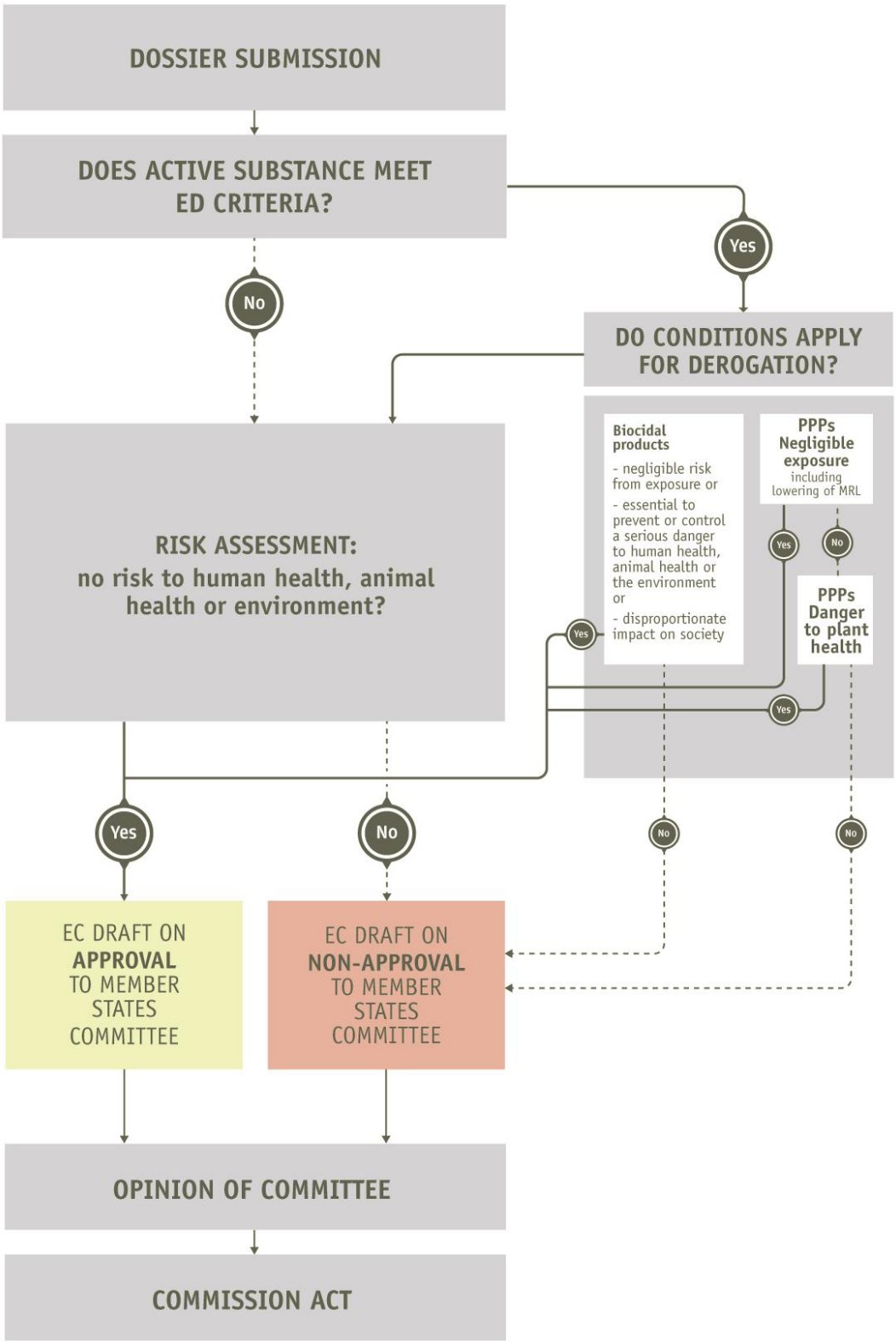


Figure 1: Regulatory decision making in the PPP and BP Regulations, under consideration of derogations for active substances identified as EDs

1.4. Problem identification

1.4.1. Problem definition: Absence of scientific criteria to identify EDs under the PPP and BP legislation – the interim criteria in place are not able to correctly identify EDs according to the latest scientific developments.

Regulation (EC) No 1107/2009 and Regulation (EU) No 528/2012 both lack scientific criteria to identify EDs, which are needed in order to be able to correctly implement the provisions set in the Regulations concerning these kind of substances (Annex II, Section 3.6.5 of the PPP Regulation and Article 5.2 of the BP Regulation).

Both legislations set a legal obligation for the European Commission to establish scientific criteria by December 2013. Until these legal obligations are fulfilled, both Regulations have set the *same* interim criteria to identify EDs.

These interim criteria are not based on the latest scientific developments on endocrine disruption, but they are based on classification of substances that are suspected of being carcinogenic and/or suspected of being toxic to reproduction (C2 and/or R2 according to Regulation (EC) No 1272/2008[35]). They are able to identify some substances with ED properties but may miss some other ED substances ("false negatives"[36]) or identify some substances as having endocrine disrupting properties which are not EDs ("false positives"[37]).

In order to protect human health and the environment, it is important to set scientific criteria which are able to identify EDs correctly. For the same reasons, the criteria should be the same for both Regulations. A harmonised definition is also important because it would enhance greater coherence between the regulatory frameworks as some chemical substances are regulated under both Regulations, since they can be used either in PPP or BP. Further, any potential endocrine disrupting property of a chemical substance does not depend on its use, but is an inherent characteristic of the substance.

The legal obligation to define criteria is only set under the PPP and BP Regulations. However, it is expected that the new criteria may also influence other EU regulatory areas, where so far no criteria for EDs have been set or requested. In light of the legal obligations, this impact assessment focusses on the PPP and BP Regulations only.

1.4.2. Affected parties

Once the criteria to identify EDs are set, they will be applied subsequently to the approvals (or the renewals of approvals) of active substances falling under the PPP and BP Regulations. This is expected to affect – directly and indirectly - society because PPP and BP are used in many ways and play an important role in some economic sectors.

The impacts on society are thus driven by the regulatory consequences for the substances which are identified as EDs which are already set under the PPP and BP Regulations. In both cases, these substances shall not be approved unless some specific conditions ("derogations") apply. The derogations and how they are implemented differ between the PPP and BP Regulations (see Figure 1 and Section 1.5 for more details). While the derogations under the BP Regulation consider negligible risk and a wider scope of socio/economic considerations,

[35] Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006

[36] False negative: test result that is incorrect because the test failed to recognise an existing condition or finding. Retrieved from http://www.dictionary.com/browse/false--negative?s=t

[37] False positive: a test result that is incorrect because the test indicated a condition or finding that does not exist. Retrieved from http://www.dictionary.com/browse/false--positive?s=t

under the PPP Regulation the derogations are mainly based on hazard (negligible exposure and almost zero exposure via food by lowering the MRLs[38] to the limit of determination) and limited socio-economic considerations (serious danger to plant health). Consequently the impacts under the PPP Regulation are expected to be higher compared to the BP Regulation.

In addition, the regulatory consequences set in both the PPP and BP Regulations must be consistent with provisions of international law, such as customary international law and treaties ratified by the EU.

The establishment of criteria under the PPP and BP Regulations, following this impact assessment, may have repercussions on other EU-chemical legislation. The BP Regulation can be taken as an illustration of what would happen for sectors where derogations taking into account risk and/or socio economic considerations apply, whereas the PPP Regulation can be taken as an illustration of what would happen for sectors where the decision making is mainly based on hazard.

As a consequence of the regulatory context described above, the health of the general population, consumers, and workers exposed to EDs (e.g. professional users) may be affected directly or via the quality of the environment or the safety of the food. However, there may also be indirect impacts for consumers in terms of variation in availability or costs for certain products including agricultural commodities.

Economic operators affected may be manufacturers, importers, exporters, traders, industries marketing chemical substances and downstream industries. In particular food chain operators (for instance those using disinfectants), health care facilities, small and medium sized enterprises and professional users like farmers producing plant or animal products are all expected to be affected. Parties may be affected to different extents depending on the type of products they produce and use and the geographical location of their activity.

MS and third countries may be affected via international trade through the lowering of the MRLs for food and feed to the default value (limit of determination, i.e. analytical zero) for substances identified as EDs, which have to be applied for EU production but also for imports. International trade is also expected to be impacted via imports of articles, because articles treated with active substances not approved in the EU for BP cannot be imported into the EU. The operability for implementing the criteria may also have an impact on national administrations because of inter alia, shorter approval periods and more complex assessments when applying the derogations.

Since the criteria that the European Commission will present under the PPP and BP Regulations may have repercussions on other EU legislation containing specific provisions governing EDs (e.g. REACH, the Water Framework Directive, the Cosmetics products legislation), parties may also be affected indirectly via these pieces of legislation.

1.5. Underlying drivers

The ***absence of scientific criteria to identify EDs*** in Regulations (EC) No 1107/2009 and (EU) No 528/2012 is a consequence of the fact that when these Regulations were drafted, the co-legislators felt that it was too early to set scientific criteria in a regulatory context and instead requested the European Commission to set them by December 2013.

[38] The levels of residues are assessed and maximum residue levels (MRL) are established under Regulation (EC) No 396/2005[38]. An MRL is the upper legally allowed concentration for a residue in food or feed, based on good agricultural practice and protection of vulnerable consumers. MRLs must be respected in commodities produced in the EU or imported into the EU, in order to ensure consumers' safety.

The interim criteria currently applicable under these Regulations may fail to identify some EDs because: 1) they only refer to certain adverse effects for human health (carcinogenicity and toxicity for reproduction) and do not consider wildlife species and 2) they do not consider the endocrine mode of action of substances. For these reasons, they may identify "false negatives" and "false positives".

The scientific criteria to identify EDs are set in a regulatory context (PPP and BP Regulations), which plays a significant role in determining the impacts of the criteria on the approval of active substances and on society in general. Thus, the ***regulatory consequences for substances identified as EDs*** are identified as an additional driver which adds complexity to the analysis of the impacts.

The regulatory consequences for substances identified as EDs are different between the PPP and BP Regulations. In both cases, substances identified as EDs shall not be approved unless some specific conditions ("derogations") apply. However, these derogations differ in their scope and possibilities of implementation (see Annex II, Section 3.6.5 and Article 4.7 of the PPP Regulation and Article 5 of the BP Regulation for details). This implies that substances identified as EDs will be subject to one of the following regulatory consequences:

- a non-approval of the active substance (BP for general public, most cases for PPP)
- approvals limited to situations where negligible exposure is assessed on a case by case basis (some PPP cases)
- approvals limited to negligible risk assessed on a case by case basis (BP professional uses)
- approvals limited to socio/economic considerations (PPP to fight a serious danger to plant health; BP professional uses when a substance is needed to prevent or control serious dangers to human health, animal health or the environment or measures would lead to disproportionate negative effects on society).

The derogations in the PPP and BP Regulations differ in their scope (exposure vs. risk because of exposure respectively, and socio-economic considerations vs. danger to plant health respectively), but also if they apply sequentially or are assessed in an integrated way, leading to differences in the implementation (see Figure 1 for more details). These differences have consequences for the approval of substances, and hence to the availability of PPP or BP, which is then expected to impact several sectors.

The regulatory consequences in the PPP and BP Regulations also differ with respect to the allowed residues. While in the PPP legislation residues (MRLs) of substances identified as EDs will be lowered to the analytical zero, the BP Regulation foresees that a treated article shall not be placed on the EU market unless all active substances contained in the biocidal products that it was treated with or incorporates are approved. These provisions are applicable to commodities and products produced in the EU but also to those imported from non-EU countries. As a consequence the provisions may also have impacts on international trade with consequences for the internal market.

1.6. Evaluations

Neither the PPP nor the BP Regulations, adopted in 2009 and 2012 respectively have so far been subject to an ex-post evaluation. However, preparations for the evaluation of Regulation

(EC) No 1107/2009 have started under the REFIT[39] programme. Regulation (EC) No 1107/2009 in its Article 82 provides for the issuance of a report which should cover, inter alia, the application of the criteria for approval as set out in Annex II (which includes the provisions on EDs) and their impacts on agriculture, human health, and environment.

2. WHY SHOULD THE EU ACT?

Defining scientific criteria for the identification of EDs is a legal obligation for the European Commission, set out in the PPP and BP Regulations, which were both adopted through the ordinary legislative procedure. The endocrine properties of an active substance to be used in PPP and BP need to be assessed for its approval. Since this approval process is done at EU level, EU action is needed for setting the criteria.

Scientific criteria to identify substances which have endocrine disrupting properties are expected to contribute to a more informed regulatory decision making which considers current scientific knowledge. This implies a regulatory decision making which considers in addition to the adverse effects (WHAT question) also the endocrine mode of action (HOW question). Knowledge on the endocrine mode of action is relatively recent and it may further accumulate in the future.

Setting *harmonised* criteria under the PPP and BP legislation will ensure a consistent level of protection of human health and the environment. A coherent approach with respect to EDs under the PPP and BP legislation will also allow legal coherence and certainty, as well as regulatory consistency and predictability. This is in particular important as some chemical substances (currently around 38 substances[40], considering only the biocides already assessed under the review programme) fall under both pieces of legislations.

3. WHAT OBJECTIVES SHOULD BE ACHIEVED?

Scientific criteria to identify EDs need to be presented in order to fulfil legal obligations set in the PPP and BP Regulations, with the aim of maintaining the high level of protection of human health and the environment and to provide consistency in these levels of protection across both sets of legislation.

The general objectives within the Treaty guide the present impact assessment, as they are the legal basis for both the PPP and BP Regulations:

- ensuring a high level of protection to human health, animal health and the environment;
- strengthening the functioning of the internal market.

For the PPP Regulation the two objectives mentioned above should be considered while improving agricultural production (see Article 1 of Regulation (EC) No 1107/2009).

The compliance with international obligations, notably under the Sanitary and Phytosanitary (SPS) and Technical Barriers to Trade (TBT) agreements under the World Trade Organisation are also important considerations.

[39] Annex II: REFIT Initiatives. Annex to Commission Work Programme 2016; No time for business as usual. Retrieved from: http://ec.europa.eu/atwork/pdf/cwp_2016_annex_ii_en.pdf

[40] Some examples are benzoic acid, bifenthrin, bromadiolone, capric acid, clothianidin, copper hydroxide, cypermethrin, cyproconazole, dazomet, deltamethrin

The following specific objectives for PPP and BP Regulations have also been considered:

- providing for legal clarity, predictability and coherence in the identification of EDs;
- providing for scientific criteria that are operational in terms of regulatory decision-making;
- offering possibility to apply these criteria across the PPP and BP Regulations.

4. WHAT ARE THE OPTIONS TO ACHIEVE THE OBJECTIVES?

As explained in previous sections, the European Commission is legally required to establish scientific criteria to identify substances with endocrine disrupting properties in the context of the PPP and BP Regulations. Four options, including the current baseline (interim criteria), have been developed. The four options are based on hazard, and consider scientific knowledge.

The regulatory consequences (i.e. implementation) of the scientific criteria to identify EDs are already set under the PPP and BP Regulations and are driving the potential impacts of the criteria (see Sections 1 for more details). The regulatory consequences differ in terms of scope and implementation, adding complexity to the impact assessment. In order to address this complexity, a 2nd set of options was developed and presented in the roadmap. Consequently, two separate sets of options were considered along two aspects:

- Aspect I: setting scientific criteria to identify EDs based on hazard under the PPP and BP Regulations;
- Aspect II: implementation of the ED criteria / approach to regulatory decision making.

The options for each aspect are described below and analysed separately. These analyses are not aimed at concluding on any preferred option for setting scientific criteria to identify endocrine disruptors, but at providing additional information to decision makers on the potential implications of these different options under the PPP and BP Regulations.

4.1. Aspect I: Setting scientific criteria to identify EDs based on hazard under the PPP and BP Regulations

All the options considered under this aspect (with exception of the baseline) are based on hazard and on the WHO/IPCS definition, for which there is a wide scientific consensus. They have been all presented in the Roadmap and are representing different views of Member States and stakeholders. These views are explained in the sub-sections below.

4.1.1. Option 1: No policy change (baseline).

No scientific criteria are specified and the interim criteria set in the PPP and BP Regulations continue to apply. The interim criteria are based on classification of substances: suspected of being carcinogenic and/or suspected of being toxic to reproduction (C2 and/or R2 according to Regulation (EC) No 1272/2008[41], respectively).

[41] Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006

The majority of the respondents to the public consultation that was carried out in the context of the impact assessment did not support Option 1 as it may fail to identify the correct EDs. There is scientific consensus that the interim criteria set in the PPP and BP Regulations are not correctly identifying EDs because they are unable to detect an ED mode of action. The interim criteria may detect "false positives" (the interim criteria identify EDs even when no ED mode of action is present) and "false negatives" (substances which have ED mode of action which cause potential adverse effects are not identified by the interim criteria).

4.1.2. Option 2: WHO/IPCS definition to identify EDs

The aim of this option is to identify, based on hazard elements, substances which meet the WHO/IPCS definition (2002). EDs are identified as substances:

a) Which show an adverse effect. An adverse effect is defined according to the definition of WHO/IPCS (2009)[42];

b) and where there is experimental evidence based on international agreed study protocols[43] (*in vivo* studies), possibly supported with other information (e.g. (Q)SAR, analogue and category approaches) that the substance has the capacity to cause endocrine-mediated adverse effects in humans or endocrine-mediated adverse effects relevant at the population level on animal species living in the environment. However:

- This evidence needs to occur in the absence of other toxic effects, or if occurring together with other toxic effects, the endocrine-mediated adverse effects should not be a non-specific secondary consequence of other toxic effects;
- where there is information demonstrating that the effects are clearly not relevant for humans and not relevant at population level to species living in the environment, then the substance should not be considered an ED.

As mentioned before, there is a wide scientific consensus on the WHO/IPCS definition for identifying endocrine disruptors. This was confirmed in the "BfR consensus statement" published on 4 May 2016[44].

However, scientists, MS and stakeholders are divided on whether this definition alone would be the best option in the context of the PPP and BP Regulations.

Some of them (most endocrinologists, some MS, health/environmental/consumers NGOs) consider that this option is the most appropriate as it would correctly identify EDs.

Others (most toxicologists, some MS, industry and third countries) consider that this option would not correctly identify EDs of actual concern under the current PPP Regulation, i.e. would not correctly assess which EDs pose an ***actual risk*** to human health and the environment because the current derogations under the PPP Regulation are mainly hazard

[42] An adverse effect is "*a change in the morphology, physiology, growth, development, reproduction, or, life span of an organism, system, or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress, or an increase in susceptibility to other influences"* (WHO/IPCS (2009)

[43] The EFSA Opinion on EDs indicated that a reasonable complete suite of standardised assays for testing EDs is currently (or will soon be) available only for vertebrate species. See footnote 33 in EFSA Scientific Committee; Scientific Opinion on the hazard assessment of endocrine disruptors: scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing effects mediated by these substances on human health and the environment. EFSA Journal 2013;11(3):3132. [84 pp.] doi: 10.2903/j.efsa.2013.3132.

[44] "Scientific principles for the identification of endocrine disrupting chemicals – a consensus statement Outcome of an international expert meeting organized by the German Federal Institute for Risk Assessment (BfR)" Retrieved from http://www.bfr.bund.de/cm/349/scientific-principles-for-the-identification-of-endocrine-disrupting-chemicals-a-consensus-statement.pdf

based. They believe that many active substances would no longer be approved although they can be used safely, i.e. they would only produce an adverse effect at unrealistic high exposure. They believe that only a subset of the identified EDs should be regulated under the current hazard based "cut-off" criteria set in the PPP, i.e. those substances which produce an adverse effect at realistic doses of exposure. Some of these diverging opinions are also reflected in the public consultation report.

4.1.3. Option 3: WHO/IPCS definition to identify EDs and introduction of additional categories based on the different strength of evidence for fulfilling the WHO/IPCS definition.

The aim of this option is to identify, based on hazard elements, substances which meet the WHO/IPCS definition, and to introduce additional categories based on the strength of the evidence. For the purpose of this impact assessment 3 categories are evaluated, as follows:

- Category I: EDs (as defined in Option 2).
- Category II: Suspected EDs, which means substances where there is some evidence that endocrine-mediated adverse effects can be produced on humans or on populations living in the environment, but where the evidence is not sufficiently strong or convincing enough to place the substance in Category I.
- Category III: Endocrine active substances, which means substances for which there is some *in vitro or in vivo* evidence indicating an interference with the endocrine system (endocrine activity) but without evidence of an adverse effect in intact organisms.

Regulatory consequences are defined in the PPP and BP Regulations for EDs (Category I), while no regulatory consequences are defined in these Regulations for suspected EDs or endocrine active substances (Categories II and III). Therefore, EDs under Option 2 and under Option 3 Category I are identical in terms of substances identified and the impacts related to their regulatory consequences are expected to be the same.

Scientists, MS and stakeholders are divided on whether this option would positively contribute to more efficacy and operability of the criteria. Most endocrinologists, some MS, health/environmental/consumers NGOs are generally in favour of this option considering that:

- the classification system would be consistent with classification under CLP regulation;
- additional categories would bring further clarity and easier classification by assessors;
- downstream users would better plan the substances to use in their products.

Most toxicologists, some MS and industry are generally against this option considering that it would raise confusion on whether all categories should be subject to regulatory consequences, while the uncertainties on taking regulatory action exclusively based on identification of a substance as an ED are already higher than usual. They believe that:

- additional categories with no specific regulatory consequences would reduce clarity and predictability;
- harmonized classification is competence of CLP regulation and not of sectorial legislation;
- additional categories are likely to lead to "blacklisting" of substances which may negatively affect innovation.

Some of these views have also been expressed in the public consultation. The views expressed in the context of Option 2 (see above) need to be also considered.

4.1.4. Option 4: WHO/IPCS definition to identify EDs and inclusion of potency as an element of hazard characterisation.

The aim of this option is to identify, based on hazard elements and in the regulatory context of the PPP and BP Regulations, substances which meet the WHO/IPCS definition and to prioritise the substances of greater concern. A prioritisation of substances is supported by farmers, the chemical industry and some EU MS. Third countries are expected to favour this option with respect to options 1 to 3. Therefore, this option was included in the Roadmap and considered in the impact assessment.

Under the PPP and the BP Regulations, if a substance is identified as an ED it will not be approved unless certain derogations apply. If a substance is not identified as an ED, it will undergo a full risk assessment focused on potential adverse effects and based on comprehensive data requirements (see Figure 1). Under this regulatory context, a prioritisation of substances of greater concern via hazard characterisation may be considered for the substances which would fall under the "hazard cut off criteria" leading to a non-approval of these substances unless derogations apply, while substances not falling under these "cut off criteria" would still be subject to a full risk assessment and only approved if considered not having adverse effects on human health, animal health or the environment. Thus, Option 4 would identify, based on hazard elements, substances which meet the WHO/IPCS definition and which have a stronger potency, being potency one of the elements of hazard characterisation.

Potency is part of hazard characterization and not of hazard identification; however it is neither a full hazard characterisation (hazard characterisation includes e.g. potency, severity, irreversibility) nor a risk assessment (risk assessment is hazard characterisation + exposure assessment). Potency is an inherent characteristic of a chemical substance. It is a scientific measurement (i.e. based on experiments) of the substance's ability to produce an (adverse) effect. In other words, the higher the potency of a substance, the lower the dose needed to produce a certain adverse effect. For instance artificial sweeteners are more potent than sugar to sweeten a cup of tea, since only a few drops are needed instead of a spoon. Another example is cyanide and table salt: both can be toxic but cyanide is far more toxic than salt.

Potency may be considered in several ways. One way would be setting a dose threshold necessary to achieve an adverse effect. For the purpose of this impact assessment potency has been defined as a threshold value based on the STOT-RE Cat 1[45] trigger values from the Regulation (EC) No 1272/2008 (see Section 5).

Considering in particular the regulatory context of the PPP Regulation (i.e. derogations based mainly on hazard) the diverging views of scientists, stakeholders and MS regarding this option are summarized below.

Most endocrinologists, some MS, health/environmental/consumers NGOs believe that:

- potency should not be part of the criteria for identification of EDs because it is part of hazard characterisation;
- considering potency in the criteria to identify EDs might reduce protection of human health and environment because EDs are suspected to produce adverse effects at low doses (i.e. EDs are suspected to act via non-monotonic dose-response curves, i.e. a safety threshold might not be identified for EDs);

[45] Specific Target Organ Toxicity - Repeated Exposure

Most toxicologists, some MS, industry and third countries believe that:

- EDs are chemicals which can be treated like any other chemicals because the available evidence does not confirm the existence of non-monotonic dose-response curves for EDs. This implies that safety thresholds can be set for EDs like for any other chemical and that regulatory decisions can be based on risk considerations.
- if risk considerations cannot be taken into account in the regulatory decision making because derogations are based mainly on hazard, it would be unscientific not to prioritize the most hazardous substances based on scientific information. The consideration of potency would be a scientific way to achieve this prioritisation.

Recent scientific reports[25,46] state that assessment of risks from ED on human health and the environment would require consideration of dose-response relationships (which includes potency considerations), exposure assessment, and risk characterisation.

There is scientific consensus that Option 4 would not identify correctly all EDs, but that potency should be used when assessing risks of EDs on human health and wildlife. Scientists agree that potency should not be considered at the step of hazard identification, but at the step of hazard characterization needed for a risk assessment of ED. This was confirmed in the "BfR consensus statement" published on the BfR website the 4 May 2016[46] (see Box 1 for more details) but has not yet been published in a scientific peer reviewed journal (the process for publication is currently on-going).

4.2. Aspect II: Implementation of the ED criteria / approach to regulatory decision making

The regulatory consequences (i.e. implementation) of the criteria to identify EDs are already set under the PPP and BP Regulations and are driving the impacts. In addition, the regulatory consequences differ in terms of scope and implementation, adding complexity to the impact assessment. For analytical purposes it was considered important to address this complexity and thus the options presented in the Roadmap were designed in order to address the difference in the derogations between the PPP and the BP Regulations.

As a consequence a very comprehensive range of options was developed which covers the entire spectrum of potential policy choices: these include the baseline (current provisions in the BP and PPP Regulations), the possibility to modify an annex of the PPP Regulation under regulatory procedure with scrutiny, and the possibility to modify the PPP Regulation under ordinary legislative procedure. The inclusion of such a wide spectrum of options has been done for analytical purposes and greater transparency, in order to allow greater comparability of the evidence gathered throughout the analysis and facilitate the identification of the most proportionate and fit for purpose policy choice.

Some Member States and all third countries replying to the public consultation support an option that will identify EDs and take regulatory decisions based on risk assessment.

[46] Expert conference on endocrine disruptors organised by the Federal Institute for Risk Assessment (BfR) and held in Berlin on 11 and 12 April 2016:
http://www.bfr.bund.de/en/press_information/2016/13/breakthrough_in_the_scientific_discussion_of_endocrine_disruptors-197254.html
The statement indicated potency is part of hazard identification. However, the assessment of the corresponding risks on human health and wildlife would further require consideration of dose-response relationships, including potency, exposure assessment, and risk characterization, including susceptible sub-populations, severity and reversibility of effects.

4.2.1. Option A: No policy change (baseline).

The regulatory consequences under the PPP and BP Regulations remain unchanged. This means that the decision making in the PPP sector is, including the derogations, mainly based on hazard while the decision making in the BP sector considers more risk and socio economic elements (except for consumers).

A decision taken based on hazard means that a substance is not-approved based on its inherent properties, while a decision based on risk considers the use of the substance and if there is actually exposure to this substance which leads to a risk. [47]

This baseline option (Option A) implicitly applies when evaluating the impacts of the options for setting scientific criteria (Aspect I) because it represents the current regulatory framework.

Most endocrinologists, some MS, health/environmental/consumers NGOs call for EU criteria to assess EDs purely based on hazard. Most toxicologists, some MS, industry, farmers and third countries disagree with hazard-based ED criteria and call for EU criteria to assess EDs which consider risk.

4.2.2. Option B: Adjustment of the PPP derogations in light of current scientific knowledge.

Option B only applies to the PPP Regulation and takes into account scientific knowledge which is based on scientific consensus. The option aims at updating the derogations foreseen in the PPP legislation while maintaining the essentially hazard-based decision making. It would contribute to increased operability of the derogations currently laid down in the PPPR and would allow implementing the criteria in a consistent manner across the PPP Regulation and the BP Regulation. See below and Figure 2 for more details.

The derogations to the non-approval of active substances, currently mainly hazard-based, would be updated in light of current scientific knowledge (e.g. recent scientific opinions of EFSA[48], Scientific Committee SCCS[49], expert meeting in Berlin[46]) to derogations which consider risk components. While the general hazard approach for EDs would be maintained, the derogations would be based on a stronger risk component compared to the current regulatory situation.

The European Commission is empowered to amend non-essential elements of the Annexes in Regulation (EC) No 1107/2009 taking into account current scientific and technological knowledge via Regulatory Procedure with Scrutiny (RPS) (cf. Article 78 of Regulation (EC) No 1107/2009). This option is therefore feasible within the remit of the mandate of the Commission as it does not imply changes by ordinary legislative procedure to the basic act.

By updating the PPP derogations to take into account current scientific knowledge, there would also be a higher alignment of the PPP Regulation to the BP Regulation (see also Section 1.5 and Annex 8 for further details on the exact working of the derogations under the

[47] For instance, a knife – a dangerous object per se - would be banned completely if the decision is taken based on hazard, while it would be allowed for certain uses or restricted (e.g. not allowed for small children) if the decision is taken based on risk.

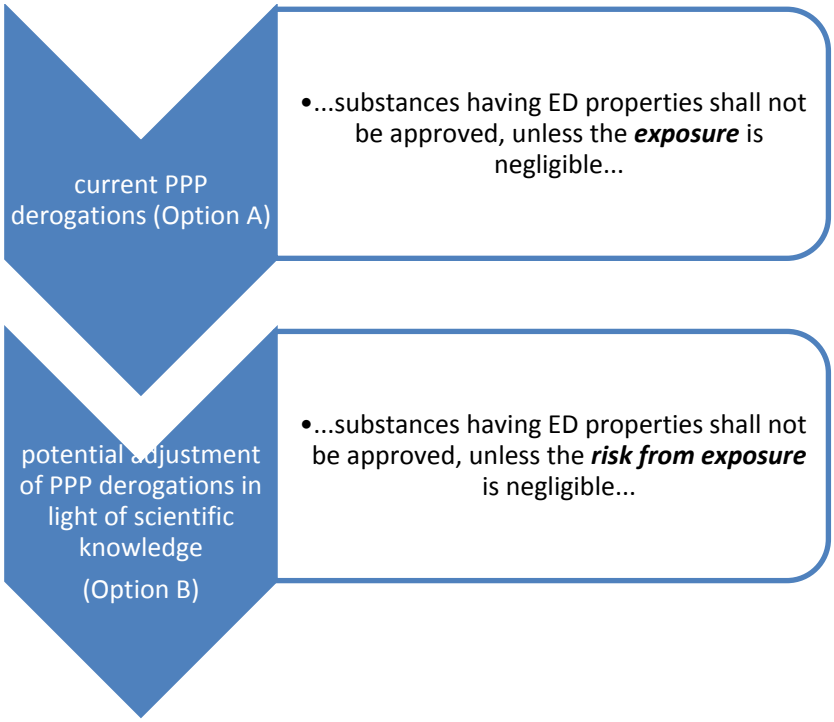
[48] The EFSA Scientific Opinion 2013 indicated that safe doses/concentrations of EDs can be established and that severity, irreversibility and potency should be evaluated in relation to degree, timing and duration of exposure, i.e. using risk assessment. EFSA also stated that EDs can be treated like most other substances of concern for human health and the environment, i.e. be subject to risk assessment and not only to hazard assessment.

[49] The Scientific Committee on Consumer Safety (SCCS) supports the use of risk assessment to assess EDs for decision making (Memorandum 2014)

PPP and BP Regulations). Such alignment would provide for more harmonisation of the implementation of the criteria. Thus, this option represents a potential contribution to a clearer and simpler regulatory environment and of an easier implementation of the criteria. It would also contribute to achieving one of the objectives of Better Regulation which is effectiveness of EU action.

Third countries replying to the public consultation support this option because it will identify EDs and take regulatory decisions based on a hazard approach which considers derogations based on science and consideration of risk elements, as requested by international obligations (notably Sanitary and Phytosanitary (SPS) and Technical Barriers to Trade (TBT)). Chemical industry, farmers, and some MS are in favour of decision making which considers risk.

Figure 2 Potential adjustment of derogations under the PPP Regulation in light of current scientific knowledge (Option B)



4.2.3. Option C: Alignment of the PPP with the BP Regulation by introducing further socio-economic considerations.

Option C only applies to the PPP Regulation, as it implies an amendment of the PPP Regulation to introduce measures similar to those in the BP Regulation as regards the derogations for non-approval of substances in case this would have a disproportionate negative impact on society (Art 5.2. of the BP Regulation).

This option would require a modification via ordinary legislative procedure of the current PPP Regulation. At a preliminary stage of the analysis it was anticipated that this option goes beyond the mandate given to the Commission for the identification of ED criteria and that it should be discarded. Nevertheless, the option was still considered relevant for analytical purposes and to support the analysis of potential future policy choices. As a consequence, it was maintained for the analysis but not further discussed in the main report. Moreover, it was part of the roadmap which was considered as the basis of this impact assessment.

5. WHAT ARE THE IMPACTS OF THE DIFFERENT POLICY OPTIONS AND WHO WILL BE AFFECTED?

5.1. Methodology applied for assessing the impacts

Once the criteria to identify EDs are set based scientific considerations, they will be applied subsequently to the regulatory process for the approval or renewal of approval of active substances falling under the PPP and BP Regulations (no derogations for SMEs are foreseen in the Regulations). The impacts are driven by the regulatory consequences foreseen for the substances which are identified as EDs. Regarding the international dimension, the impacts need to be assessed considering provisions set in international law, such as customary international law and treaties ratified by the EU.

Due to this situation, the impacts have been assessed in a two-step procedure as described in the subsections below.

5.1.1. Step 1: Number of substances identified as ED – the screening study

In a first instance, the **number of substances which would be identified as EDs** under the various options has been estimated via a screening study performed by an external contractor (Specific Contract SANTE/2015/E3/001). The study was based on a scientific method developed by the Joint Research Centre (JRC). The JRC monitored and assisted the screening process performed by the contractor. The methodology, the results of the screening, and the contractor's details will be published once the screening is finalised, which is expected by end June 2016.

The screening study served as a case study and constitutes the basis for the assessment of the impacts on different policy areas. It resulted in a quantifiable estimation regarding how many and which chemical substances used in PPP and BP may be identified as EDs under Options 1 to 4. It also gave an estimate of the extent of the overlap between the options allowing a comparison of the options. Further, both the method and the experience applying it might be used at a later state as a starting point for practical guidance to apply the criteria.

However, the results of the screening do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. The results of the study cannot be used for regulatory purposes because for identifying a substance as ED for taking regulatory decisions a more in depth assessment in line with the provisions of the respective Regulations would be required.

5.1.2. Step 2: Direct and indirect impacts in different policy areas

Building on the results of the screening study (i.e. the chemical substances identified as ED under each of the Options 1 to 4) and the regulatory consequences foreseen in the PPP and BP Regulations (non-approval of active substances unless the derogations apply), the direct and indirect impacts in different policy areas have been assessed. The policy areas covered in the assessment were human health, environment, economic operators, users, MS and third countries.

For assessing these impacts and because they are multifactorial, the evidence of the screening study was complemented with additional information. However, the availability of reliable

and sound data to assess the impacts on agriculture, trade, health and environment was scarce and highly variable. Also the identification of plausible and reliable case studies to be used for assessing the impacts was difficult. In particular:

- Basic agricultural/trade data were either not available, not ready, or not easy to use (e.g. information on uses of active substances per crop and per pest were not available for all EU MS; yield decreases in crop production due to the absence of a PPP - crucial for any estimation of agricultural and end consumers impacts - could only be estimated with significant uncertainties; extrapolation from case studies based on few Member States to the whole EU was not considered appropriate due to e.g. differences in climate conditions; some agronomic impacts cannot be quantified for example resistance to target organisms).
- Regarding health data, no active substance identified in the options can be linked directly to hormone related diseases and disorders because of the acknowledged limitations of the reviewed health studies. Also, studies trying to quantify the health cost associated to EDs' exposure rely upon controversial assumptions and models adapted from other sectors. Further, due to the already high protection of health in the PPP and BP legislations (no use of substances that pose a serious health or environmental concern would be authorised), a comparison between Option A and Option B (approaches to regulatory decision making) would be difficult.
- Assessing environmental impacts, e.g. on biodiversity/ecosystems, is also difficult, in particular because evidence to link environmental data to particular active substances is in general not possible, as confirmed by the recent study on benefits of chemical legislation (RPA, 2015)[50].

The preliminary assessment of the evidence concluded that it would not be possible to quantify impacts, as data would neither be of sufficient quality nor reflect reality due to the high level of uncertainties and assumptions made. In addition, some approaches to estimate impacts would - as a consequence of the variable data availability in the different areas – create a strong imbalance between the assessments of the areas. Thus, under consideration of the Better Regulation Guidelines and in light of the complexity of the areas and the potential impacts (including key impacts listed in Tool #16), as well as the evidence and data available, a **Multi-Criteria Analysis (MCA**, Better Regulation Guidelines' Tool #55[51]) was considered as the most appropriate analytical method to compare and rank the options against the areas considered because:

- it is useful when impacts cannot be fully quantified or monetised;
- it allows impacts to be reconciled with policy objectives;
- it can capture distributional impacts (e.g. in terms of stakeholder types);
- it enables to judge the pros and cons of options along the criteria chosen for the comparison;

[50] Risk and Policy Analysts (RPA) et al. 2015. Study on the Calculation of the Benefits of Chemical Legislation on Human Health and the Environment, Final report for DG Environment, March 2016, Loddon, Norfolk, UK

[51] The analytical methods listed in Tool #55 are: Cost Benefit Analysis (CBA), Least Cost Analysis (LCA), Multi-Criteria Analysis (MCA), Cost-Effectiveness Analysis (CEA), Counterfactual Analysis, and SWOT Analysis. Cost-Benefit Analysis, Least Cost Analysis and Cost-Effectiveness Analysis were discarded because robust assumptions for quantifying and monetising the impacts were not available. The Counterfactual analysis was discarded as it is more appropriate for evaluations as it looks at what would have happened in the absence of an intervention. The SWOT analysis was discarded as it is not an analytical method per se, but it is used to identify Strengths, Weaknesses, Opportunities and Threats in relation to a project/organisation.

- it allows the selected criteria to determine the results obtained by assigning weights to them.

Although a MCA is complex and might be difficult to communicate, it has also many advantages over informal judgement. Advantages are in particular that performance scores and weights are explicit and developed according to established techniques; that a sensitivity analysis can be performed, highlighting how the weights assigned to MCA-criteria and changes in performance of the options influence the final result; and that the scores and weights used provides an audit trail.

The performance scores applied in the MCA methodology of this impact assessment for Options 1 to 4 (i.e. the assessment of the impacts for each of the MCA-criteria) are based on the results of the screening combined with the additional evidence available in each of the dimensions analysed (e.g. human health, agriculture, trade). It is assumed that Options 1 to 4 are applied under the current PPP and BP Regulations (Option A).

In order to assess the potential impacts of Options B and C (Option C was discarded but kept for methodological reasons, see Section 4.2.3), a 2nd MCA was carried out which compares qualitatively the current regulatory framework with potential different regulatory decision making. Thus, the MCA was carried out in a step-wise approach, as there were two sets of options with the aim to simplify the already very complex analysis:

- Step 1: the MCA methodology applied to Options 1 to 4 (Aspect I)
- Step 2: the MCA methodology applied to Options A to C (Aspect II)

The same MCA parameters (criteria, weights, performance assessment methods, etc.) were used for both steps.

The MCA-methodology is detailed in Annex 6 and includes a sensitivity analysis which considers different scenarios based on the availability of evidence, different priority setting (weight) to the different dimensions (e.g. giving a higher weight / priority to human health), and/or different performance of the options. In the sub-sections below the key steps of the MCA are summarised.

5.1.3. MCA methodology: selection of the MCA-criteria

The MCA-criteria need to be operational so that they assess how well each option meets the objectives expressed by the MCA-criteria. The number of MCA-criteria should be kept as low as is consistent with making a well-founded decision.

The MCA-criteria were developed as the first MCA-step by the procedure summarised in this section and in more detail in Annex 6:

1) The MCA-criteria were designed so that effectiveness, efficiency and coherence of each option can be assessed, by following Tool #8 of the Better Regulation Guidelines (see below). In particular:
    a) Link with the objectives (effectiveness): the MCA-criteria were selected considering the objectives described in Section 3 and which are: 1) ensuring of high level of protection of human health, animal health and the environment; and 2) strengthening the functioning of the internal marked while improving agricultural production. Criteria on the social and environmental impacts are linked to the first objective, whereas criteria on the economic, effectiveness and coherence impacts are linked to the second objective. Further, the compliance with international obligations and specific objectives were also considered (see Section 3).

b) Areas with significant impacts (efficiency): the MCA-criteria were selected to cover the areas were significant impacts could be expected. This was done by following Tool #16 – "Identification/screening of impacts" for identifying the key economic, social and environmental impacts.

c) Consistency with other EU legislation (coherence): the MCA-criteria selected include consideration of international treaties that the EU needs to abide by (WTO and Codex Alimentarius) or the coherence between PPP and BP legislation.

Table 1: MCA-criteria listed by dimension and by impacts they address

Impacts		Dimensions and MCA-criteria
EFFECTIVENESS & COHERENCE		**EFFECTIVENESS & COHERENCE**
		Legal certainty and proportionality:
		Operability for regulatory decision making:
		Coherence between BP and PPP legislation:
		Compliance with international obligations of the EU:
EFFICIENCY	Economic	**SECTORIAL COMPETITIVENESS: EU AGRICULTURE**
		Number of PPP affected:
		Crops affected:
		Existence of alternatives / risk of resistance of pests:
		SECTORIAL COMPETITIVENESS: PPP, BP AND RELATED INDUSTRIES
		Functioning of the single market:
		Innovation and research:
		SME's:
		INTERNATIONAL TRADE
		Import of food:
		Import of feed:
		Import of treated articles:
	Social	**HUMAN HEALTH**
		Hormone related diseases and disorders:
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides:
		Food safety:
	Environment	**ENVIRONMENT**
		Chemical quality of water:
		Wildlife vertebrate populations:
		Animal welfare:

2) The availability of evidence was crucial for the selection of MCA-criteria in order to be able to use the criteria to assess the performance of the options. As mentioned before, the data availability was highly variable, with some fields benefiting from more detailed data while others being characterised by the prevalence of qualitative data or the lack of data (see Table 2).

3) The MCA-criteria were assessed against a range of qualities: completeness, redundancy, operationality and mutual independence.

4) The MCA-criteria were checked against the Public Consultation Report to ensure that all relevant potential impacts mentioned by stakeholders are covered.

5) The MCA-criteria were discussed with the members of the Impact Assessment Steering Group (IASG) at the meeting of 1st February 2016, in order to ensure that all relevant potential impacts are covered.

5.1.4. MCA methodology: assessment of the options and sensitivity analysis

In a second MCA-step, the performance of the options was assessed for each of the MCA-criteria. The performances reflect the impacts expected for each criterion.

The assessment of the performance (impacts) was based on the outcome of the screening study (number and, where possible, identity of AS identified as EDs under each option). Additional evidence was also considered to the extent possible for the analysis of the impacts and for assessing the performance of the options under the current regulatory framework (Option A). A summary of the evidence used for each criterion is given in Table 2 and described in more detail in the respective Annexes.

Some of the impacts (MCA-criteria for EU agriculture and international trade) could be assessed based on case studies which were based on the substance-specific outcome of the screening study (identity of the substance) and additional evidence. For other criteria, where less evidence was available, a more descriptive approach had to be followed so that the evidence compiled via the screening study played a more prominent role because of the assumptions taken during the assessment of the potential impacts. Assumptions played also a prominent role when assessing the potential impacts of Options B and C (Option C was discarded but kept for methodological reasons, see Section 4.2.3). The reason for this is that the comparison of the impacts of these options with those under the current regulatory framework (Option A) could only be done qualitatively. Exact evidence could only be collected once the regulatory process is finalised for each substance, which usually takes 2 to 3 years and is therefore not possible to be assessed in the context of this impact assessment.

The impacts described in Sections 5.3 and 5.4 translate into the performance of the options and have been structured the same way as the dimensions used for the MCA:

- Achievement of effectiveness and coherence (Annex 8)
- Human Health-Hormone related diseases and disorders (Annex 9)
- Human Health-Transmissible diseases and food safety (Annex 10)
- Environment (Annex 11)
- Sectorial competitiveness: EU agriculture (Annex 12 and 13)
- Sectorial competitiveness: PPP, BP and related industries (Annex 14)
- International Trade (Annex 15)

Table 2: Description and underlying evidence for the MCA-criteria listed by dimension

MCA-CRITERIA	ADDITIONAL EVIDENCE CONSIDERED WHEN ASSESSING PERFORMANCE OF THE OPTIONS IN THE MCA	DESCRIPTION AND ASSUMPTIONS OF THE MCA-CRITERIA
EFFECTIVENESS & COHERENCE		
Legal certainty and proportionality: *degree to which legal certainty is ensured*	current experience implementing the PPP and BP Regulations and their derogations.	Legal certainty would in principle be achieved by all options. However, the application of case-by-case derogations is expected to lead to more uncertainty to applicants and stakeholders. The introduction of categories may decrease legal certainty as AS placed under Category II or III have no regulatory consequences under the PPP and BP Regulations.
Operability for regulatory decision making: *additional efforts required to public authorities and applicants resulting from implementing derogations and a revision of categories*	current experience implementing the PPP and BP Regulations and their derogations.	The application of derogations for approving substances identified as EDs would decrease operability for regulatory decision making. Additional burden may be expected because of the application of case-by-case derogations.
Coherence between BP and PPP legislation	current experience implementing the PPP and BP Regulations and their derogations as some substances fall under both legislations.	The application of case-by-case derogations (currently different between BP and PPP and currently clearer and easier to implement under BP), is expected to lead to less coherence between the PPP and BP Regulation. An alignment of derogations is assumed to lead to higher coherence and better implementation.
Compliance with international obligations: *compliance with international obligations (WTO and Codex Alimentarius)*	Provisions of - The Agreement on Technical Barriers to Trade (TBT Agreement) - The Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement).	It is assumed that the more the implementation of criteria is based on risk rather than hazard, the more compliant is the EU with its international obligations.
HUMAN HEALTH		
Hormone related diseases and disorders (potentially ED related diseases and disorders): *health risks potentially related to hormonal axes (EATS)*	- No evidence available to establish a causal link between currently approved AS and potentially ED related diseases. - Incidence of potentially ED related diseases in the EU based on literature review and data from Eurostat, OECD, and WHO. - Current experience implementing the PPP and BP Regulations and their derogations.	All options based on the WHO definition are considered to be equally protective. Option 1 is considered not fit for purpose as not able to identify an ED mode of action. i) An active substance is only approved following a risk assessment. As a consequence, it can be assumed that no harmful or unacceptable effects on human health are expected for approved substances. It can be assumed that human health is protected regardless the number of AS identified as ED. ii) exposure zero scenario: it is assumed that only a hazard based approach can protect human health. Thus, it is assumed that any exposure to an AS with ED properties is harmful and the longer the list of *relevant* AS with ED properties, the higher the protection of human health.
Transmissible diseases: health risks caused by lack of appropriate disinfectants (e.g. in hospital settings) or insecticides (e.g. mosquito borne public health treats)	- Expert advice on transmissible diseases was provided by the European Centre for Disease Prevention and Control (ECDC). - Current experience implementing the BP Regulation and its derogations.	It can be assumed that the expected impact is proportional to the number of BP identified as ED as there is a need for a wide spectrum of disinfectants (there is no single universal disinfectant) and insecticides to control transmissible diseases
Food safety: *risk of contamination of food (e.g. by mycotoxins)*	- The Rapid Alert System for Food and Feed (RASFF) data - EFSA database on Collection on	The impact on food safety with regards to mycotoxins includes large elements of uncertainty. It can be assumed that the likelihood of having an impact on health will be higher if less PPP relevant for the control of fungi

MCA-CRITERIA	ADDITIONAL EVIDENCE CONSIDERED WHEN ASSESSING PERFORMANCE OF THE OPTIONS IN THE MCA	DESCRIPTION AND ASSUMPTIONS OF THE MCA-CRITERIA
	Contaminant Occurrence Data - No detailed data is available on the monetary impact of mycotoxins in the EU.	producing mycotoxins are available.
ENVIRONMENT		
Chemical quality of water: *contamination of ground, surface, and drinking water with ED chemicals used as PPP or BP*	No direct evidence available to establish a link between the use of PPP and BP and chemical quality of water. This criterion assumes that the quality of the water is inversely proportional to the number of active substances present in it, irrespectively of their levels. It aims at zero exposure from active substances.	It is assumed that the higher the number of AS removed from the market or restricted, the higher the likelihood of an improvement in the chemical status of water.
Wildlife vertebrate populations: *decrease of wildlife vertebrate populations because of ED mediated adverse effects*	No direct evidence available to establish a link between the use of PPP and BP and the adverse effect on vertebrate populations.	All options based on the WHO definition are considered to be equally protective. Option 1 is considered not fit for purpose as not able to identify an ED mode of action. It is assumed that a decision making based on risk assessment is equally protective for wildlife populations as a decision making based on hazard. Differently, the inclusion of socio-economic considerations may consider a risk/benefit analysis and, therefore, it is assumed to protect the environment to a lesser extent. Exposure zero scenario: it is assumed that only a hazard based approach can protect environment. Thus, it is assumed that any exposure to an AS with ED properties is harmful and the longer the list of relevant AS with ED properties, the higher the protection of environment
Animal welfare: *number of animal tests needed*	Number of tests required in the application dossiers.	All the options perform the same, no matter how many substances they identify as ED. It is however assumed that the inclusion of additional categories under option 3 might trigger additional animal testing, as companies or authorities would wish to verify whether the chemicals classified as Category II or III are actual EDs or not.
SECTORIAL COMPETITIVENESS: EU AGRICULTURE		
Number of PPP affected: *number of PPP authorised at national level that will be affected as a consequence of the non-approval of affected AS identified as EDs*	Data on authorised PPP from 8 MS collected via PPPAMS but evidence is lacking in order to quantitatively assess the impacts in terms of yield losses of the potential disappearance of one single substance.	After an AS is approved under the PPP Regulation, MS can authorise products containing this AS. Consequently, if an AS is no longer approved, the PPPs containing this AS will no longer be authorised. Data to assess this, at AS level, were available from 8 MS and were used as case studies. It is assumed that the higher the number of PPP that will disappear from the market, the higher the negative impacts on EU agriculture.
Crops affected: *number of crops affected by the disappearance of certain AS*	Data on authorised PPP uses on crops from 8 MS collected via PPPAMS	After an AS is approved under the PPP Regulation, MS can authorise products containing this AS which are used on specific crops against specific pests. Data to assess this, at AS level, were available from 8 MS and were used as case studies. It is assumed that the longer the list of crops affected, the higher the negative impacts on EU agriculture.
Existence of alternatives / risk of resistance of pests: *number of PPP alternatives existing for each crop / risk of appearance of resistance in pests resulting from a lower number of available PPP*	Eurostat data concerning statistics on pesticides (Regulation (EC) No 1185/2009).	The data available in the context of Regulation (EC) No 1185/2009 were used to analyse the percentage of AS (in terms of sales) affected per chemical class and per major group. It is assumed that the higher the percentage of a chemical class affected, the lower the number of alternatives existing. For some crops, only one particular AS is

MCA-CRITERIA	ADDITIONAL EVIDENCE CONSIDERED WHEN ASSESSING PERFORMANCE OF THE OPTIONS IN THE MCA	DESCRIPTION AND ASSUMPTIONS OF THE MCA-CRITERIA
		effective/efficient and therefore its loss might lead to higher impacts for the crop production than the data shown in the assessment but the level of detail and of reliability of additional data at the disposal of the Commission did not allow for such a detailed analysis.
SECTORIAL COMPETITIVENESS: PPP, BP AND RELATED INDUSTRIES		
Functioning of the single market (in particular when exceptions apply):	Current experience implementing the PPP and BP Regulations and their derogations, in particular the effect on national authorisations and mutual recognitions.	Derogations may be applied at MS level where it is necessary and subject to specific conditions that only applies in some MS and not in others. Thus, it can be assumed that the higher the number of AS removed from the market or approved under restricted conditions, the more specific national conditions would apply, which consequently would impact negatively on the functioning of the single market.
Innovation and research: *change of innovation, research, and technical development in PPP and BP industry, pesticide application industry, food industry, others*	General information available on the costs to develop and market PPP and BP, but evidence is lacking in order to quantitatively assess the impacts on innovation and research.	Considering the current drivers for innovation and the market structure, it can be assumed that the non-approval of an AS will probably not trigger substantial innovation.
SME's: *Burden to SMEs*	- Eurostat data on the size of farms, both in terms of hectares and full-time equivalent jobs per holding, in the EU. All agricultural holdings qualify as SMEs. - No data available on SMEs operating in the BP sector. - Not data available on SMEs operating in the PPP industry sector	It is assumed that the higher the impacts on farmers, the higher the impacts on SMEs, as all farmers are SMEs – see also impacts for agriculture. Any increase in costs and demand of staff is assumed to negatively affect the market position of SMEs because larger firms have greater financial capacity and are better able to e.g. spread risks. SMEs have in general smaller portfolios of active substances than larger companies and therefore they are relatively more vulnerable to the withdrawal of AS identified as ED.
INTERNATIONAL TRADE		
Import of food: *volume of imports of food potentially affected by lowering the MRLs at the limit of determination (LOD).*	- The EU Pesticide Database on MRLs (at AS and crop basis). - COMEXT trade databases from Eurostat for volumes and value of imports of crops from third countries, but evidence is lacking in order to quantitatively assess the impacts on third countries' economies of the possible trade disruption resulting from lowered MRLs	The PPP Regulation provides that for AS identified as ED, the MRLs in products imported to the EU is set at the default level (no risk assessment). This implies that some MRLs already set (information available via the EU Pesticide database) will need to be lowered to the default value, i.e. to the limit of determination (LOD). This MCA criterion was evaluated based on information available. For each AS identified as ED and for a sample of the more relevant crops imported in the EU (COMEXT database), it was evaluated how many MRLs would be lowered to the LOD for a crop. It can be assumed that the higher the number of MRLs lowered, the worse the impacts on trade. Also, the higher the value of imports of impacted crops, the worse the impacts on trade.
Import of feed: *volume of imports of feed potentially affected by lowering the MRLs at the LOD*		
Import of treated articles: *volume of imports of goods which may be affected as a consequence of implementing the BP Regulation in relation to treated articles*	Eurostat COMEXT data used to analyse the country of origin, value and volume of textiles imported to the EU	With the non-approval of a BP, it is assumed that manufacturers and importers have to make an effort to adapt to the new requirements. It can therefore be assumed that the more AS identified as ED used in treated articles, the higher the volume of imports may be affected.

5.2. Direct impacts on the number of PPP and BP active substances falling under Options 1 to 4

For determining whether an active substance would be identified as ED under each of the options, a screening study was performed by an external contractor. This study provides evidence regarding which substances and how many of the substances used in PPP and BP may be identified as EDs under each of Options 1 to 4. Please refer to Annex 3 for a method description, Annex 4 for the list of substances screened and Annex 5 for the detailed results of the screening study.

The screening study was carried out in the context of this impact assessment to evaluate the impacts associated to options for criteria to identify endocrine disruptors under the regulations on plant protection products and biocidal products. The screening was based on available evidence (no additional testing) and needed to be carried out in a limited time. The screening methodology was developed for the purpose of the screening exercise.

The results of the screening therefore do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances identified in the screening are considered as endocrine disruptors within the meaning of the EU legislation.

The screening was based on hazard classification according to Regulation (EC) No 1272/2008, scientific data available in regulatory assessment reports[52], and information from databases[53] focusing on endocrine effects and including non-regulatory scientific studies (see Annex 3 for a method description). The methodology used was developed by the Joint Research Centre (JRC, European Commission) and was based on the WHO/IPCS definition of an ED and international guidance on assessment of EDs (2012 OECD technical guidance on assessment of EDs[54]). Considering the internationally validated testing methods available[55], the methodology only focused on the estrogenic, androgenic, thyroidal and steroidogenic modalities of the endocrine system (EATS modalities) and on population-relevant effects in animal vertebrate species.

The screening of chemical substances used in PPP or BP resulted in the same number of active substances identified as EDs under Option 2 and Option 3 Category I, while the number of substances identified under Option 4 is a subset of these (see Table 2 and Figure 2). This trend was expected since it is related to the design of the options and the method used for the screening, however the results indicate the magnitude of the difference between the options and which substances or substance groups are likely to be affected. This information was not available before performing the screening study.

[52] EFSA conclusions, Member State (MS) Draft Assessment Reports, MS Competent Authority Reports, REACH restriction dossiers, Support documents for identification of SVHC and opinions of the SCCS.

[53] JRC's Endocrine Active Substances Information System, TEDX, SIN list, ToxCast, EDSP WoE analyses and targeted literature searching

[54] OECD Guidance document on standadised test guidelines for evaluating chemicals for endocrine disruption. No. 150. Retrieved from: http://www.oecd.org/chemicalsafety/testing/oecdguidancedocumentonstandardisedtestguidelinesforevaluatingchemicalsforendocrinedisruption.htm

[55] EFSA Scientific Committee; Scientific Opinion on the hazard assessment of endocrine disruptors: scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing effects mediated by these substances on human health and the environment. EFSA Journal 2013;11(3):3132. [84 pp.] doi: 10.2903/j.efsa.2013.3132.

All **PPP active substances** that are currently on the market were screened, with some exceptions (such as the exclusion of micro-organisms) which are explained in Annex 4. In total, 347 PPP active substances were screened.

For PPP, Option 1 (interim criteria) identifies almost twice as many substances than Option 2 or Option 3 Category I, but only a small overlap (5 substances) exists between them. A total of 37 substances are identified under Option 1 as ED, but they are not overlapping with the substances identified under options 2, 3 Category I, or 4. Consequently they are considered to be **false positives** because they are identified as EDs under Option 1 without appearing to have ED properties under Options 2 to 4. This is because the approach followed for Option 1 and Options 2, 3 Category I, and 4 differ: while the interim criteria are based on categorisation of substances as suspected of being carcinogenic (C2) or suspected of being toxic for reproduction (R2), Options 2 to 4 are based on implementation of the WHO definition of EDs (adverse effects, mode of action and causal link).

Table 3. Number of active substances used in PPP or BP identified as EDs under the screening study[56] preformed for this impact assessment (substances identified as ED and classified as C1 or R1, thus falling under the "cut-off" criteria, are not included in the PPP numbers). In total, 347 PPP and 98 BP were screened.

	NUMBER OF SUBSTANCES IDENTIFIED AS EDS				
	OPTION 1	OPTION 2 / OPTION 3 CAT I	OPTION 3 CAT II	OPTION 3 CAT III	OPTION 4[57]
Active substances used in PPP	42	26	82	45	11
Active substances used in BP	16	5	26	8	2

The results also show that Option 1 (interim criteria) did not identify all active substances that were considered ED under Options 2, 3 Category I, or 4. These 21 substances are **false negatives** because substances identified as ED using the WHO definition are not identified under Option 1 (however this identification is only the 1st step in regulatory decision making). This result confirms that Option 1 is not effective to identify all substances with endocrine-properties. However, it should be kept in mind that most of the adverse effects caused by these "false negatives" would be addressed via the "standard" risk assessment needed in any case under the PPP and BP Regulations, which is focused on potential adverse effects (WHAT question), being the mode of action (HOW question) known or not.

It should be noted that the number of substances identified under Option 1 is based on *harmonised* CLP[58] classification as suspected of being carcinogenic (C2) or suspected of being toxic for reproduction (R2) and in addition on proposals for such classification by the EFSA which are more recent than the *harmonised* classification. This further increased the number of substances classified as C2 or R2 and therefore as EDs under Option 1.

[56] The screening study includes substances falling under REACH, Cosmetics Regulation, and Water Framework Directive (see Annex 4). The results of the screening of these substances were neither available nor relevant in the context of this impact assessment report. They will be published in the report of the screening study.

[57] In the screening, potency-based STOT-RE Cat 1 trigger values from the Regulation (EC) No 1272/2008 were used as cut-off criteria to evaluate potency. The most sensitive endocrine specific endpoint was compared to the potency cut-off values taken from the STOT-RE, according to the route of exposure (oral, dermal, inhalation). The doses were time-adjusted to a 90-day study. The same value was used for all species and no adjustment for different sizes (body weights) or life spans was done.

[58] Regulation (EC) No 1272/2008

In order to avoid "double-counting" from a regulatory perspective and with respect to potential impacts, substances identified in the screening as EDs and already falling under one of the "cut-off" criteria (R1, C1, and persistent/toxic and bio-accumulative substances), are identified separately (see Annex 5). Although this confirms that some EDs are already regulated via the consideration of the adverse effects, they have been excluded from the analysis of the impacts in the different areas (in particular agriculture and trade).

A total of 98 **BP active substances** were screened. The BP substances selected for the screening were linked to the availability of data at EU level, which is related to the on-going review programme of existing biocidal substances on the market and resulted in different percentages of product groups screened, for instance only 17% of active substances used in disinfectants were screened compared to 52% of the pest control substances. Thus, any result of the screening of BP substances should be cautiously interpreted for the potential impact on all product types on the market. Nevertheless, the overall trend (see Table 3) that Option 1 identifies more substances (16 substances) than Options 2 and 3 Category I (5 substances) is confirmed also for BP, as well as the fact that Option 4 identifies a subset of Option 2 and Option 3 Category I.

The number of false positives and false negatives show the same trend for BP as for PPP. A total of 13 substances are identified under Option 1 for BP but not under Option 2 and 3 Cat I (false positives). The interim criteria failed to identify two substances that have endocrine modes of actions (false negatives) that were identified as EDs under Option 2 and 3 Cat I.

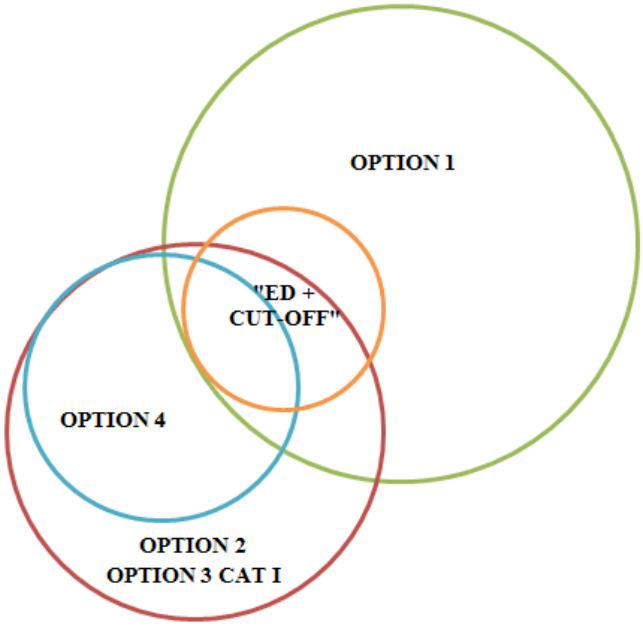


Figure 3. Relation between the chemical substances used in PPP identified as EDs under Option 1, Option 2 and Option 3 Category I, and Option 4. The circle "ED + cut off" represents substances that are identified as ED and also classified as C1 or R1 and therefore falling under the cut-off criteria in the PPP Regulation.

Table 4. False positives and false negatives identified for Option 1 by the screening.

	PPP	BP
False positives (identified under Option 1 but not under Options 2 to 4)	37	13
False negatives (identified under Options 2 to 4 but not under Option 1)	21	2

5.3. Direct and indirect impacts in different policy areas expected after implementing the scientific criteria in the current regulatory PPP and BP Regulations (Aspect I)

Once the new scientific criteria are defined, they will be applied in the context of the review or renewal of approval programmes foreseen in the PPP and BP Regulations for active substances. As a consequence, they are expected to impact the number of active substances which are on the market to be used in PPP and BP. This will then lead to impacts on several areas in particular human health, environment, sectorial competitiveness including agriculture, and trade, as summarised below.

- The health of the general population, consumers, and workers would be affected directly or indirectly via the occurrence of PPP and BP or their metabolites in food or in the environment, by the availability of PPP or BP (e.g. disinfectants), by the availability of certain products for which production PPP or BP may not be longer available, or by the variation in costs for products including agricultural commodities.
- Economic operators may also be affected. Besides the chemical industry, impacts are also expected for downstream users of PPP and BP (e.g. food operators, farmers, health facilities) because of availability of PPP and BP. Consumers and international trade may also be affected.
- Potential impacts of the different options on legal certainty, proportionality and operability for regulatory decision making, coherence between the PPP and the BP legislation, as well as the coherence with international treaties and/or obligations, were also considered in the assessment.

The potential impacts are summarised in the subsections below, which reflect the dimensions identified to perform the Multi Criteria Analysis (MCA) (see Table 1). More detailed discussion on the respective impacts can be found in the respective Annexes.

5.3.1. Achievement of effectiveness and coherence (Annex 8)

The criteria to define EDs will be applied in the framework of the current PPP and BP Regulations. The effectiveness of the options to fulfil the objectives of these Regulations was assessed considering legal certainty and operability, while coherence was assessed considering the coherence between the PPP and BP Regulations and the compliance with international obligations of the EU (WTO and Codex Alimentarius).

Legal certainty would in principle be achieved by all options. However, the case-by-case assessment of derogations for the approval decision process of substances identified as EDs would decrease legal certainty for all involved parties and also decrease **operability** regarding regulatory decision making.

The introduction of categories (Option 3, WHO definition with categories), may decrease legal certainty because the current legislation for PPP and BP does not foresee specific provisions regarding the application of categories for ED substances. It is likely that MS and

stakeholders may interpret differently regulatory consequences for substances placed under Category II or III, which would decrease legal certainty for operators. Further, substances falling under Categories II and III may be "black listed".

In addition, using categories similar to those used for classification under Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP Regulation) may lead to confusion. It may be misinterpreted that substances categorised under the criteria to identify EDs as EDs Category II or EDs Category III are classified as such under the CLP, while this would not be the case. The criteria to identify EDs were mandated by the co-legislators only for PPP and BP. It may be confusing with respect to other overarching pieces of EU legislation (CLP), and thus negatively affect legal certainty and operability, in particular because the categories foreseen under Option 3 (Cat I, II and III) do not follow the same rationale as those used in the CLP Regulation.

Summarising, the more substances identified under an option which is implemented under the current legal framework (Option A), the more likely the derogations would be applied and legal certainty would therefore be decreased. Therefore and based on the results of the screening, the options would perform 4>2>1>3. With respect to operability, it can be expected that the more substances are identified as EDs, the more case-by-case derogations are expected which would lead to higher operability difficulties and additional burden, implying that the options rank 4 > 2/3 > 1.

Coherence between the PPP and BP legislation on the implementation of the ED criteria is not achieved under the current regulatory decision making (Option A) because the current derogations differ in these two pieces of legislation for approval of substances identified as EDs. This is particularly important as some chemical substances (currently 38) fall under both the PPP and BP legislation. The more substances identified, the more cases for derogations are likely to arise, and the less the coherence between the PPP and BP Regulations is obtained. Thus, the options would perform this way: 4>2/3>1.

Compliance with international obligations (e.g. those under the WTO-Sanitary and Phytosanitary (SPS) agreement and Codex Alimentarius) was also considered. The issue of the assumed non-compliance of options to set ED criteria based on hazard (Option A for PPP) has been raised increasingly by WTO Members at every Technical Barriers to Trade (TBT) and SPS Committee meeting since October 2013. In the public consultation, six public authorities and six governments from non-EU countries gave their comments. One of the main issues they stressed was the potential impact on trade triggered by ED criteria based on hazard alone, whereas the SPS agreement lays down that measures have to be based on risk assessment.

Options 1, 2 and 3 are all based on the identification of hazard. However, Option 4 will perform comparatively better than the others in terms of compliance with WTO rules as it goes one step further in the direction of risk assessment by including potency as one element of hazard characterization. This implies a ranking of options 4 > 2/3/1.

5.3.2. Human health (Annexes 9 and 10)

Protection of human health is a Treaty objective (Art 168.1) and a key objective for both the PPP and BP Regulations. In the context of this impact assessment, impacts and evidence regarding hormone related diseases were analysed, but also impacts on transmissible diseases caused by lack of appropriate disinfectants or insecticides and food safety (in particular contamination by mycotoxins).

In the public consultation, concerns regarding food safety and public health were raised by public authorities, professional associations, and NGOs. Some EU MS (France, Denmark, Sweden), health, environmental and consumer NGOs call for EU criteria to identify EDs based on hazard that would also include additional categories based on the different strength of evidence for fulfilling the WHO/IPCS definition (Option 3). On the other hand, some EU MS (Germany, UK) support risk assessment (Option B, see Section 5.4) or Option 4 (WHO definition and inclusion of potency).

The association between incidence of certain human diseases and exposure to EDs have been raised in some international reports (WHO-UNEP, 2012[59]) or stakeholder statements (Endocrine Society, 2009[60], 2015[61]). Evidence, including EU data, is scattered and its interpretation difficult. The evidence available which aims at demonstrating effects of ED, is often linked to substances which are already banned in the EU. Epidemiological information, including cohort studies and systematic reviews, suggests that a causal link between the exposure to PPP and certain human diseases is not proven or not applicable to the regulatory situation in the EU with respect to PPP and BP (EFSA[62]; "AgriCan"[63]). Also the recent RPA study[64] stresses that health outcomes are often the results of the synergies of multiple factors. For long latency diseases a number of assumptions is required which seriously limits the value of any indicator trying to measure the contribution of chemicals legislation in lowering exposures.

Estimates on costs of diseases related to exposure to EDs which were recently published should be taken with caution. There are concerns over the validity of these estimates and the methods used to calculate them, which are linked to the scattered evidence. Moreover performing a Cost of Illness (CoI) analysis is always very challenging (Annex 9).

Further, it needs to be acknowledged that science is still evolving and that controversy between scientists still exists regarding some key aspects which are not relevant for the identification of EDs but are relevant for the assessment of EDs. This controversy is also reflected in recent meetings and events, for instance the "meeting with the former Chief Scientific Advisor of the European Commission Ms Ann Glover" (2013)[65], the conference "EDs: criteria for identification and related impacts" (1st June 2015, Brussels)[66], and the "Expert Meeting to Reach Scientific Consensus on EDs" (April 2016, Berlin, chaired by the German Federal Institute for Risk Assessment).

Summarising, the evidence related to **endocrine mediated diseases** and associated costs shows that under the existing EU regulatory framework with respect to PPP and BP robust

[59] World Health Organization (WHO) 2012. State of the science of Endocrine Disrupting Chemicals 2012. Summary for Decision-Makers. Ed. Bergman Å., Heindel, J.J., Jobling S., Kidd, K.A., and Zoeller R.T. Retrieved from http://www.unep.org/pdf/WHO_HSE_PHE_IHE_2013.1_eng.pdf

[60] Diamanti-Kandarakis E. et al. 2009 Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement. Endocrine Reviews 30(4):293-342, doi:10.1210/er.2009-0002, available on: https://www.endocrine.org/endocrine-press/scientific-statements

[61] Gore, A.C., et al. 2015. EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals. Endocrine Reviews 36 (6) doi.org/10.1210/er.2015-1010

[62] European Food Safety Authority. 2010. Application of systematic review methodology to food and feed safety assessments to support decision making. EFSA Journal 8(6):1637. [90 pp.]. doi:10.2903/j.efsa.2010.1637

[63] Levêque-Morlais, N., et al. 2015. The AGRIculture and CANcer (AGRICAN) cohort study: enrolment and causes of death for the 2005–2009 period. International Archives of Occupational and Environmental Health. 88 (1): 61-73. DOI 10.1007/s00420-014-0933-x

[64] Risk and Policy Analysts (RPA) et al. 2015. Study on the Calculation of the Benefits of Chemical Legislation on Human Health and the Environment, Final report for DG Environment, March 2016, Loddon, Norfolk, UK

[65] European Commission. 2013. Minutes of the expert meeting on endocrine disruptors. Retrieved from: http://sciences.blogs.liberation.fr/files/glover-u-s-perturbateurs-endocriniens.pdf

[66] European Commission. 2015. Conference "Endocrine disruptors: criteria for identification and related impacts". Retrieved from: http://ec.europa.eu/health/endocrine_disruptors/events/ev_20150416_en.htm

conclusions cannot be drawn on the link between exposure to EDs and increased incidence of endocrine mediated diseases. Nevertheless, protection of human health remains the highest priority as it is a main objective in the PPP and BP Regulations, and thus guides this impact assessment. Protection of human health was therefore analysed under consideration of the current regulatory framework of the PPP and BP Regulations.

The EU authorisation system for PPP and BP is based on prior approval (a "positive list"), i.e. substances are deemed hazardous until proven otherwise.30 This also applies to the assessment of **adverse effects linked to EDs.** Most of the adverse effects associated with endocrine disruption are covered by the "standard" risk assessment carried out for a substance even if this substance is not identified as an ED (for example, reproductive adverse effects). This is confirmed by the high number of PPP commonly associated with the endocrine mediated diseases which have already been banned for years in the EU (see Table 3 in Annex 9). It is also confirmed by the fact that Member States could not find an agreement on whether it would be appropriate under REACH Regulation to identify some substances as EDs for their adverse effect human health: several Member States in fact argue that the *very same* adverse effects triggering the identification as EDs of those substances are already considered via the classification as substances toxic for reproduction. These Member States clearly argue that identification as EDs would mean *double-counting* the same effects with no added in a regulatory context.

The substances identified under the ED criteria defined in Options 1 to 4, under the current PPP and BP Regulations (Option A), may be approved subject to conditions if the foreseen derogations apply. However, in case a substance is not identified as an ED under any of these criteria, it still goes through a "standard" risk assessment, which includes assessment of human health (see Figure 1). A substance with endocrine disrupting properties, whether identified as an ED or not, would only be approved if it has no harmful or unacceptable effects on human health. As a consequence, even if Option 2, 3 and 4 identify a different number of EDs, it can be assumed that the approval procedure of the substance will act as a safety net and ensure that human health is protected to the same extent for any of these options. This assumption can be also applied to "false negatives", i.e. substances which are not identified as ED under Options 1 or 4 but are identified as ED under Option 2 or Option 3 Category 1. However, Option 1 fails to detect some modalities, e.g. thyroid modality. Although these "false negative" substances would be covered by the "standard" risk assessment under the PPP and BP Regulations, nevertheless Option 1 can be considered as not fit for purpose to detect ED because some modalities are not covered. In addition, Option 1 identifies “false positives”, i.e. substances with no endocrine mode of action. These substances would be removed from the market (unless derogations apply) although they are not EDs according to the WHO/IPCS definition. This might in turn have negative impacts on human health because of higher risks of occurrence of mycotoxins and transmissible diseases, while not identifying the correct EDs. Therefore, with respect to endocrine mediated diseases the options are considered to perform as follows: 2/3/4>1.

In addition, a sensitivity analysis which includes a variation of the performance of the options was performed. The MCA-scenario "aim: exposure zero" assessed the performance of the options based on a different assumption which only aims at minimizing exposure: the higher the number of active substances identified as EDs, the better the performance of the option for human health with respect to exposure (without consideration of any risk assessment). As a consequence, within this scenario, the options perform as 2/3 > 4 > 1 only based on exposure considerations.

Transmissible diseases can be passed from person to person or from a host/product to a person. This can occur by direct contact, by food or through a vector (for example mosquitos).

Disinfectants are extensively used in hospitals or other health care setting to prevent and control diseases. Disinfectants are also extensively used in the food industry to ensure the microbial safety of food products. Insecticides are used to control insects which transmit human diseases. In the screening of biocidal active substances one of the 44 included disinfectants (Iodine) and one of the 49 the included pest control substances (Cypermethrin) was identified as an ED. However, the results of the screening should be very cautiously interpreted as it is not possible to judge how representative the screening results are for biocides. For example, the screening did cover only 44 of 266 disinfectants. In addition, not only the number of substances but also which substances are important to consider, as they may target different disease agents. The results indicate that the different options may results in different numbers of disinfectants or insecticides identified as ED.

The case of iodine (used as disinfectant) is interesting. In the screening it is identified as ED under Options 2, Option 3 Category I and Option 4. Iodine is a physiologically essential element and it is required for the synthesis of the thyroid hormones. This means that both iodine deficiency as well as excess iodine can affect thyroid hormone levels. This substance was identified in the screening as an ED, since it can produce adverse effects via an endocrine mode of action. At the doses used as disinfectant, it would unlikely pose any risk to human health and the environment. However, if identification as an ED was confirmed in a formal assessment, it would be regulated as an ED under the BP Regulation.

Although the BP Regulation provides the possibility of applying derogations for the approval of an ED substance, it can be assumed that the number of disinfectants or substances available to control vectors[67] may decrease for professional users, even if derogations may be granted. Nonetheless several disinfectants remain available on the market, this may have a health impacts as there is a need for a wide spectrum of disinfectants (there is no single universal disinfectant which kills all pathogenic micro-organisms). Critical impacts may in particular occur if key substances would not be available and no appropriate alternatives could be found or developed. Based on the current information it cannot be excluded neither properly estimated whether non-approval of key biocidal substances for transmissible diseases will occur. Notwithstanding the high uncertainties it can be assumed that the impacts would be associated to the number of biocides that would be identified as ED. Therefore, it can be assumed that, with respect to transmissible diseases, an option would perform worse if it identifies a higher number of EDs, i.e. options perform as follows: 4>2/3>1.

Food safety of agricultural products or derived products may be at risk of **contamination by mycotoxins**. Mycotoxins are dangerous substances produced during storage or plant growth by fungi species (moulds). They are one of the most important categories of biologically produced natural toxins, including some which are EDs like zearalenone found on several foods and feeds in temperate regions worldwide.[68] To protect humans and animals from the dangerous effects of mycotoxins (e.g. liver cancer), the European Commission has set maximum levels in food and feed products.

PPP are used on certain crops in order to limit the growth of fungi and consequently the contamination by mycotoxins. Other methods to reduce the presence of mycotoxins are crop rotation (growing different crops on a field in different years) and using resistant plant varieties.

[67] A vector is an organism, often an invertebrate arthropod, that transmits diseases (it transmits a pathogen from reservoir to host).

[68] Zinedine, A. et al. 2007. Review on the toxicity, occurrence, metabolism, detoxification, regulations and intake of zearalenone: an oestrogenic mycotoxin. Food Chem Toxicolo 2007; 45(1):1-18. Retrieved from: http://www.ncbi.nlm.nih.gov/pubmed/17045381

The screening of PPP for endocrine disrupting properties resulted in a varying number of PPP identified under the four options (see Annex 5). In all the options PPP were identified belonging to the group of azoles (for example, cyproconazole, tebuconazole, tetraconazole, see Table 3 in Annex 5). This group of fungicides is considered to be important for mycotoxin control in the EU. Depending on the option, the group of azoles would be impacted between 5% and 35%. Option 4 identified both the lowest number of PPP as EDs and the lowest number of substances belonging to the group of azoles (see Figure 3 and Table 3 in Annex 5). An analysis of the identified substances under each option points out that substances in the same group of PPP remain available to manage fungi (see Annex 5, Table 2 analysing the outcome of screening for groups of PPP). However, it is unclear whether these alternatives are equally effective to control the fungi producing mycotoxins and whether the efficacy will be reduced in the short term because of the development of resistance (see Annex 13). So, it is not possible to quantify to which extent the loss of one or more PPP, including substances belonging to the group of azoles, would lead to higher levels of contamination of crops and consequently higher levels of mycotoxins in food and feed in the future as many factors influence the occurrence of mycotoxins. Notwithstanding the uncertainties it could be assumed that the likelihood of having an impact on health will be probably higher if an option results in less PPP active substances available on the market belonging to a group of PPP relevant for the control of fungi producing mycotoxins. This implies that Option 4 appears relatively the best option in relation to control mycotoxin contamination of food and feed, followed by Option 2 and Option 3, i.e. the options perform 4 > 2/3 > 1.

5.3.3. Environment (Annex 11)

In general terms, the use of chemicals may have environmental effects. In addition, human health might be affected via environmental exposure. Animal welfare (animal testing) is also considered in this chapter. It was a concern for several respondents to the public consultation who specifically called for the development and use of methods that do not rely on animal testing in order to produce safety data.

A recent study carried out for the European Commission[69], concluded that it was not possible to identify robust and reliable environmental impact indicators in relation to ecosystem services or species level effects. The indicators that could be developed for the environment were limited inter alia because of the lack of monitoring data.

For the purpose of this impact assessment, exposure via water (groundwater, drinking water and surface water) was considered, as well as the potential effects on vertebrate populations. In addition, animal welfare, in the context of animal testing required for regulatory purposes, was considered in line with Tool # 16 of the Better Regulation Guidelines.

Regarding the MCA-criterion **"*chemical* quality of groundwater, drinking water and surface water"**, the assessment was carried out under the assumption that any potential presence of active substance is to be avoided and that the chemical quality of the water is inversely proportional to the amount of any active substance potentially present in it. Under this assumption, it could be concluded that the higher the number of substances removed from the market or restricted, the higher the likelihood that the chemical status of the water improves. The options would therefore perform: 1>2/3>4. However, it should be noted that this approach does not take into account the fact that for groundwater, strict thresholds

[69] RPA et al. 2015. Study on the Calculation of the Benefits of Chemical Legislation on Human Health and the Environment, Final report for DG Environment, March 2016, Loddon, Norfolk, UK

already apply and that for surface water, levels of chemicals below certain thresholds would actually pose no risk to aquatic organisms.

In order to carry out a sensitivity analysis which includes a variation of the performance of the options, the MCA-scenario "aim: exposure zero" was developed. It assessed the performance of the options based on an assumption that aims at minimizing exposure: the higher the number of active substances identified as EDs, the better the performance of the option for the environment with respect to exposure (without consideration of any risk assessment). As a consequence, within this scenario, the options perform 1>2/3>4 only based on exposure considerations.

Decline in some **wildlife vertebrate populations** might be at least partially due to exposure to EDs in the environment. However, a number of other factors including overexploitation, loss of habitat and climate change are also likely to be contributing causes to this decline.

PPP and BP are the most "data rich" regulated product groups in the EU. A detailed list of data requirements has to be submitted by the applicant before any approval of the active substance or authorisation of a product containing the approved substances can be considered. These core data requirements include testing of several non-target species, cover several ecological compartments and, include assessment of reproductive effects. It can thus be assumed that effects on wildlife species, in terms of potential reproductive effects which may be relevant for population effects, are assessed. Tests which cover endocrine disrupting endpoints have been added recently to the data requirements. Moreover, evidence shows that most substances generally linked to ED effects have already been banned in the EU or have been approved subject to strict conditions in recent years, reflecting the regulatory system in place in the EU and its focus, inter alia, on protecting the environment. As a consequence, it can be assumed that wildlife vertebrate populations are equally protected by the standard risk assessment foreseen under the PPP and BP Regulations, irrespectively of how many substances are identified as ED under different options of the criteria. However, Option 1 fails to detect some modalities, e.g. thyroid modality. Although these "false negative" substances would be covered by the "standard" risk assessment under the PPP and BP Regulations, nevertheless Option 1 can be considered as not fit for purpose to detect ED because some modalities are not covered. The performance of options for wildlife vertebrate populations is therefore: 2/3/4 > 1.

In order to carry out a sensitivity analysis which includes a variation of the performance of the options, the MCA-scenario "aim: exposure zero" was developed. It assessed the performance of the options based on an assumption that aims at minimizing exposure: the higher the number of active substances identified as EDs, the better the performance of the option for the environment with respect to exposure (without consideration of any risk assessment). As a consequence, within this scenario, the options perform 2/3 > 4 > 1 only based on exposure considerations.

In terms of **animal welfare**, all options rank the same, irrespective of the number of substances they identify as ED. However, Option 3 with the inclusion of additional categories, might trigger additional animal testing by third parties which would want to verify if the chemicals, classified in Category II or III, are EDs or not. This would not be in line with the objectives of Directive 2010/63/EU on the protection of animals used for scientific purposes. The ranking of the options is therefore considered to be 1/2/4>3.

5.3.4. Sectorial competitiveness: EU agriculture (Annexes 12 and 13)

Agriculture plays a critical role in the EU, providing food security, high quality food and also generating jobs in the farming, food and related sectors. The use of PPP plays an important role in agricultural production, and the availability of sufficient tools to control pests and weeds is crucial to farmers. Farmers are usually agricultural holdings with less than 250 employees and can therefore qualify as SMEs.

In their answers to the public consultation, farmers generally expressed concerns about the yield losses that would result from the potential disappearance of key PPP, the development of resistance that might occur (if only a few similar types of PPP remain available) and expressed their preference for a more proportionate decision making concerning EDs that would include elements of risks (Option B, see Section 5.4).

The current legislative framework foresees a non-approval of active substances identified as EDs used in PPP, unless derogations apply. Thus, an impact on the number of PPP available to farmers is expected as a consequence of the non-approval of active substances identified as ED. This impact will also have consequences on the cultivation of crops for which some PPP may no longer be available, and the number of available alternatives to fight a given pest or disease. This latter aspect is important from an agricultural point of view, as recognised by on-going international activities focusing on this topic, carried out by the European and Mediterranean Plant Protection Organisation (EPPO)[70] or the Food and Agriculture Organisation of the United Nations (FAO)[71]. A reduction in the number of active substances with a different mode of action is expected to increase the risk of development of resistance in pests and diseases, since the exclusive reliance on a single active substance and the lack of diversity of available control measures are agronomic factors which increase the risk of resistance (EPPO, 2015).[72] Resistance may decrease the efficacy of a whole chemical group of PPP, leaving farmers with insufficient alternatives to tackle plant health problems.

Considering the three MCA-criteria chosen for assessing impacts on agriculture, it appears in the case studies carried out to assess the performance of the options that Option 4 would have the lowest impact. Option 1 and Option 2/3 Category I perform differently depending on the criterion chosen and, for PPP authorised and crops affected, the MS analysed. Intuitively, one would think that the higher the number of actives substances identified as ED, the higher the number of PPP authorisations and the number of crops that would be affected. Such an assumption would lead to Option 1 (the one identifying the highest number of active substances as ED) being the one performing the worst. However, the evidence available for the 8 MS which provided data did not confirm this in most of the cases. In almost all the 8 MS analysed, Option 1 is the second best performing option and has less impact in terms of PPP and crops affected than Options 2/3 Category I. Thus, as a result of the case studies the options perform 4>1>2/3.

The availability of alternatives and the risk of developing resistance was analysed based on the data available under Regulation (EC) No 1185/2009 concerning statistics on pesticides. In a first step, the chemical classes that would be affected by the potential non approval of the active substances identified as endocrine disruptors (EDs) under the different options were analysed in terms of percentage of active substances that would be affected per chemical class

[70] EPPO activities on resistance to plant protection products. Retrieved from: https://www.eppo.int/PPPRODUCTS/resistance/resistance.htm

[71] For instance FAO Guidelines on Prevention and Management of Pesticide Resistance. International Code of Conduct on the Distribution and Use of Pesticides. September 2012.

[72] EPPO 2015. PP 1/213 (4) Resistance risk analysis. Bulletin OEPP/EPPO Bulletin (2015) 45 (3), 371–387 ISSN 0250-8052. DOI: 10.1111/epp.12246.

and major group (e.g. herbicides, fungicides, and insecticides). It is assumed that the higher the percentage of chemical class affected, the lower the number of alternatives existing. Similar calculations were performed for the volumes of sales of these active substances. As a result of the analyses, Option 2/3 Category I is expected to have less impact than Option 1. Overall, the options perform this way: 4 > 2/3 >1.

5.3.5. Sectorial competitiveness: PPP, BP, and related industries (Annex 14)

Sectorial competitiveness is particularly important in the context of the current EU priorities: boosting jobs, growth and investment. This applies to the various sectors involved, e.g. producers of raw materials, formulators of PPP and BP, downstream users (e.g. farmers, food processors, the paint and coating industry, healthcare facilities like hospitals), related industries (application equipment), and consumers. Sectorial competitiveness has been assessed considering in particular the impact on research and innovation, the burden to SMEs and the functioning of the single market.

Before analysing the impacts it is important to refer to the general discussion about the impact of stricter rules on innovation. Many companies and industry organizations consider stricter rules as having a negative impact on innovation and competitiveness as it diverts personnel and resources away from R&D and production activities. On the other hand, it is argued that regulation can have a positive effect on innovation and growth: for example, requirements could promote innovation by encouraging the replacement of hazardous chemicals with more sustainable alternatives. Both views were expressed by respondents in the public consultation. In their answers to the public consultation, industry representatives generally expressed their preference for a decision making concerning EDs based on risk (Option B, see Section 5.4) as they believe that further elements of hazard characterisation (severity, (ir)reversibility, potency and lead toxicity) should be included in the criteria (potency is included in Option 4).

Competitiveness and innovation in companies in the supply chain is driven by a wide range of factors (energy prices, labour costs and productivity, infrastructure, taxation, regulatory environment etc.). It is stressed that setting criteria for EDs is just one issue that may affect the innovative capacity or competitiveness of EU companies. Information is lacking in order to compare the size of the impact of setting EDs in relation to those other factors impacting competitiveness and innovation. Also should be considered that in general, not linked to the setting of criteria for EDs, a decrease of the number of active substances and BP and PPP available on the market in the EU has taken or is still taking place.

The criteria for EDs may lead to additional costs and increase the time it takes to put PPP and BP on the market as more tests and data may be required to evaluate whether a chemical for which an endocrine mode of action is determined can be considered an ED. It is expected that setting the ED criteria would imply that some substances incorporated in PPP or BP will be non-approved or approved under more restrictive conditions. Taking into account the current drivers for innovation (energy prices, labour costs and productivity, infrastructure, taxation, regulatory environment etc.) and the market structure (for instance, multinationals focus their R&D on growth markets), this may not necessarily trigger substantial **innovation** for replacing these by alternative substances for use in PPP and BP or alternative techniques. For downstream users and formulators it is difficult to judge whether the proposals will lead to additional innovation because of the many factors involved. For example, many major industrial sectors are relying on the use of BP. This market is segmented and consists of highly diverse group of enterprises that may respond differently. It will also depend on the substance in question. For key substances in the supply chain probably quicker increased R&D will occur. It is important to note that replacing a chemical in an article or a mixture can

imply that companies need to change their technologies or processes. It can also imply to establish new relations with suppliers.

With respect to the functioning of the **single market**, the derogations foreseen in the PPP and BP Regulations are expected to create new complexity (specific conditions that would apply in each MS and the interpretation and the enforcement of those conditions). As a consequence, the availability of PPP and BP to downstream users (farmers, professional users, health care sector and food chain producers, industry, etc.) may differ between MS, creating an unequal playing field for downstream users.

SMEs play an important role both in the PPP and BP sector, as well as in downstream and related industries. In general it can be concluded that any increase in costs and demand in human resources would negatively affect the market position of SMEs because SMEs are less able than larger firms to accommodate such costs and additional demand in personal resources and expertise. Moreover, SMEs in general have less active substances in their portfolio than larger companies, therefore making them more vulnerable to the non-approval of substances identified as ED. This could lead to a reduction of SMEs, to even further concentration in the BP and PPP-sector and to less competition.

To sum up, the impacts on all aspects on sectorial competitiveness are related to the number of substances identified as ED. Therefore the options would perform this way: 4>2/3>1.

5.3.6. International trade (Annex 15)

Trade is essential to economic growth and job creation in the EU. Around two thirds of EU imports are raw materials, intermediary goods and components needed for companies' production processes. Imports on food, feed, and treated articles are the three commodity groups used as MCA-criteria for trade in this impact assessment. These groups cover many products imported to the EU and are essential for food security and important to a wide range of trading partners. While impacts on food and feed imports are mainly related to PPPs, impacts on treated articles are mainly related to BP.

Exporters to the EU have to comply with the food and feed safety standards of the EU. An active substance identified as an ED may lead to impacts on trade as the allowed Maximum Residue Levels (MRLs) of the substance in products imported in the EU would have to be lowered to the limit of determination (LOD) in accordance with point 3.6.5 of Annex II of Regulation (EC) No 1107/2009. In practice, this means that many of the active substances for which the MRLs are lowered cannot be used in the production of food or feed in third countries.

In the public consultation, third countries raised concern over the potentially significant trade implications of setting criteria to identify EDs based on hazard, and asked for a risk-based approach to be taken (Option B, see Section 5.4). They reminded the European Commission that any decision on EDs needs to respect the principles of the WTO (notably Article 5 of the SPS agreement). The topic of setting ED criteria by the different options has raised attention in the WTO Technical Barriers to Trade (TBT) and Sanitary and PhytoSanitary (SPS) Committees since 2013, where an increasing number of WTO Members are taking the floor to express concerns.

Examples of countries and crops that may be affected are wine from Chile, bananas from Latin America, soybeans imported for the production of feed, as well as citrus fruit from South Africa, to name just a few.

It is difficult to quantify precisely the potential impacts on trade. However, an analysis was carried out by using the screening results (see Section 5.2 and Annex 5) and then quantitatively assessing the number of MRLs that would be lowered to LOD for a selection of the most valuable imported crops under the four options. Data from the EU Pesticide Database on MRLs and Eurostat COMEXT trade databases were used to carry out the analysis. To determine how the options rank against each other it is assumed that the more MRLs lowered for a certain crop, the greater negative impact. Furthermore, the higher the value of imports expected to be affected, the worse an option performs. Therefore, the analysis of trade impacts can be considered as set of case studies which is based on the identity of substances identified under each option, and the MRLs which would be consequently lowered for a number of imported crops. For BPs, textiles have been selected as case study in order to illustrate potential impacts.

For the most **imported food crops** in terms of value, Option 4 consistently has the least impacts on trade. Looking beyond the best performing option, it is clear that all other options will have significant negative impacts on trade but it is highly dependent on the crop, e.g. citrus fruits will be more heavily impacted under Option 2/3 Category I, while wheat and barley is more impacted by Option 1. The overall performance is therefore 4 > 2 / 3 / 1.

The most impacted food crops in absolute terms would be tomatoes under Option 1 with 17 MRLs lowered. This represents 12 % of the total number of MRLs for tomatoes. Another crop highly impacted by Option 1 is barley with 15 MRLs lowered (13% of the MRLs set). Crops with high expected impacts under Option 2/3 Category I are wine and pears with 15 MRLs lowered. This represents 11% and 12% of the MRLs set, respectively.

The EU is highly dependent on **imports of feed**, and an increase in feed costs could weaken the competitiveness of the EU livestock sector. A trade disruption could amplify the current EU protein deficit for the livestock sector and the need for alternative sources. The analysis focused on four imported products mainly used for feed; soybeans, maize, rapeseed and cottonseed. Option 4 would have the least negative impacts, followed by Option 2/3 Cat I, with Option 1 having the most negative impacts on trade. The performance is 4 > 2 / 3 > 1

In the BP Regulation, an article containing a BP ("**treated article**") shall not be placed on the EU market unless all active substances that it incorporates are approved in the EU. This is expected to have consequences on imported products. Textiles are used as a case study to analyse the potential impacts because 80% of the textile articles used in the EU are imported, mainly from Asia. Textiles could be treated to prevent growth of mould during storage and transport or to create special functions, such as anti-odour in sportswear. One impact of non-approval of a biocidal active substance could be higher prices of treated articles as a limited number of companies would be able to supply treated articles of the same quality. Another possible impact may be the removal of certain treated articles from the EU market because of the lack of alternatives. The impact of the options are assumed to be correlated with the number of AS identified as ED, thus, Option 4 performs better than Option 2/3 Cat I which performs better than Option 1.The performance is 4 > 2 / 3 > 1.

5.4. Direct and indirect impacts in different policy areas expected under consideration of different implementation of the ED criteria and different approaches to regulatory decision making (Aspect II)

The regulatory consequences (i.e. implementation) of the criteria to identify EDs are already set under the PPP and BP Regulations and are driving the impacts of the criteria, as detailed in Section 5.3.

Because the regulatory consequences differ in terms of scope and implementation under the PPP and BP Regulations, adding complexity to the impact assessment, a second set of options was developed (Aspect II). This set of options under Aspect II considers in particular the implementation of the ED criteria into the PPP and BP Regulations and their different approaches to regulatory decision making. For methodological reasons the options developed cover the entire spectrum of potential policy choices and address the difference in the current derogations between the PPP and the BP Regulations. Two options were developed in addition to the current provisions in the BP and PPP Regulations (Option A): the possibility to modify an annex of the PPP Regulation under regulatory procedure with scrutiny (Option B), and the possibility to modify the PPP Regulation under ordinary legislative procedure (Option C). Obviously, Options B and C are not relevant for the BP Regulation.

At a preliminary stage of the impact assessment it was anticipated that Option C should be discarded, nevertheless it was maintained for the analysis of the impacts for methodological reasons (see Section 4.2.3 and Annexes 6 and 7). The impacts discussed in this section only refer to Option B compared to Option A, and are only applicable to the PPP Regulation as mentioned above (see also Section 4.2.2).

The impacts are expected to cover the same areas as those discussed under Section 5.3, which addresses the implementation of the criteria to identify EDs under the current regulatory framework. In the current section addressing the options under Aspect II, it was evaluated if potential changes to regulatory decision making would lead to the same, more or less impact for the different areas. Therefore, the comparison of Options B or C with the current regulatory framework (Option A) could only be done qualitatively, as robust evidence on the outcome of regulatory decision making takes usually 2 to 3 years for each substance evaluated, which is outside the timeframe for this impact assessment.

Option B, i.e. taking regulatory decisions based on risk assessment, is supported by some Member States and all third countries replying to the public consultation. Industry and farmers also indicated to support a regulatory decision making based on risk considerations.

5.4.1. Achievement of effectiveness and coherence (Annex 8)

The effectiveness of the options to fulfil the objectives of these Regulations was assessed considering legal certainty and operability, while coherence was assessed considering the coherence between the PPP and BP Regulations and the compliance with international obligations of the EU (WTO and Codex Alimentarius). It was assumed that clearer derogations based on current scientific knowledge (Option B) would increase legal certainty and lead to higher operability because of less controversial discussions during the regulatory decision making foreseen under the PPP Regulation. As a consequence, for both criteria the options are ranked B > A.

Coherence between the PPP and BP legislation on the implementation of the ED criteria is not achieved under Option A (no changes to the regulatory decision making), as the current derogations differ in these two pieces of legislation for approval of substances identified as EDs. An alignment of the PPP derogations to the BP derogations (Option B) would ensure more coherence between these two pieces of legislation in terms of consideration of risk, and would ensure that the criteria to identify EDs would be implemented consistently. This is particularly important as some chemical substances (currently 38) fall under both the PPP and BP legislation. Thus, the options would perform B > A.

Compliance with international obligations (e.g. those under the WTO-Sanitary and Phytosanitary (SPS) agreement and Codex Alimentarius) was also considered. The issue of

the assumed non-compliance of options to set ED criteria based on hazard (Option A for PPP) has been raised increasingly by WTO Members at every Technical Barriers to Trade (TBT) and SPS Committee meeting since October 2013. In the public consultation, six public authorities and six governments from non-EU countries gave their comments. One of the main issues they stressed was the potential impact on trade triggered by ED criteria based on hazard alone, whereas the SPS agreement lays down that measures have to be based on risk assessment. In Option A, the decision making is mainly based on hazard, while Option B considers the inclusion of further elements of risk assessment in the derogations of the PPP Regulation. Therefore, the options regarding decision making would perform B > A.

5.4.2. Human health (Annexes 9 and 10)

Protection of human health is a Treaty objective (Art 168.1) and a key objective for both the PPP and BP Regulations. In the context of this impact assessment, impacts and evidence regarding hormone related diseases were analysed, but also impacts on food safety (in particular contamination by mycotoxins). Potential impacts on transmissible diseases are not considered relevant in this section because they are only related to the availability of BP, which are not relevant as explained in Section 5.4.

In the public consultation, concerns regarding food safety and public health were raised by public authorities, professional associations, and NGOs. Some EU MS (Germany, UK) support risk assessment (Option B).

Potential impacts on human health are described in detail in Section 5.3.2. Summarising, the evidence related to **endocrine mediated diseases** and associated costs shows that under the existing EU regulatory framework with respect to PPP and BP robust conclusions cannot be drawn on the link between exposure to EDs and increased incidence of endocrine mediated diseases. Protection of human health was therefore analysed under consideration of the current regulatory framework of the PPP and BP Regulations. The EU authorisation system for PPP and BP is based on prior approval (a "positive list"). This implies that most of the adverse effects associated with endocrine disruption are covered by the "standard" risk assessment carried out for a substance even if this substance is not identified as an ED (for example, reproductive adverse effects). This is confirmed by the high number of PPP commonly associated with the endocrine mediated diseases which have already been banned for years in the EU (see Table 3 in Annex 9).This is also confirmed by the fact that Member States could not find an agreement on whether it would be appropriate under REACH Regulation to identify some substances as EDs for their adverse effect human health.

Recent available Scientific Opinions from EU Agencies and Scientific Committees regarding EDs argue in favour of the use of risk assessment decision making in order to maximise available information to protect human health compared to decision making that is based on hazard alone. Also recent WHO reports (2014[73], 2015[74]) recommend to identify risks from exposure to EDs. Considering that the current rules (i.e. the risk assessment step following identification or non-identification of a substance as an ED) ensure that authorised products do not have unacceptable effects on the health of humans, it can be assumed that Option A and B have the same impact with regard to potential adverse effects caused by exposure to EDs. As a consequence, with respect to endocrine mediated diseases, the options A and B perform the same: A/ B.

[73] WHO 2014. Identification of risks from exposure to EDCs at the country level.
[74] WHO. 2015. Identification of risks of EDCs: overview of existing practices and steps ahead. Report of a meeting in Bonn, Germany 7-8 July 2014

In order to carry out a sensitivity analysis which includes a variation of the performance of the options, the MCA-scenario "aim: exposure zero" was developed. It assessed the performance of the options based on a different assumption which only aims at minimizing exposure: the higher the number of active substances identified as EDs, the better the performance of the option for human health with respect to exposure (without consideration of any risk assessment). The assessment to evaluate the options under Aspect II was based on the number of correctly identified ED substances which will not be approved. As Option A would take from the market (non-approval) more substances identified as EDs than Options B, it is assumed that it would perform the best in a scenario only based on exposure considerations.

Food safety of agricultural products or derived products may be at risk of contamination by mycotoxins. Mycotoxins are one of the most important categories of biologically produced natural toxins, including some which are EDs like zearalenone found on several foods and feeds in temperate regions worldwide.[75] PPP are used to limit the growth of fungi and consequently the contamination by mycotoxins.

The screening of PPP for endocrine disrupting properties resulted in a varying number of PPP identified under the four options (see Section 5.3.2. and Annex 5). In all the options PPP were identified belonging to the group of azoles, a group of fungicides considered important for mycotoxin control in the EU. The group of azoles would be impacted between 5% and 35%. Notwithstanding the uncertainties it could be assumed that the likelihood of having an impact on health will be probably higher if an option results in less PPP active substances available on the market belonging to a group of PPP relevant for the control of fungi producing mycotoxins. This implies that Option B (which considers derogations based on risk) performs better than Option A (which considers derogations based mainly on hazard).

5.4.3. Environment (Annex 11)

In general terms, the use of chemicals may have environmental effects. In addition, human health might be affected via environmental exposure. Animal welfare (animal testing) is also considered in this chapter. It was a concern for several respondents to the public consultation who specifically called for the development and use of methods that do not rely on animal testing in order to produce safety data.

A recent study carried out for the European Commission[76], concluded that it was not possible to identify robust and reliable environmental impact indicators in relation to ecosystem services or species level effects. The indicators that could be developed for the environment were limited inter alia because of the lack of monitoring data. For the purpose of this impact assessment, exposure via water (groundwater, drinking water and surface water), the potential effects on vertebrate populations and animal welfare, in the context of animal testing required for regulatory purposes, was considered.

Potential impacts on **chemical quality of groundwater, drinking water and surface water** were evaluated assuming that any potential presence of active substance is to be avoided and that the chemical quality of the water is inversely proportional to the amount of any active substance potentially present in it. Under this assumption, it could be concluded that the higher the number of substances removed from the market or restricted, the higher the

[75] Zinedine, A. et al. 2007. Review on the toxicity, occurrence, metabolism, detoxification, regulations and intake of zearalenone: an oestrogenic mycotoxin. Food Chem Toxicolo 2007; 45(1):1-18. Retrieved from: http://www.ncbi.nlm.nih.gov/pubmed/17045381

[76] RPA et al. 2015. Study on the Calculation of the Benefits of Chemical Legislation on Human Health and the Environment, Final report for DG Environment, March 2016, Loddon, Norfolk, UK

likelihood that the chemical status of the water improves. However, this approach does not take into account the fact that for groundwater, strict thresholds already apply and that for surface water, levels of chemicals below certain thresholds would actually pose no risk to aquatic organisms. Options A and B are considered to rate equally assuming that both would lead to chemical qualities which fulfil the strict thresholds provided under the PPP Regulation and would not pose a risk to organisms.

In order to carry out a sensitivity analysis which includes a variation of the performance of the options, the MCA-scenario "aim: exposure zero" was developed. This scenario aims at minimizing exposure and considers that the higher the number of active substances identified as EDs, the better the performance of the option for the environment with respect to exposure (without consideration of any risk assessment). The assessment was based on the number of correctly identified ED substances which will not be approved. As Option A would take from the market (non-approval) more substances identified as EDs than Options B, it is assumed that it would perform the best based on exposure considerations only.

Decline in some **wildlife vertebrate populations** might be at least partially due to exposure to EDs in the environment. However, a number of other factors including overexploitation, loss of habitat and climate change are also likely to be contributing causes to this decline.

PPP and BP are the most "data rich" regulated product groups in the EU. A detailed list of data requirements has to be submitted by the applicant before any approval of the active substance or authorisation of a product containing the approved substances can be considered. These core data requirements include testing of several non-target species, cover several ecological compartments and, include assessment of reproductive effects. It can thus be assumed that effects on wildlife species, in terms of potential reproductive effects which may be relevant for population effects, are assessed. Tests which cover endocrine disrupting endpoints have been added recently to the data requirements. Moreover, evidence shows that most substances generally linked to ED effects have already been banned in the EU or have been approved subject to strict conditions in recent years, reflecting the regulatory system in place in the EU and its focus, inter alia, on protecting the environment. As a consequence, it can be assumed that wildlife vertebrate populations are equally protected by the standard risk assessment foreseen under the PPP and BP Regulations, irrespectively of how many substances are identified as ED under different options of the criteria. Recent available Scientific Opinions from EU Agencies and Scientific Committees regarding EDs support the use of risk assessment decision making in order to maximise available information compared to decision making that is based on hazard alone. Therefore, Options A and B have the same impact with regard to potential adverse effects caused by exposure to EDs.

In addition, under the MCA-scenario "aim: exposure zero" which assesses the performance of the options aiming at minimizing exposure, it is assumed that Option A would take from the market (non-approval) more substances identified as EDs than Options B. Thus, Option A performs the best with respect to exposure only.

In terms of **animal welfare**, no difference is expected in terms of the number of required animal tests for Options A and B because the data requirements under the PPP and BP Regulations are already set.

5.4.4. Sectorial competitiveness: EU agriculture (Annexes 12 and 13)

Agriculture plays a critical role in the EU, providing food security, high quality food and also generating jobs in the farming, food and related sectors. The use of PPP plays an important role in agricultural production, and the availability of sufficient tools to control pests and

weeds is crucial to farmers. Farmers are usually agricultural holdings with less than 250 employees and can therefore qualify as SMEs.

In their answers to the public consultation, farmers generally expressed concerns about the yield losses that would result from the potential disappearance of key PPP, the development of resistance that might occur (if only a few similar types of PPP remain available) and expressed their preference for a more proportionate decision making concerning EDs that would include elements of risks (Option B).

The current legislative framework foresees a non-approval of active substances identified as EDs used in PPP, unless derogations apply and MS agree with the derogations. Thus, an impact on the number of PPP available to farmers is expected as a consequence of the non-approval of active substances identified as ED. This impact will also have consequences on the cultivation of crops for which some PPP may no longer be available, and the number of available alternatives to fight a given pest or disease, as described more in detail in Section 5.3.4.

Considering the three MCA-criteria chosen for assessing impacts on agriculture and with respect to Aspect II, all options applied under the current legislative framework in the PPP sector (Option A) may lead to an impact on agriculture (see for more details Section 5.3.4). These impacts depend on the option chosen. Option B would allow decision making based on derogations which consider risk elements and would thus have less impact on agriculture than Option A. Thus, the options would perform this way for all MCA-criteria related to EU agriculture: B>A.

5.4.5. Sectorial competitiveness: PPP, BP, and related industries (Annex 14)

Sectorial competitiveness is particularly important in the context of the current EU priorities: boosting jobs, growth and investment. This applies to the various sectors involved, e.g. producers of raw materials, formulators of PPP and BP, downstream users (e.g. farmers, food processors, the paint and coating industry, healthcare facilities like hospitals), related industries (application equipment), and consumers. Sectorial competitiveness has been assessed considering in particular the impact on research and innovation, the burden to SMEs and the functioning of the single market. In their answers to the public consultation, industry representatives generally expressed their preference for a decision making concerning EDs based on risk (Option B).

Competitiveness and innovation in companies in the supply chain is driven by a wide range of factors (energy prices, labour costs and productivity, infrastructure, taxation, regulatory environment etc.) which are discussed more in detail in Section 5.3.5. In general, not linked exclusively to the setting of criteria for EDs, a decrease of the number of active substances and BP and PPP available on the market in the EU has taken or is still taking place.

The criteria for EDs may lead to additional costs and increase the time it takes to put PPP and BP on the market and would imply that some substances incorporated in PPP or BP will be non-approved or approved under more restrictive conditions. Taking into account the current drivers for innovation (energy prices, labour costs and productivity, infrastructure, taxation, regulatory environment etc.) and the market structure (for instance, multinationals focus their R&D on growth markets), this may not necessarily trigger substantial **innovation**. For downstream users and formulators it is difficult to judge whether the proposals will lead to additional innovation because of the many factors involved. Many major industrial sectors are relying on the use of BP. This market is segmented and consists of highly diverse group of enterprises that may respond differently. For key substances in the supply chain probably

quicker increased R&D will occur. It is important to note that replacing a chemical in an article or a mixture can imply that companies need to change their technologies or processes. It can also imply to establish new relations with suppliers.

With respect to the functioning of the **single market**, the derogations foreseen in the PPP and BP Regulations are expected to create new complexity (specific conditions that would apply in each MS and the interpretation and the enforcement of those conditions). As a consequence, the availability of PPP and BP to downstream users (farmers, professional users, health care sector and food chain producers, industry, etc.) may differ between MS, creating an unequal playing field for downstream users.

SMEs play an important role both in the PPP and BP sector, as well as in downstream and related industries. In general it can be concluded that any increase in costs and demand in human resources would negatively affect the market position of SMEs because SMEs are less able than larger firms to accommodate such costs and additional demand in personal resources and expertise. Moreover, SMEs in general have less active substances in their portfolio than larger companies, therefore making them more vulnerable to the non-approval of substances identified as ED. This could lead to a reduction of SMEs, to even further concentration in the BP and PPP-sector and to less competition.

To sum up, the impacts on all aspects on sectorial competitiveness are related to the number of substances identified as ED which is leading to the non-approval of substances unless derogations apply. Therefore, Option B which considered derogations based on risk elements, is expected to have less impacts than Option A (derogations based mainly on hazard),

5.4.6. International trade (Annex 15)

Trade is essential to economic growth and job creation in the EU. Around two thirds of EU imports are raw materials, intermediary goods and components needed for companies' production processes. Imports on food, feed, and treated articles are the three commodity groups used as MCA-criteria for trade in this impact assessment. These groups cover many products imported to the EU and are essential for food security and important to a wide range of trading partners. While impacts on food and feed imports are mainly related to PPPs, impacts on treated articles are mainly related to BP. Treated articles are not assessed because Option B is not applicable for the BP Regulation (see Section 5.4).

Exporters to the EU have to comply with the food and feed safety standards of the EU. An active substance identified as an ED may lead to impacts on trade as the allowed Maximum Residue Levels (MRLs) of the substance in products imported in the EU would have to be lowered to the limit of determination (LOD) in accordance with point 3.6.5 of Annex II of Regulation (EC) No 1107/2009. In practice, this means that many of the active substances for which the MRLs are lowered cannot be used in the production of food or feed in third countries.

In the public consultation, third countries raised concern over the potentially significant trade implications of setting criteria to identify EDs based on hazard, and asked for a risk-based approach to be taken (Option B). They reminded the European Commission that any decision on EDs needs to respect the principles of the WTO (notably Article 5 of the SPS agreement). The topic of setting ED criteria by the different options has raised attention in the WTO Technical Barriers to Trade (TBT) and Sanitary and PhytoSanitary (SPS) Committees since 2013, where an increasing number of WTO Members are taking the floor to express concerns.

Examples of countries and crops that may be affected are wine from Chile, bananas from Latin America, soybeans imported for the production of feed, as well as citrus fruit from South Africa, to name just a few.

It is difficult to quantify precisely the potential impacts on trade. An analysis was carried out by using the screening results and then quantitatively assessing the number of MRLs that would be lowered to LOD for a selection of the most valuable imported crops under the four options (see Section 5.3.6 for a more detailed description).

Depending on the option for the criteria chosen, food imports are expected to be affected in different extent under the current PPP Regulation (see Section 5.3.6). Also feed imports will be affected in a similar way than food. Since the EU is highly dependent on imports of feed, an increase in feed costs could weaken the competitiveness of the EU livestock sector. A trade disruption could amplify the current EU protein deficit for the livestock sector and the need for alternative sources. For both food and feed imports, Option B would take into account elements of risk in the foreseen derogations and would thus have less impact than Option A. The options are thus performing as B>A.

6. HOW DO THE OPTIONS COMPARE?

This section is not concluding on any preferred option for setting scientific criteria to identify endocrine disruptors, but aims compiling the information on the potential implications of these different options under the PPP and BP Regulations.

Under Section 6.1 Options 1 to 4 (Aspect I: setting scientific criteria to identify EDs) were compared via an MCA which included a sensitivity analysis under consideration of different weight scenarios (ranging from either equally distributed weight to giving different weights to different policy areas). The comparison of Options 1 to 4 implies that the current regulatory decision making applies (Option A of Aspect II). For more details please refer to Section 5.1 and Annex 6.

Under Section 6.2, the independent analysis carried out for the options of Aspect II (implementing ED criteria / approach to regulatory decision making) is presented, which is a MCA with the same criteria and scenarios for the sensitivity analysis as for the options under Aspect I. For reasons related to the MCA-methodology and in order to maintain consistency between the two MCAs, Option C was maintained for the analysis of the impacts although at a preliminary stage of the impact assessment it was discarded (see Section 4.2.3 and Annexes 6 and 7).

Under Section 6.3 a final summary discussion on the options is given.

6.1. Policy ranking of Options 1 to 4 for setting scientific criteria to identify EDs under the current regulatory decision making (Aspect I) - MCA results

Option 4 ranks consistently as the best in the MCA, followed by Option 2. Option 1 scores consistently the worst (see Annex 7).

Options 2 to 4 are all based on the WHO definition, which is currently recognised by most scientists. These options offer the same high level of protection to human health regarding EDs for PPP and BP under the current Regulations. Option 3 adds additional categories to the WHO definition, which seem to be difficult to implement in the current PPP and BP legislation and may add additional burden to administration and businesses, with uncertain benefits. Compared to the other options, Option 4 prioritises some substances based on some

elements of hazard characterisation and as a consequence minimises the socio-economic impacts on, for example, agriculture and trade.

Option 1 is the baseline (interim criteria) and not considered fit for purpose as it is based on classification and not based on science regarding EDs. Option 1 results in the incorrect identification of substances as EDs, i.e. it is likely to identify a certain number of false positives. Option 1 would also fail to identify some substances which would be identified as ED under Options 2 to 4 (false negatives), however the adverse effects caused by these substances are expected to be covered by the "standard" risk assessment under the PPP and BP Regulations. Further, the Commission has been mandated to replace Option 1 in the PPP and BP regulations, and it has been shown clearly in the public consultation that this option is not supported by any of the stakeholders.

The policy ranking remains the same throughout the sensitivity analysis, which considers different weights ("priorities") for MCA-criteria and different assessment of the performance of the options (see Annex 6 and 7 for more details).

6.2. Policy ranking of the options related to different implementation of the ED criteria and different approaches to regulatory decision making (Aspect II) – MCA results

Option A represents the current regulatory decision making in place, i.e. the PPP and BP Regulations .The additional options discussed under Aspect II are only applicable to the PPP Regulation (please refer to Section 4.2 for more details). For reasons related to the MCA-methodology and in order to maintain consistency between the two MCA, Option C was maintained for the analysis of the impacts although at a preliminary stage of the impact assessment it was anticipated that it should be discarded (see Section 4.2.3 and Annexes 6 and 7).

The MCA policy ranking clearly identifies Option C (alignment of PPP with BP regarding socio-economic considerations) as the best option, followed by Option B (adjustment of the PPP derogations in light of current scientific knowledge). However, as mentioned before, Option C was discarded at a preliminary stage and only kept for methodological reasons, which as a consequence implies that Option B is consistently ranked as the best policy option compared to A.

Option B corresponds to an adjustment of the derogations foreseen under the PPP Regulation in light of current scientific knowledge and would align the PPP with the BP Regulation with respect to the foreseen derogations. Recently, EU Panels of experts like those of the EFSA[25] and the Scientific Committee for Consumer Safety[26] stated that decisions regarding EDs should be based on risk assessments in order to make the best use of the available information with the aim of protecting human health. Amendments in light of scientific evidence of non-essential elements of the act are foreseen in Article 78 of the PPP Regulation and can be done with measures adopted in accordance with the regulatory procedure with scrutiny.

An alignment of the derogations between the PPP and BP legislation would be better received in the context of international obligations (such as WTO and Codex Alimentarius) which the EU must respect when exercising its powers. In accordance with these international obligations any draft legal proposals on setting criteria to identify EDs need to be notified to WTO under the prescribed procedures to allow third countries to comment.

The policy ranking remains the same throughout the sensitivity analysis, which considers different weights ("priorities") for MCA-criteria and different assessment of the performance of the options (see Annex 6 and 7 for more details).

6.3. Summary

This section is not concluding on any preferred option for setting scientific criteria to identify endocrine disruptors, but aims compiling the information on the potential implications of these different options under the PPP and BP Regulations.

The options considered in this impact assessment for setting scientific criteria to identify EDs under the current PPP and BP Regulations are Option 1 (interim criteria), Option 2 (WHO definition), Option 3 (WHO definition + categories), and Option 4 (WHO definition + potency). In addition, Option B (adjustment of the PPP derogations in light of current scientific knowledge, Aspect II) is considered.

However, given the scientific (fit for purpose) and legal implementation aspects discussed in the previous section, Option 1 is not considered to be a viable alternative at the present time. It is also the option which ranks worse in the MCA. Thus, the range of options which could be selected for the setting the criteria to identify EDs is reduced – with no particular ranking order – to 2, 3, and 4 under the current PPP and BP Regulations. In addition, Option B (adjustment of the PPP derogations in light of current scientific knowledge, Aspect II) could be considered in combination with any of these options.

All options offer the same high level of protection to human health regarding EDs under the current PPP and BP Regulations because they are all based on the WHO definition (currently recognised by most scientists) and because the Regulations are based on a prior approval system and on a highly comprehensive set of data requirements. Indeed, as explained earlier, under the PPP and BP Regulations, no active substance – whether its mode of action is known or not – would be authorised in the EU if an unacceptable risk of causing adverse effects to human health or the environment is identified.

On **Options 2 and 3** there is agreement amongst the various Member States, scientists and stakeholders that the two options would, from a scientific point of view, correctly identify EDs. Both options, implemented under the current PPP and BP Regulations, will have the highest impacts on sectorial competitiveness, agriculture, and trade.

The implementation of **Option 3** may be challenging in the context of the PPP and BP legislation, which are not designed for "categories", i.e. they do not foresee any regulatory consequences for the additional categories. Option 3 may lead to legal uncertainty, unpredictability and lack of operability because MS and stakeholders may interpret differently regulatory consequences for substances placed under Category II or III. It may be also misinterpreted that substances categorised as Category II or Category III are classified as such under Regulation (EC) No 1272/2008 (Classification, Labelling, Packaging), while this would not be the case. For these reasons, Option 3 may also reduce harmonisation in the single market. Further, Option 3 is expected to lead to additional animal testing, which would not be in line with the objectives of Directive 2010/63/EU on the protection of animals used for scientific purposes. Indeed, this option may encourage economic players to find substitutes for substances “suspected EDs” (Category II) and “endocrine active substances” (Category III) or may lead to the need of confirmation of the substance as an ED and thus, following further animal testing, to a transfer to a different Category. Finally, option 3 may lead to "black listing" of substances falling under Categories II and III and may then impose additional burden to economic sectors.

Option 4 is contested by some Member States, some stakeholders and some scientists because the less potent EDs would not be identified as EDs (although these substances are expected to fall under the "normal" risk assessment and would be regulated based on the assessment of the potential adverse effects). In light of a very recent scientific consensus

paper (see "BfR consensus statement" referred to in Sections 1.2.1 and 4.1.4), potency should not be considered in the identification of endocrine disruptors. This implies that Option 4, although fully taken into account in the assessment, should no longer be considered a feasible option for the scientific criteria to identify endocrine disruptors under the PPP and BP Regulations. Further, the way potency is considered may still be subject to a political decision (e.g. on whether or not to fix a cut-off and eventually at which level). Although Option 4 is expected to lead to fewer impacts compared to options 2 and 3 because it would allow a prioritisation of substances, if applied under the current legislative framework it would not be in line with international obligations because of the decision making based mainly on hazard under the PPP Regulation.

Option B, in combination with any of the other options, is based on science because the derogations would be based on a scientific consideration of risk applied on a case-by-case basis[77], while the hazard based approach in the PPP Regulation is maintained. This option would also be in line with international obligations. Based on the previous paragraphs, Option B in combination with Option 2 (WHO definition) is expected to reach the widest consensus amongst scientists, Member States and stakeholders because the criteria for identification of EDs are based on the WHO definition and the derogations under the PPP Regulation would be adjusted to current scientific knowledge (based on 2013-2015 Scientific Opinions by EU Agencies/Scientific Committees and the "BfR consensus statement" published in May 2016). Further, the adjustment of the derogations under the PPP Regulation would provide more clarity/operability and would allow implementing the criteria consistently across the PPPR and the BPR.

7. HOW WOULD IMPACTS BE MONITORED AND EVALUATED?

The legal acts which will be presented as a consequence of this impact assessment are secondary legislation under Regulation (EC) No 1107/2009 and Regulation (EU) No 528/2012. Monitoring and evaluation of secondary legislation shall not be carried out per se, but should be done in the context of the primary legislation. Regarding the implementation of the criteria, sufficient time should be allowed in order to evaluate the regulatory consequence.

In terms of effects on human health or the environment, it needs to be considered that either positive or negative effects related to EDs will only be visible on the medium or even long term. As a consequence, sufficient time would need to be allocated in order to be able to see any effects via monitoring.

The data used in this impact assessment for agriculture and trade, could be used also in future to evaluate impacts on these areas. In addition, other monitoring data are currently collected or will be collected over the coming years. All these data could be used to monitor and evaluate, for instance, exposure levels to EDs and impacts on different sectors. In particular, the data collected under the following pieces of legislation, EU initiatives and other sources could be considered in order to evaluate the impact of the legislation:

- Data concerning human health collected by EUROSTAT or through registries (e.g. Cancer registries, rare disease registries), for instance those described in Section 1.1. of Annex 9 of this impact assessment.

[77] Risk assessment is one of the pillars of the precautionary principle: Communication from the Commission on the precautionary principle /* COM/2000/0001 final */

- Data on workplace health and occupational health collected as follow up to Commission Recommendation 2003/670/EC[78] and activities related to this (e.g. Commission exercise to establish a list of occupational diseases for a pilot study, with the objective of overcoming certain discrepancies linked to the diversity of occupational diseases' systems across the EU; European opinion polls on occupational safety and health at work carried out by the European Agency for Safety and Health at Work[79]).
- To address the lack of information about exposure of citizen to chemicals, Horizon 2020 Societal Challenge 1 has published a call in the work programme 2016-2017 for a joint European programme on HBM[80] (the European Human Biomonitoring Initiative – EHBMI). The goals of the programme are to coordinate existing HBM initiatives in Europe, to establish a single European reference hub, and to build capacity and understanding of the nature and level of chemical exposure of EU citizens and the associated potential health risks. A strong EU-wide evidence base of comparable and validated exposure and health data for sound policy-making at EU and national level is expected to be established.
- Pesticides residues analysis data collected under the coordinated multiannual union control and national control programs to ensure compliance with the maximum residue levels in food, summarised in the annual EFSA scientific reports on pesticides residues in food.
- EU water basins are monitored under the Water Framework Directive for priority chemical substances and could be used to determine the presence of certain substances in the environment.
- In addition, the 'Information Platform for Chemical Monitoring' (IPCheM)[81] designed and implemented by the European Commission, offers a single access point to chemical monitoring data collections managed by and available to European Commission bodies, MS, international and national organisations and researchers.
- Data collected under Regulation (EC) 1185/2009 (pesticide statistics) by MS and transmitted to the European Commission (Eurostat) could be used to improve understanding of exposure to certain active substances.
- In future, data collected via the PPP Application Management System, currently developed by the European Commission and expected to be fully operational in the near future.
- Trade data, e.g. COMEXT databases (Eurostat).
- Data from the audits carried out by the European Commission (DG SANTE) in the MS for the purpose of verifying the implementation and enforcement of the rules on pesticides, including emergency authorisations, marketing and use, formulation analysis and sustainable uses.

[78] Commission Recommendation 2003/670/EC of 19 September 2003 concerning the European schedule of occupational diseases, OJ L 238, 25.9.2003, p.28

[79] Information about the European opinion polls on safety and health at work can be found on the EU-OSHA website. Retrieved from: https://osha.europa.eu/en/surveys-and-statistics-osh/european-opinion-polls-safety-and-health-work

[80] Horizon 2020 Societal Challenge 1 call in the work programme 2016-2017 for a joint European programme on HBM (the European Human Biomonitoring Initiative – EHBMI).

[81] European Commission. JRC. Information Platform for Chemical Monitoring Data (IPCheM). Retrieved from: https://ipchem.jrc.ec.europa.eu/RDSIdiscovery/ipchem/index.html

- Feedback received from stakeholders and MS authorities on the implementation of Regulation (EC) No 1107/2009 and Regulation (EC) No 396/2005.

In case the data collected through the above sources shows that further data might be needed to determine the impact of the initiative, the European Commission might decide to carry out an impact check or a specific evaluation to check the long term impacts of the criteria in the PPP and BP regulatory framework. However, it is still premature to affirm whether this specific assessment on the criteria will be needed as the necessity would derive from the strength and completeness of the data collected.

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PART 2/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annex 1 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

{COM(2016) 350 final}
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ANNEX 1: PROCEDURAL INFORMATION

Contents

1. ORGANISATION AND TIMING

The European Commission decided in 2013 to perform an impact assessment with DG ENV and DG SANCO (now DG SANTE, Health and Food Safety) co-responsible for it. The corresponding Roadmap was published in June 2014.

Since November 2014, DG SANTE is the lead DG in the preparation of this initiative as an immediate consequence of the internal re-organisation of the European Commission and as the responsibility for the BP Regulation was transferred from DG ENV to DG SANTE.

Other DGs contributed to the preparation of this impact assessment via an IA Steering Group set up in 2013. The IA Steering Group (IASG) comprised members of DGs AGRI, CLIMA, COMP, CNECT, ENV, EMPL, GROW, JRC, LS, MARE, RTD, TRADE, SANTE and SG. The IASG discussed all aspects related to the preparation of the impact assessment. A total of 11 IASG meetings took place on the following dates:

IASG MEETINGS	**ISSUES DISCUSSED**
20 January 2014	▪ Scope of the roadmap ▪ Scope and details on the IA
22 February 2014	▪ Roadmap
23 July 2014	▪ Public consultation draft questionnaire
12 September 2014	▪ Public consultation draft questionnaire
10 December 2014	▪ Transfer of biocides file to DG SANTE ▪ Update on court case T- 521/14 ▪ Update on planned IA studies
19 March 2015	▪ Update on on-going and planned IA studies ▪ Presentation of the draft JRC methodology (1st study) ▪ Communication events foreseen (round-tables, conference)
21 May 2015	▪ Update on communication events ▪ Update on the progress of the public consultation report ▪ Update on the on-going and planned IA studies
17 July 2015	▪ Endorsement of the public consultation report ▪ Update on the on-going and planned IA studies
19 January 2016	▪ Update on the screening of substances (1st study) ▪ 2nd phase of the IA (presentation of the MCA-methodology) ▪ Timeline and general planning ▪ Follow up to the ruling of the General Court
1 February 2016	▪ Update on the general planning ▪ Discussion on the MCA-criteria
4 April 2016	▪ IA report

The initiatives under the PPP and BP Regulations are included in Agenda Planning under the references 2015/SANTE/001 (Implementing Regulation on Plant Protection Products to specify criteria to identify endocrine disruptors) and 2016/SANTE/045 (Delegated act biocides endocrine-disruptors), respectively. Moreover, in the European Commission Work

Programme for 2016, the European Commission has committed to "*conclude the complex preparatory work already under way to protect Europeans from the dangers of endocrine disruptors and follow up on it*."[1]

In July 2014 Sweden sued the Commission for failure to act (case T-521/14) regarding setting new scientific criteria for defining EDs in the Biocidal Products Regulation (EU) No 528/2012 by end of 2013. The European Parliament, the Council and individual Member States such as France, the Netherlands, Finland and Denmark intervened in favour of Sweden during the case. In its judgement of 16 December 2015, the EU General Court ruled that the European Commission breached EU law by failing to set criteria to identify EDs. The Court stated that according to the Biocides Regulation, the Commission had a clear, precise and unconditional obligation to adopt delegated acts as regards the criteria by December 2013.

2. EXTERNAL EXPERTISE AND SUPPORTIVE EVIDENCE

This impact assessment builds on preparatory work – listed below - which focused on EDs and which was carried out over the last few years by the European Commission or mandated by the European Commission to EU agencies or external contractors via public procurement rules.

Additional sector-specific data sources were used for the assessment of the impacts in some sectors, and are detailed in the corresponding Annexes.

2.1. Scientific Committees and Expert Groups chaired by the European Commission

In 2010, two expert groups were established with the aim of exchanging information on various scientific and policy aspects related to EDs. Both groups included representatives of industry associations, non-governmental organisations, European Commission Services, European Agencies and Member States.

The "***EDs Expert Advisory Group*", chaired by the JRC**, was set up to provide advice on scientific criteria for the identification of endocrine disrupting substances. The outcome is summarised in the two reports summarised below.

- **JRC Expert Advisory Group Report "Key scientific issues relevant to the identification and characterisation of endocrine disrupting substances" (2013)** [2]**.** The aim of the report is to capture the expert opinions expressed in the Expert Group. It acknowledges that consensus was not required and different views were presented. For instance, the report summarises that agreement was not reached on whether elements of hazard characterisation (potency, severity, lead toxicity, irreversibility) should be considered or not when identifying EDs of real concern. Those who

[1] Annex II: REFIT Initiatives. Annex to Commission Work Programme 2016; No time for business as usual. Retrieved from: http://ec.europa.eu/atwork/pdf/cwp_2016_annex_ii_en.pdf

[2] JRC Scientific and policy reports. Key scientific issues relevant to the identification and characterisation of endocrine disrupting substances. Report of the Endocrine Disrupters Expert Advisory Group. Retrieved from: http://www.fhi.no/dokumenter/623e53f70d.pdf

disagreed with such consideration were of the opinion that these elements can only be considered in the context of risk assessment. Others believed that, when decision making is based on hazard assessment, these elements should be considered altogether at the step of hazard identification/assessment to prioritise substances of higher concern. As regards availability of test methods, the Working Group agreed that existing standardised assays are mainly available only for the four modalities: estrogenic, androgenic, thyroid and steroidogenic (EATS). The Working Group also agreed that overall tests were lacking for birds and invertebrates.

- **JRC Expert Advisory Group Report "Thresholds for EDs and Related Uncertainties" (2013)** [3]**.** The Expert Group was asked to gather views on the likelihood of existence of thresholds for a biological adverse response of an organism to an ED. The question was posed in relation to a review of the REACH Regulation concerning the treatment of EDs under authorisation, but it was also considered of general relevance to the evaluation of an ED. Consensus was welcome but not necessary. The experts could not reach a consensus on whether a threshold or non-threshold approach was to follow in the evaluation of EDs. There were both points of agreement and disagreements.

  Experts agreed that lack of consensus exists regarding the evidence for low-dose effects and on occurrence and relevance of non-monotonic dose-response curves. Most experts agreed that thresholds of adversity are likely to exist for EDs but may be very low for certain EDs and during foetal development. Several experts also agreed that, although thresholds may exist, they might be difficult to measure with the current available test methods. Some experts considered that, even during foetal development, a threshold for adversity must exist and can be estimated with appropriate testing. Other experts considered that uncertainties in estimating thresholds would be higher for EDs than for other non-genotoxic toxicants.

  Some experts supported a "non-threshold approach" because: 1) endocrine related endpoints are missing in current test guidelines; 2) using additional dose groups in animal testing may help but it is hindered by animal welfare considerations; 3) potential additional effects of mixtures will increase uncertainty in estimating thresholds.

  Other experts considered a "threshold approach" appropriate and justified because: 1) test guidelines can be updated with relative sensitive endocrine-related endpoints; 2) appropriate dose spacing in animal testing can increase confidence in threshold estimates; 3) case-by-case assessment is the most appropriate approach, as thresholds can be estimated when adverse effects and mode of action are identified.

The "***Ad hoc working group of Commission Services, EU Agencies and Member States", chaired by DG ENV***, focussed on policy issues. In February 2013, a first draft for criteria was proposed by DG ENV to the Ad-Hoc Working Group. This draft working document did

[3] JRC Scientific and policy reports. Thresholds for Endocrine Disrupters and related uncertainties. Report of the Endocrine Disrupters Expert Advisory Group. Retrieved from: http://publications.jrc.ec.europa.eu/repository/bitstream/JRC83204/lb-na-26-068-en-n.pdf

not reach consensus among Commission Services, Member States and stakeholders and a formal Inter Service Consultation was not started.

Further, the **Scientific Committee on Consumer Safety (SCCS) issued a "Memorandum on EDs"** in 2014 [4]. The Memorandum supports the EFSA Opinion on use of risk assessment to assess EDs for decision making. The SCCS adds that "*due to the ban on animal testing for cosmetic ingredients effective since 2013, it will be extremely difficult in the future to differentiate between a potential ED and an ED, if the substance is registered solely for use in cosmetics products. The replacement of animal test methods by alternative methods in relation to complex toxicological endpoints (such as endocrine disruption) remains scientifically difficult, despite the additional efforts launched at various levels. With regard to substances with endocrine activity (potential EDs), the assessment of their impact to human health without the possibility to use animal data remains a challenge*."

2.2. European Commission mandates to agencies

In August 2012, the European Commission mandated the European Food Safety Authority (EFSA) to issue a **"*Scientific Opinion on the Hazard Assessment of EDs*"**, which was published on March 2013[5].

The EFSA opinion supports the WHO/IPCS definition for EDs and a case-by-case risk assessment approach to assess EDs for decision making. EFSA states that "*to inform on risk and level of concern for the purpose of risk management decisions risk assessment (taking into account hazard and exposure data/predictions) makes best use of available information. EDs can therefore be treated like most other substances of concern for human health and the environment, i.e. be subject to risk assessment and not only to hazard assessment*".

Further, EFSA clarified that for mixtures, critical windows of susceptibility and non-monotonic dose-response curves were general issues applicable to all chemicals (and not specific to EDs). The EFSA Opinion also concluded that "*a reasonably complete suite of standardised assays for testing the effects of EDs is (or will soon be) available for the estrogenic, androgenic, thyroid and steroidogenic (EATS) modalities in mammals and fish, with fewer tests for birds and amphibians".* There are no standardised mechanistic assays for any modalities in invertebrates. Although some apical tests[6] are available for invertebrates, none of these apical tests is able to provide a firm diagnosis of a specific endocrine activity linked to a given adverse effect.

In 2016 the European Commission requested the European Centre for Disease Prevention and Control (ECDC) to **provide information of certain diseases** for public health and the

[4] Scientific Committee on Consumer Safety (SCCS) Memorandum on Endocrine Disruptors. Retrieved from: http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_009.pdf

[5] EFSA Scientific Committee; Scientific Opinion on the hazard assessment of endocrine disruptors: scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing effects mediated by these substances on human health and the environment. EFSA Journal 2013;11(3):3132. [84 pp.] doi: 10.2903/j.efsa.2013.3132.

[6] Apical test: A test or assay aimed at detecting/measuring apical endpoints: generally in vivo testing describing a response by the organism as a whole (e.g. generally death, reproductive failure, or developmental dysfunction). For apical endpoints see the glossary.

importance of biocidal products to prevent them. The request focused on 1) infectious diseases in healthcare facilities (in particular hospitals), 2) infectious diseases (e.g. respiratory tract viruses and norovirus outbreaks) in community settings (e.g. schools, day care centers and childcare facilities), and 3) mosquito-borne diseases (West Nile Fever, Dengue, Chikungunya and Malaria). The request concerns only the situation of health in the Union. The provided information served as basis for Annex 10 (human health, transmissible diseases and food safety.

2.3. European Commission public procurement projects

The "State of the Art Assessment of EDs" Report (Kortenkamp, 2011)[7]

In 2009, the project "State of the Art Assessment of EDs" was commissioned through public procurement by the European Commission.

The report summarises advances in the state of the science from 2002 to 2011 and maps ways of addressing EDs in important pieces of EU chemicals legislation (e.g. PPP Regulation, BP Regulation, REACH). It warned that the data required in EU chemicals legislation did not capture the range of endocrine disrupting effects that can be measured with internationally agreed and validated test methods. However, the PPP data requirements have been updated since the publication of the report, including updated test guidelines which also consider EDs (Regulations 283/2013 and 284/2013 on data requirements for PPP active substances and PPP formulations and the respective Communications 2013/C 95/01 and 2013/C 95/02 listing relevant test methods and guidance documents)[8].

Overall the report considers critical windows of susceptibility a key issue for EDs, which would *justify consideration of EDs as substances of concern equivalent to carcinogens, mutagens, reproductive toxicants and PBT* (persistent, bioaccumulative and toxic) *chemicals*. However, as mentioned above the EFSA Opinion[5] clarified that mixtures, critical windows of susceptibility and non-monotonic dose-response curves are general issues applicable to all chemicals and not specific to EDs.

The report considers that EDs should be identified according to the 2002 WHO-IPCS definition[9] and using a weight of evidence approach which considers all the elements of hazard characterisation together, i.e. potency together with other factors such as severity, lead toxicity, specificity of effect and irreversibility. Rigid potency-based cut-off values as decisive decision criteria are not recommended.

[7] Kortenkamp, Martin, Faust, Evans, McKinlay, Orton, Rosivatz. 2011. State of the art assessment of endocrine disrupters. Final Report, Project Contract Number 070307/2009/550687/SER/D3. Retrieved from: http://ec.europa.eu/environment/chemicals/endocrine/pdf/sota_edc_final_report.pdf

[8] European Commission. Legislation on Plant Protection Products (PPP). Retrieved from: http://ec.europa.eu/food/plant/pesticides/legislation/index_en.htm

[9] WHO/IPCS. 2002. Definition of an Endocrine Disruptor: *an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations.*

Screening of chemicals to evaluate if they would be identified as EDs under each of the proposed options (on-going, results for PPP and BP available, see Annexes 3 to 5)

In order to provide robust evidence on the potential impacts, approximately 600 chemicals are being screened by an external independent contractor in order to evaluate if they would be identified as ED under each of the options identified in the Roadmap. The screening covers chemicals falling under the PPP, BP, REACH, Cosmetics or WFD in this sequential order. The rationale for selection of the chemicals has been published and it is available in Annex 4. The study is still on-going, but all the evidence for PPP and BP is already available and has been used in this impact assessment.

The screening is based on available evidence (desk work) and is being carried out by a contractor selected following public procurement rules using the Framework Contract (FWC) SANCO/2012/02/011. The work started in May 2015 and presented final results for PPP active substances in January 2016 and for BP active substances in February 2016. Remaining results are expected by the end of April 2016 for a subsample of chemicals falling under the legislation for REACH, cosmetics and the WFD.

As a basis for this exercise, the Joint Research Centre of the European Commission (JRC) developed a screening methodology, which is summarised in Annex 3. The JRC also monitored the progress of the screening in cooperation with DG SANTE. The European Chemicals Agency (ECHA) and the EFSA were consulted in the elaboration of the methodology.

The final report of the study is planned to be published together with this impact assessment report. The results cannot however be used for regulatory purposes as for this a more in depth assessment would be required following the respective EU legislations.

3. CONSULTATION OF THE REGULATORY SCRUTINY BOARD

A draft impact assessment report was submitted to the Regulatory Scrutiny Board (RSB) on 13 April 2016. The meeting with the RSB took place on 12 May 2016. A negative opinion was issued by the RSB on the ground that there were several shortcomings in the report, which would limit its contribution to an informed decision making.

Based on the revised report submitted the 3 June 2016 the RSB issued a positive option with recommendations to be integrated in the report. These recommendations and how they have been addressed in the report are summarised below.

The RSB asked to further clarify in the report that (i) the criteria for the identification of EDs should be specified only on the basis of the relevant scientific evidence and irrespective of the economic and social impacts and that (ii) the proposed analysis of impacts is provided only with a view to informing about the implications of the different options for the specification of EDs in a given regulatory context and not to influencing the selection of the preferred option for the criteria to identify EDs. As a response to this recommendation, clarifications have been added to the impact assessment report on sections 1.1, 4, 6 and 6.3, as well as to the Annexes 6 to 15 to clarify that the impact assessment is not concluding on any preferred

option for setting scientific criteria to identify endocrine disruptors, but aims at providing additional information to decision makers.

The RSB recommends discarding Option 4 from the impact assessment in view of the emerging scientific consensus according to which potency is not relevant for the identification of a substance as endocrine disruptor. The emerging scientific consensus refers to the consensus paper signed by scientists as a consequence of the meeting carried out the 11 and 12 of April 2016. This consensus paper has been referenced throughout the report, including a citation of its most relevant parts and a particular consideration on the final discussion of the options to set scientific criteria to identify EDs. However, it has to be considered that the impact assessment report was submitted on 13 April 2016 and that the consensus paper was made available via the BfR website on the 4 May 2016 but has not yet been published in a scientific peer reviewed journal. Discarding retroactively an option of the impact assessment, which is the preferred option for some stakeholders including some Member States, on the basis of a scientific publication which has not yet been published, does not seem appropriate at this stage. However, in particular in Sections 1.2.1, 4.1.2, 4.1.4, and 6.3, clear reference to the emerging scientific consensus has been introduced and strengthened.

The RSB recommends clarifying the potential regulatory changes in the derogations under the PPP Regulation foreseen under Option B. In response to this, Figure 2 has been added to Section 4.2.2, as well as cross references to Section 1.5 (main report) and Annex 8, where the derogations under the PPP and BP Regulations are explained in detail. These amendments quote the corresponding parts of the regulations and explain in particular the different derogation approach between the BP Regulation (substances shall not be approved unless the risk from exposure is negligible) and the PPP Regulation (substances shall not be approved unless the exposure is negligible).

The RSB recommends clarifying further the methodology used for comparing the options, in particular Options A and B. Additional clarifications were added to Sections 5.1.2, 5.1.4, 5.4. The two-step procedure for assessing the impacts (screening study + Multi Criteria Analysis (MCA)) was better explained, as well as why the MCA methodology mentioned in the Better Regulation Guidelines Toolbox was chosen to evaluate the impacts. It was also further clarified in Section 5.1.3 how the MCA-criteria were developed: considering Tools #8 and #16 of the Better Regulation Toolbox, the availability of evidence, responses received via the public consultation (see Annex 2), and discussions between the General Directorates involved in the Impact Assessment Steering Group. An overview table with the evidence available for each MCA-criterion – in addition to the screening study results which played an important role in the assessment - was added (Table 2 in Section 5.1.4). It was also emphasised that the MCA was carried out sequentially in 2 steps: one MCA focusing on the impacts expected when implementing the criteria to identify EDs (Options 1 to 4) under the current regulatory framework (Option A), and a 2nd MCA where it was assessed whether these expected impacts would remain the same or not under consideration of different regulatory implementations (Options A to C; Option C was discarded but kept for methodological reasons). For this 2nd MCA, assumptions played a more prominent role due to the fact that the evaluation could only be done qualitatively in the context of the impact assessment. In addition, Section 6, including its subsections 6.1, 6.2 and 6.3, was adapted and details of the MCA only

mentioned in the corresponding Annexes (Annexes 6 and 7). Finally, a clarification was added to each of the Annexes 6 to 15, giving an overview of the application of the MCA methodology and, where applicable, its link with the assessment of the impacts (i.e. "performance" of the options).

A clarification regarding the selection of supporting evidence mentioned in Section 1.2.1. was added, as recommended by the RSB. The relevant WHO reports, including the WHO 2012 report, were/are mentioned at the very beginning of the impact assessment report (2nd paragraph of section 1). An additional section listing the cited literature has been added to the main report, and a summary of the literature cited in the main report and the Annexes has been added to Annex 16.

Editorial comments were fully taken over.

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PART 3/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection product regulation and biocidal products regulation

Annex 2 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

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Annex 2

Stakeholder consultation

Contents

Besides involvement of stakeholders via the Expert Groups chaired by the European Commission between 2010 and 2013 (see Annex 1), a public consultation and a series of targeted events were carried out in order to involve stakeholders.

What is clear from these consultations is that diverging views and interests exist between NGOs, third countries, farmers, and industry, adding to the scientific and regulatory complexity addressed in this impact assessment.

The events and public consultation are summarised briefly below.

1. DIALOGUE WITH STAKEHOLDERS VIA TARGETED EVENTS

In addition to the minimum standards and in order to involve interested parties, the following events were organised during 2015. The aim was to allow the European Commission to listen to the diverging views of the different stakeholders in preparation of the assessment of impacts.

- A **conference** "EU Conference on EDs: Current challenges in Science and Policy" was carried out in Brussels on 11 and 12 of June 2012. The conference attracted more than 300 participants including policy makers and experts from EU Member States and outside the EU, scientists, academics, industry groups, trade organisations and NGOs.

- **Three roundtables** were organised in 2015: on 25 March with stakeholders, on 24 April with Member States and on 12 May with Members of the European Parliament (MEPs). The aim was to have a targeted dialogue regarding the impact assessment with these parties.

- A **conference** "EDs: criteria for identification and related impacts" was held on 1 June 2015 with the presence of around 300 participants (MEPs, Member States' representatives, advisors to political parties, third countries' representatives, NGOs, industry, trade associations, consumer associations and journalists). At this conference, as well as being informed about the impact assessment process and objectives, key stakeholders were invited to present their respective views (industry, NGOs, third countries, and scientists with divergent views).

- A **technical meeting** took place on 6 November 2015 in Brussels at which the JRC methodology for evidence screening of chemicals developed in the context of the Impact Assessment on criteria to identify EDs was presented. Approximately 140 participants attended including MEPs, representatives from Member States and countries from outside the EU and stakeholders.

For the events carried out since 2015, the respective minutes, video-recordings and presentations are available on the dedicated webpages for EDs.[1]

[1] European Commission. Endocrine Disruptors website. Stakeholders' dialogue on endocrine disruptors. Retrieved from: http://ec.europa.eu/health/endocrine_disruptors/stakeholders_dialogue/index_en.htm

2. PUBLIC CONSULTATION

A **public consultation**[2] on defining criteria for identifying EDs in the context of the implementation of the PPP Regulation and the BP Regulation took place from 26 September 2014 to 16 January 2015 via an on-line consultation questionnaire (published on the European Commission public consultation page Your Voice in Europe, with a link from the dedicated webpage for EDs). The usual consultation period (12 weeks) was extended to provide stakeholders with sufficient time for comments. Responses were accepted in any official EU language, as well as via e-mail. The report of this public consultation was published on 24 July 2015 on the ED dedicated website.

The objective of this consultation was to gather data (e.g. methodologies used to select endocrine disrupting substances or the socioeconomic impact of identified EDs) and not the views of stakeholders. As a result, none of the questions asked for the opinion of respondents. This objective was reached as many respondents did provide information consisting of scientific articles, studies, reports, views and legal opinions.

Participants were invited to read the roadmap for background information before answering the questionnaire. This on-line consultation was open to all interested parties. In order to ensure all relevant stakeholders were informed the European Commission published a press-release at the launch of the public consultation.[3] The public consultation generated over 27 000 responses which illustrates the significant public interest in this issue and also indicates that all relevant stakeholders had an opportunity to contribute. The submissions received online can be found on DG SANTE's website.[4] Participation in the consultation was acknowledged.

Respondents came from various parts of society and included doctors, farmers, non-governmental organisations, chemical, electronic, food and medical devices industry, water companies and scientists) showing the diversity of use of these chemicals. Individual responses (as opposed to responses of behalf of organisations) accounted for more than 90% of the responses received. Of these individual responses, 88% came from seven Member States (Austria, Denmark, France, Germany, Spain, Sweden and the United Kingdom). 863 responses were made on behalf of an organisation and 64% of these came from one Member State (United Kingdom). Almost 26% of the responses on behalf of an organisation came from an industry or trade organisations and 5% from consumer/non-governmental organisations. Only one health institution and one hospital responded. Three EU-governments

[2] The Commission's minimum standards have all been met: the usual consultation period (12 weeks) was extended to provide stakeholders with sufficient time for comments. Submissions were accepted in any official EU language. Responses could be transmitted through the online questionnaire, as well as via e-mail.

[3] European Commission press release. Commission consults the public on criteria to identify Endocrine Disruptors. Retrieved from: http://europa.eu/rapid/press-release_IP-14-1057_en.htm

[4] Public Consultation on defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection product regulation and the biocidal products regulation. Retrieved from: http://ec.europa.eu/dgs/health_food-safety/dgs_consultations/food/consultation_20150116_endocrine-disruptors_en.htm#CD and the database for received contributions is available at: https://ec.europa.eu/eusurvey/publication/ED-consultation

as well as 18 national authorities sent comments. Six public authorities and six governments from non-EU countries gave their comments.

The opinions of respondents varied significantly on the options for criteria for determination of endocrine disrupting properties (Options 1, 2, 3, or 4) and for approaches to regulatory decision making (Options A, B or C). The public consultation report provides an overview on the submitted arguments by respondents in favour and against the options as included in the roadmap. In general, respondents expressed diverging views on how to define criteria and how EDs should be regulated. Overall, responses suggested that there is a need for the EU to establish definitive criteria for EDs. Option 1 (no policy change, the interim criteria set in the PPP and BP Regulations continue to apply) was therefore not supported by the consultation.

Many respondents raised issues in relation to food safety, the threat that endocrine disrupting substances might pose to human health and/or the environment and the impact of the different options proposed in the roadmap on agriculture, industry, health and environment. In particular farmers and agri-business highlighted the potential high implications of setting criteria to identify EDs on agriculture. Authorities from non-EU countries stressed the potential impact on trade and noted that any decision on EDs must respect the principles of the World Trade Organisation. A risk-based approach for regulating EDs was proposed by many respondents who identified themselves as farmers, private companies, industrial or trade organisations, or authorities in non-EU countries. Many respondents supported the use of the WHO/IPC 2002 definition as a starting point for defining an ED.

The public consultation provided an overview of the type and size of impacts that may occur if a chemical would be identified as an ED, the methodologies that may be used to obtain this type of information and also data and references to studies and articles to be considered in the impact assessment. The outcome of the public consultation provided useful input for the impact assessment process that addresses the economic, environmental and health impacts of the different policy options.

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PART 4/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection product regulation and biocidal products regulation

Annex 3 out of 16

Accompanying the document

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ANNEX 3

SCREENING METHODOLOGY TO IDENTIFY ENDOCRINE DISRUPTORS ACCORDING TO DIFFERENT OPTIONS IN THE CONTEXT OF AN IMPACT ASSESSMENT

Contents

1. INTRODUCTION

As specified in the roadmap[1], and in Section 4 of the main impact assessment report, four different policy options are outlined for identifying endocrine disruptors (EDs). To determine which substances would be tentatively identified as ED under the different options, the methodology summarised below has been developed by the Joint Research Centre of the European Commission (JRC). The method is being applied by an external SANTE contractor to approximately 600 substances selected from the total lists of substances subject to the Regulations on Plant Protection Products (PPP Regulation), Biocidal Products (BP Regulation), Chemicals (REACH), Cosmetic Products and priority substances under the Water Framework Directive (WFD).

2. AIM AND SCOPE OF THE METHODOLOGY

The screening methodology was developed to assess in a limited amount of time the potential ED properties for approximately 600 substances previously selected (see Annex 4). Therefore, the methodology was applied to existing data only.

The development of this methodology comprised the following steps:

- Identification of data sources.
- Selection of relevant data types to be collected and relevant to inform on the potential ED properties of a substance.
- Definition of a data analysis procedure to categorise substances under the four policy options.

Each step comprises a well-defined set of activities, which are elaborated in the following sections; Figure 1 provides a schematic representation of the methodology.

The assessment focused on humans and wildlife and unless specifically stated otherwise, all mammalian toxicity data were regarded as being relevant for both humans and mammals in the environment. As the understanding regarding the disturbance of the endocrine system of many invertebrate species is limited, the effects on wildlife were limited to the effects observed in mammals, fish, amphibians, and to a very limited extent in birds.

The endocrine relevant effects were limited to effects on the estrogenic, androgenic, thyroid and steroidogenesis (EATS) pathways, as these are relatively well understood and consensus guidance on the interpretation of effects observed in OECD Test Guidelines is available from the OECD Guidance Document (GD) 150.[2] Perturbations of other non-EATS pathways – while potentially relevant for ED - were beyond the scope of this methodology. Human epidemiological and *in silico* data (such as (Q)SAR predictions) were also not considered.

[1] European Commission. 2014. Defining criteria for identifying Endocrine Disruptors in the context of the implementation of the PPP Regulation and BP Regulation. Retrieved from: http://ec.europa.eu/smart-regulation/impact/planned_ia/docs/2014_env_009_endocrine_disruptors_en.pdf

[2] OECD. 2012. Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption, OECD Environmental Health and Safety Publications, Series on Testing and Assessment n°150, Organisation for Economic Cooperation and Development, Paris. Retrieved from: http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono%282012%2922&doclanguage=en

Existing data on the EATS pathway may also be scarce for many substances and the available test guidelines do not consider all relevant species, pathways, or timeframes of exposure. Moreover, within the time constraints of the project it was not possible to assess in detail the quality of individual studies nor to carry out an in depth weight of evidence assessment across all available data for each substance.

As a result of the limitations in its scope, this screening methodology is neither equivalent to nor intended to replace an in-depth assessment process as usually carried out for regulatory purposes. The results obtained are not intended to pre-empt in any way the formal regulatory conclusions that may eventually be made under different pieces of EU legislation.

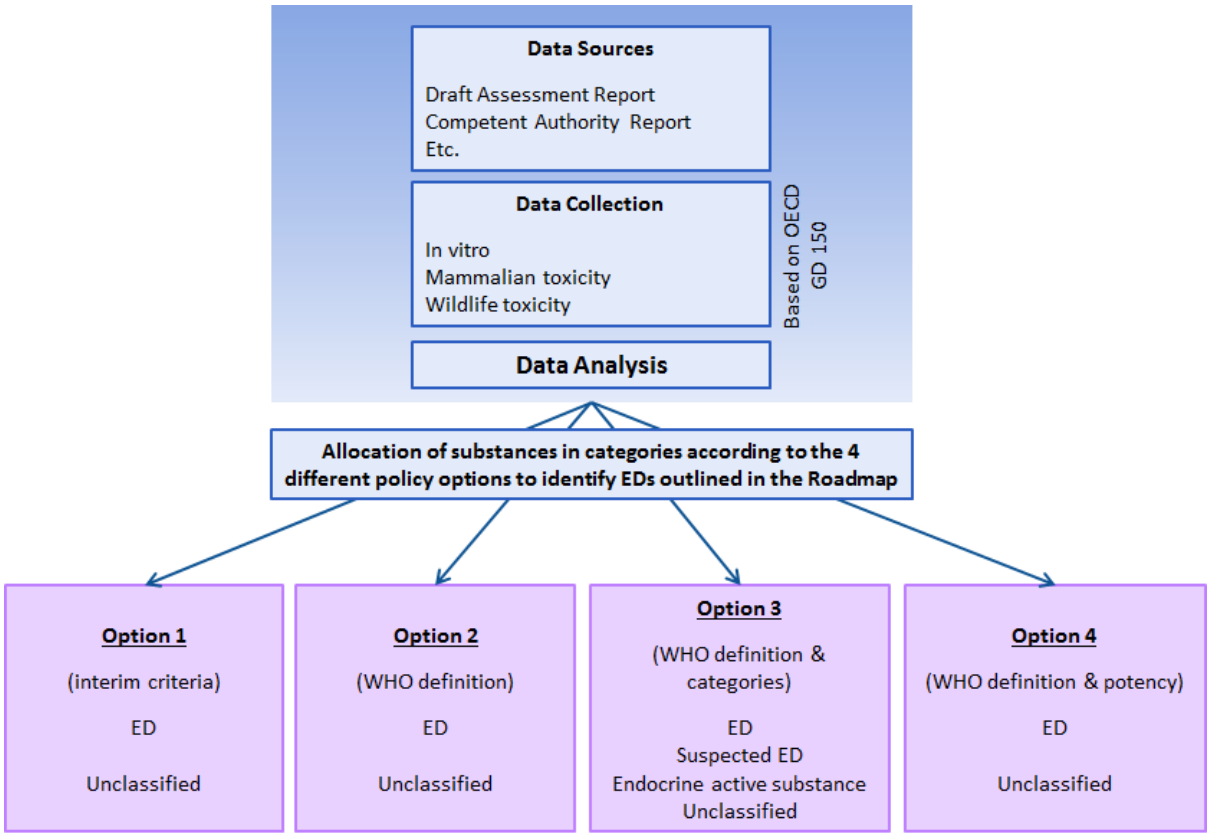

Figure 1. Schematic representation of the screening methodology to tentatively identify which substances would be identified as EDs under four policy options

3. SUBSTANCE SELECTION

Substances were selected as described in Annex 4. This information was also published on the DG SANTE website[3] in December 2015.

[3] European Commission. 2015. Selection of substances to be screened in the context of the impact assessment on criteria to identify endocrine disruptors. Retrieved from: http://ec.europa.eu/health/endocrine_disruptors/docs/impactassessment_chemicalsubstancesselection_en.pdf

4. DATA COLLECTION

Figure 2 provides a schematic representation of which data sources were used to collect relevant data which were then organised in a template to support the data analysis in order to categorise each substance under the four policy options.

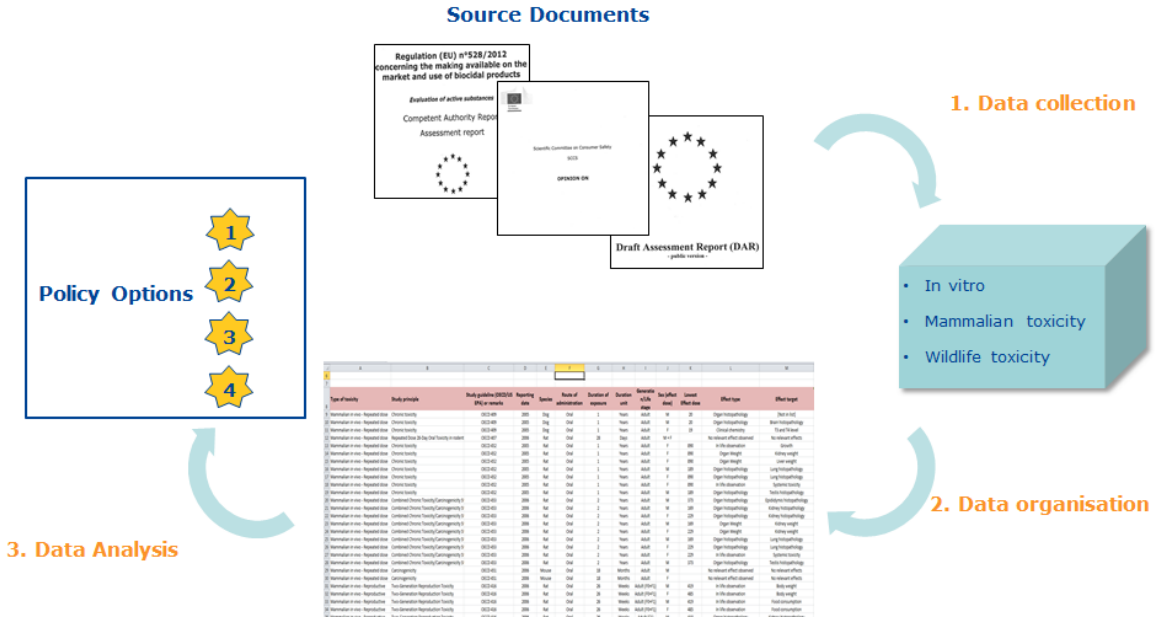

Figure 2. Schematic representation of the workflow from identification of data sources to data analysis

1.1. Information on adverse effects

To determine whether a substance would classify as an ED under each of the four different policy options, different types of information were needed (See Figure 3):

- **Option 1 (interim criteria):** assessment based on the CLP classification (as carcinogen category 2 or toxic for reproduction category 2, harmonised and proposed) and toxicity to endocrine organs. As "endocrine organ" is not defined in the interim criteria, for the purpose of this impact assessment it constitutes the organs that secrete hormones as well as the target organs that express the receptors for the sex hormones and thyroid hormones and are included in the OECD GD 150.
- **Option 2, 3 and 4 (all based on the WHO definition):** all relevant effects are captured that provide information on potential interference with the endocrine system, according to the interpretation given in OECD GD 150. Results are obtained from existing studies on developmental toxicity, reproductive toxicity, carcinogenicity and (sub)acute and (sub)chronic (repeated dose) toxicity.

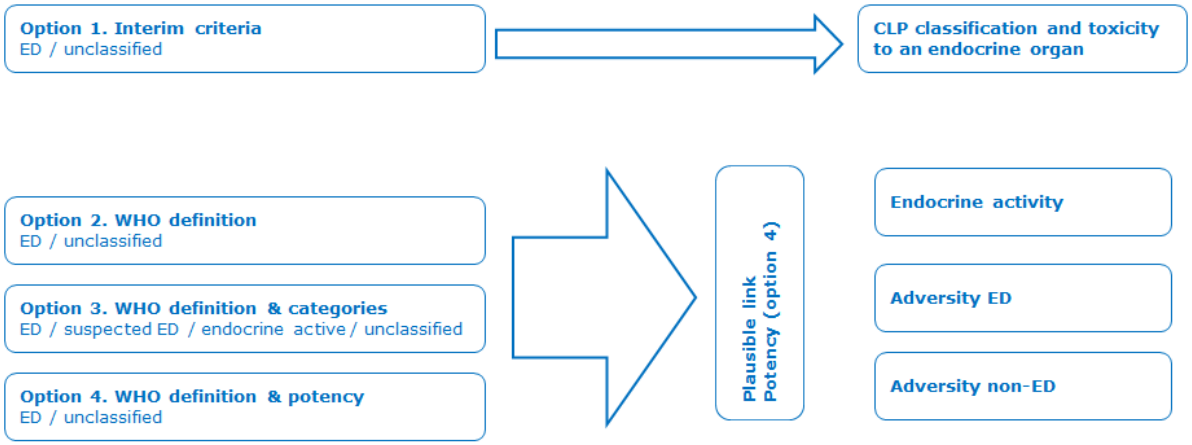

Figure 3. Data requirements for the four different policy options. For option 1, data is required on the CLP classification and the toxicity to an endocrine organ. For option 2, 3, and 4, in vivo and in vitro data are required that show a likelihood of endocrine mediated effects (in the absence of general overt toxicity).

1.2. Information sources

For option 1 (interim criteria), the hazard classification of a substance according to Regulation (EC) No 1272/2008[4] (CLP Regulation) was obtained from the ECHA Classification & Labelling Inventory. If no harmonised classification was available, but a classification was proposed in the regulatory documents (e.g. EFSA Conclusions), then the proposed classification was used. If the proposed classification was more recent than the harmonised classification, both were recorded.

The (eco)toxicological data, mostly obtained from laboratory animals (*in vivo*), was initially collected from evaluated data from the existing regulatory assessment reports, including: EFSA conclusions, MS Draft Assessment Reports, MS Competent Authority Reports, REACH restriction dossiers, Support documents for identification of SVHC and opinions of the SCCS. As the data in these documents have been assessed independently by the MS Competent Authorities, they are assumed to be of high quality and relevant by default.

This information was then supplemented by additional information, gathered from databases focusing on endocrine effects including non-regulatory studies, including:

1. Endocrine Active Substances Information System (EASIS): JRC Database of study reports on substances related to endocrine activity;
2. Substitute It Now (SIN) list: substances that have been identified by the NGO ChemSec as being substances of concern. Endocrine disrupting activity is included as a category for reason of concern;

[4] Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures (CLP Regulation), OJ L 353 31.12.2008, p. 1. Retrieved from: http://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX%3A02008R1272-20150601

3. The Endocrine Disruption Exchange (TEDX) list: potential Endocrine Disruptors; developed by the US Organisation TEDX;
4. ToxCast Database (including ToxCast ER prediction model): data for substances tested in one of the 26 *in vitro* assays that are considered to be relevant for the EATS pathways, developed by US EPA.

All data obtained from these sources are considered to be reliable by default, unless there are clear indications to the contrary. Thus, no additional quality check was performed on these data. Data from these databases and the published scientific literature gathered in the targeted search are considered valuable because they are specifically designed to investigate whether a substance has activity towards the endocrine system (EATS pathways).

Data that inform on how a substance exerts its toxic effects are described as *mechanistic* or *mode of action* data. Such data may be derived from *in vivo* or *in vitro* studies. In the case of endocrine disruption, these data are needed as evidence that a substance alters the endocrine system in accordance with the WHO definition.

1.3. Data extraction and organisation

All effect data from *in vitro* and *in vivo* studies that are potentially informative on ED action were captured. The list of relevant effects was based on a list provided in the OECD GD 150, supplemented with effects from similar *in vivo* and *in vitro* tests, also focusing on the EATS pathways. Some additional effects were captured that are not directly linked to endocrine disruption, e.g. effects occurring at the same dose as (or lower than) the endocrine effects, which help with the interpretation of the specificity of the endocrine related effects.

The data captured included the following information:

- general substance information, including chemical name, CAS Registry Number, current CLP classification (harmonised and proposed), and specific remarks in the regulatory source documents relevant to ED assessment;
- study information, including the type of toxicity test (*in vitro, in vivo*, mammalian, fish, birds, amphibians), the study principle including the protocol used (e.g. OECD or US EPA test guidelines and deviations from these guidelines), and the source of the data (e.g. the specific database from which the regulatory document was retrieved), including the primary reference given within this source and the reporting date;
- study details, including the test species and strain (for *in vitro* assays, the test system used), number of animals per group, the doses administered, the route and method of administration, duration of exposure and the purity of the substance;
- effect details, including the sex, generation and/or life stage for which the effect was observed. The lowest dose at which the specific effect was observed, including the direction of the effect and classification of the effect (optional additional details to further specify the observation). In the case of *in vitro* studies, generally the lowest effect dose is generally not reported, so median values (EC50/AC50/IC50) derived from the concentration-response relationships were captured instead.

5. DATA ANALYSIS AND EVALUATION

All effects captured were codified as providing one of the following types of evidence: *in vitro* mechanistic [A], *in vivo* mechanistic (including hormone levels)[B], EATS specific adverse effects [C], non-specific adverse effects (may or may not be related to EATS) [D] and general adverse effects (not ED-related).

In addition, the consensus interpretation regarding linkage of each effect to one or more of the EATS pathways is indicated. Because of the limited scope of the screening and absence of relevant data for many substances, it is not possible to conclude that a substance is not an ED, hence all substances that cannot be categorised on the available information are considered to be *Unclassified*.

For Option 1 (interim criteria), the identification as ED is based on the interim criteria and depends on the answers to the questions shown in Figure 4 below.

Both the harmonised classification (when available) and the proposed classification (when relevant) have been considered for the substance categorisation under Option 1.

The final categorisation considering the available harmonised and/or proposed classification for each substance as ED or not (unclassified) was based on the scheme shown in Figure 4 below:

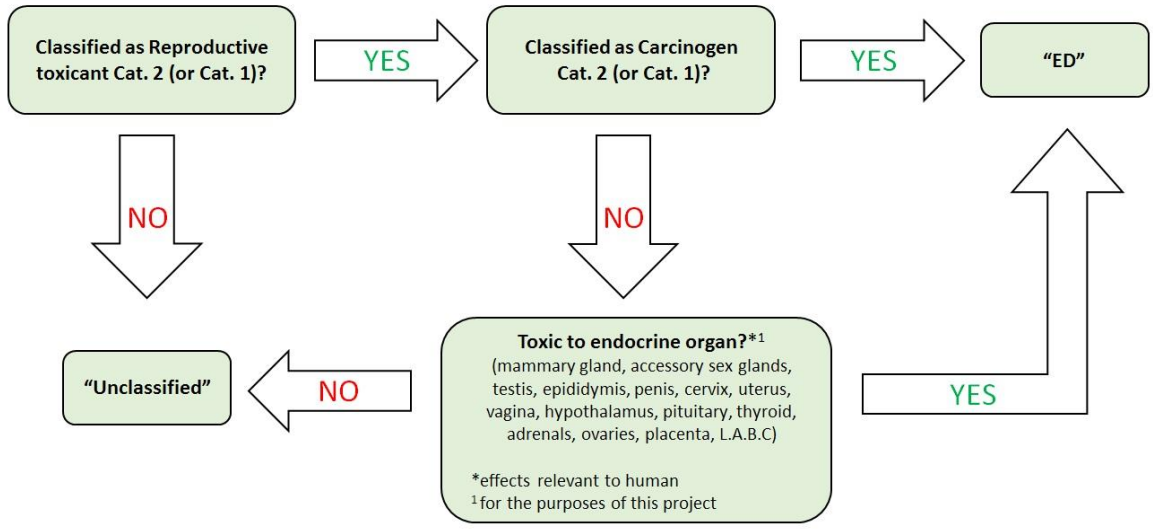

Figure 4. Decision tree, leading to the different ED categorisations according to the interim criteria as stated in the PPP Regulation and the BP Regulation.

Regarding the interpretation of "toxic to endocrine organs", endocrine organs were considered to be those that secrete hormones as well as the target organs that express the receptors for the sex hormones and thyroid hormones and are included in the OECD GD 150. This includes: mammary gland, accessory sex glands (e.g. Cowper's gland, seminal vesicles, prostate gland, bulbourethral glands, Glans penis), testis, epididymis, penis, cervix, uterus (endometrium),

vagina, hypothalamus, pituitary, thyroid, adrenals, ovaries, placenta, Levator ani/bulbocavernosus muscles (LABC).

For Option 2 (WHO definition) **and Option 3** (WHO definition + categories), all effects were collated to determine whether there was sufficient evidence that the substance "alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations".[5]

Depending on the evidence, substances were categorised as Cat I, II III, or Unclassified according to the decision tree in Figure 5. Higher weight was given to EATS specific adverse effects compared to non-specific adverse effects and, in relation to mechanistic data, higher weight was given to *in vivo* mechanistic data than to *in vitro* mechanistic data. Although not covering every situation, generally the type of evidence leading to categorisation into one of the four categories was as follows:

- Cat I: confirmed ED. Adverse effects with plausible link (i.e. same pathway) to mechanistic (endocrine mode of action) information or, in some specific cases, the pattern of adverse effects may be diagnostic of an ED mode of action
- Cat II: suspected ED. Specific adverse effects indicating endocrine disruption but without supporting mechanistic evidence, or *in vivo* mechanistic evidence without evidence for adverse effects
- Cat III: endocrine active. No *in vivo* evidence indicating endocrine adverse effects but mechanistic information *in vitro*
- Unclassified: No (existing) *in vivo* or *in vitro* data that indicate endocrine adverse effects.

[5] WHO/IPCS. 2002. Global Assessment of the State-of-the-science of Endocrine Disruptors. World Health Organization/International Programme on Chemical Safety. WHO/PCS/EDC/02.2, 180 pp. Retrieved from: http://www.who.int/ipcs/publications/new_issues/endocrine_disruptors/en/

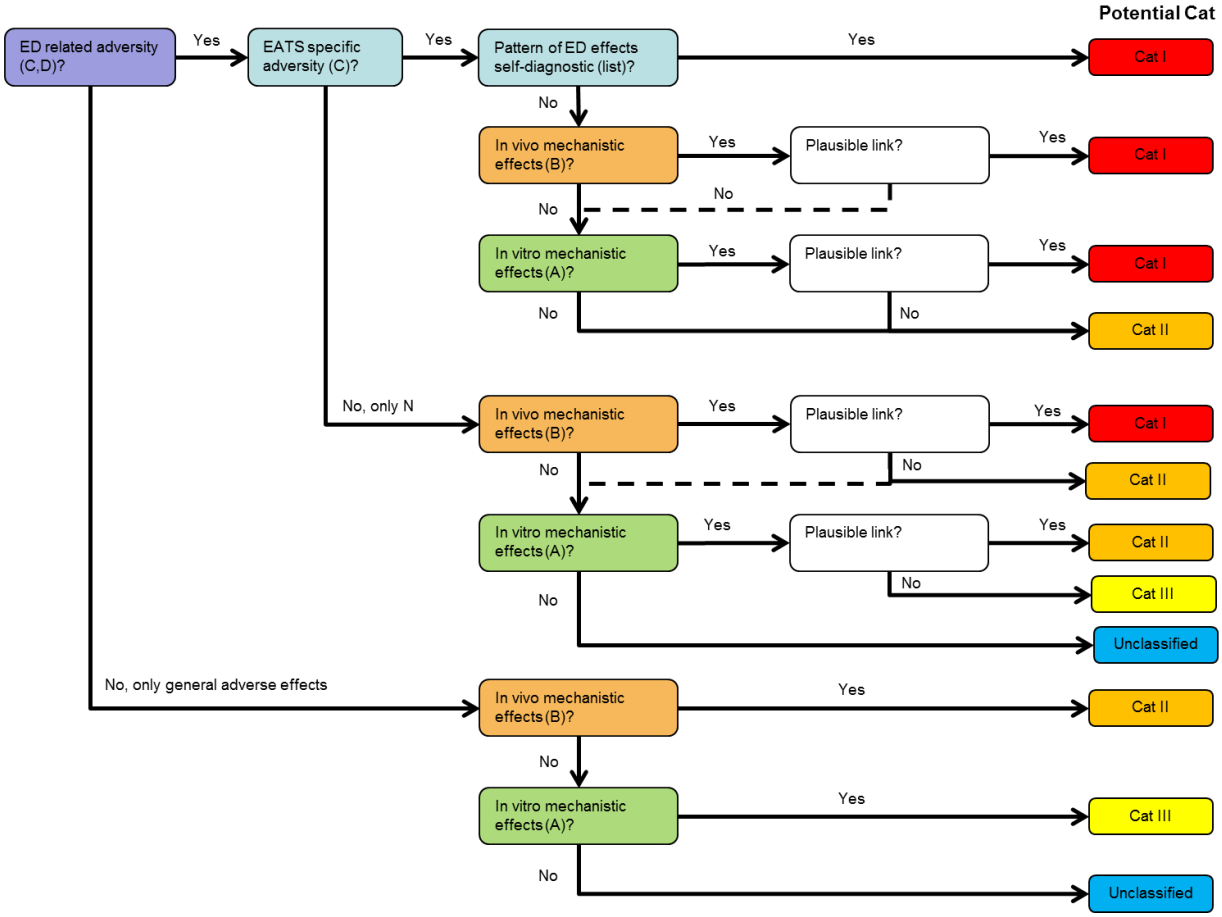

Figure 5. Decision tree for policy options 2 and 3: endocrine disruption according to the WHO definition. A limited weight of evidence based on expert judgement was applied at the Yes/No decision points.

If the decision tree is applied independently of the weight of evidence supporting each of the elements in the decision tree, it may lead to an overestimation of the number of substances identified as EDs. Therefore, a limited weight of evidence approach was applied at the Yes/No decision points in the decision tree.

This limited weight of evidence approach was based, among others, on the following considerations:

a) the magnitude and nature of the adverse effects;
b) the pattern and coherence of adverse effects observed at different doses within and between studies of a similar design and across different species;
c) the weight of certain studies with respect to others: e.g. long term/chronic/repeated-dose studies versus short term/acute studies; *in vivo* tests versus *in vitro* tests; studies with clear study-design versus poorly detailed studies;
d) the biological plausibility of a causal relationship between the induced endocrine activity and the adverse effect(s);
e) the presence of overt toxicity together with the potential ED-related effects;
f) the data available on the human relevance of the effects and mode of action observed.

Thus an isolated effect of low magnitude in one species not observed in other studies of similar design with the same species (provided the effect had been measured) would have lower weight than a case where a clear pattern of effects was seen across a number of studies and in more than one species. As this largely depends on expert judgement, this part could not be codified into the decision tree.

When potential ED-related effects were observed in the presence of overt toxicity, these effects were not considered to be informative of an endocrine mode of action.

Identification as ED under Option 4 (WHO definition + potency) takes into account the potency aspect. Potency depends on the endpoint, but also on the dose, on the duration and timing of exposure.[6]

Option 4 applies only to those substances that are identified under Option 2 or 3 Category I. To categorise a substance under Option 4 for the purpose of this impact assessment, it was agreed to use a trigger value as cut-off value.

The potency of a substance was assessed in this methodology by evaluating if the dose at which an endocrine-related-effect was observed (effect used to categorise that substance in Option 2 or 3 Category I) was above or below a relevant cut-off value. If the ED-related endpoint was below this cut-off value, the substance was considered to satisfy the potency criteria under option 4 and it was thus considered an ED. If it was above the potency cut-off, it was considered as unclassified.

In this methodology, potency-based STOT-RE Cat 1 trigger values from the Regulation (EC) No 1272/2008[7] are proposed as cut-off criteria to evaluate potency. The most sensitive endocrine specific endpoint was compared to the potency cut-off values taken from the STOT-RE, according to the route of exposure (oral, dermal, inhalation). As the duration of *in vivo* assays is variable, the doses were time-adjusted to a 90-day study. However, the same value was used for all species and no further adjustment was applied to take into account the different sizes (body weights) or life spans of different species.

The following decision tree was used to categorise substances under Option 4 by using the defined cut-off value (Figure 6).

[6] EFSA. 2013. EFSA Scientific Committee; Scientific Opinion on the hazard assessment of endocrine disruptors: scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing effects mediated by these substances on human health and the environment. EFSA Journal 2013;11(3):3132. [84 pp.] doi: 10.2903/j.efsa.2013.3132.

[7] Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures (CLP Regulation), OJ L 353 31.12.2008, p. 1. Retrieved from: http://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX%3A02008R1272-20150601

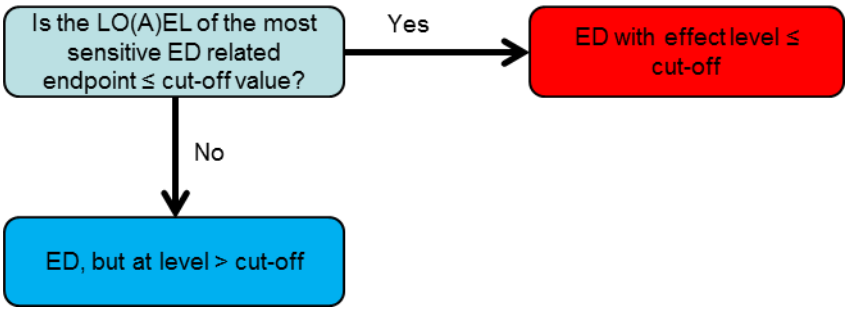

Figure 6. Decision tree, leading to ED categorisation according to option 4.

Table 1 shows the potency-based STOT-RE Cat 1 trigger values for different routes of exposure that were used as cut-off values.

Table 1. Guidance values for STOT-RE Cat 1 for sub chronic and other medium-term studies.

Route of exposure	**STOT-RE Cat 1**
Oral (rat)	10 mg/kg bw/day
Dermal (rat or rabbit)	20 mg/kg bw/day
Inhalation (rat) gas	50 ppmV/6h/day
Inhalation (rat) vapour	0.2 mg/l/6h/day
Inhalation (rat) (dust/mist/fume)	0.02 mg/l/6h/day

The assessment took into consideration the duration of exposure by applying commonly used extrapolation factors: e.g. for a 28-day study the guidance values reported in Table 1 were increased by a factor of three; for a 2-year study, the guidance values were decreased by a factor of eight. Based on the approach followed by the ECHA Risk Assessment Committee (RAC), the same guidance values for rat, mouse and dog studies were used.[8]

Having used such extrapolations, substances categorised as ED under Option 2 or under Option 3 Category I on the basis of evaluation of mammalian data remained classified as EDs for Human Health under Option 4 if the effect dose was lower than the adjusted potency cut-off value (Figure 6) or characterised as unclassified if the effect dose was higher than the adjusted potency cut-off value.

For the ecotoxicological evaluation under Option 4, substances categorised as ED under Option 2 or under Option 3 Category I were treated as follows.

If the plausible link was established on the basis of mammalian data only, then the same cut-off values as in human health assessment were used.

[8] ECHA. 2012. RAC Opinion ECHA/RAC/CLH-O-0000002970-73-01/F, September 2012

If vertebrate wildlife other than mammalian data (i.e. avian, fish, amphibian data) were used, these substances were categorised as ED under Option 4. In other words, the cut-off value was assumed to be very high.

Under Options 2, 3 and 4, the evidence was assessed for human health and for wildlife separately. For human health, all mammalian effects were assumed to be relevant. For wildlife, the data from fish, amphibians and birds were used in addition to the mammalian data. However, only the effects that are considered to have population relevance (i.e. developmental and reproductive effects) were used to categorise a substance.

6. SUMMARY AND CONCLUSIONS

A screening methodology was developed to assess, in a limited amount of time, the potential endocrine disrupting properties for approximately 600 substances. The substances were selected from the total lists of substances subject to different pieces of EU legislation related to management of risks to human health and environment, including the PPP Regulation, BP Regulation, Chemicals (REACH), Cosmetic Products and Water Framework Directive (WFD).

Bearing in mind the time and financial constraints on the study, the methodology was designed to be feasible, scientifically robust and transparent, allowing traceability of data and conclusions. It was necessary to limit the scope of the methodology, as described above, to the modes of action and adverse effects that are better understood and investigated in existing regulatory assessments. Every effort was made to codify the data collection and evaluation process, and document all assumptions made, while recognising that any chemical assessment inevitably involves a degree of expert judgement that cannot be codified. As a consequence, this screening methodology is neither equivalent to nor intended to replace an in-depth assessment process, and the results obtained are not intended to pre-empt in any way the formal regulatory conclusions that may eventually be made under different pieces of EU legislation.

In developing this screening methodology, it was foreseen that the results for pesticide and biocidal active substances would serve as an input to a second study comparing the impacts of the different policy options on substances falling under the PPP Regulation and the BP Regulation.

GLOSSARY

A	Androgenic pathway
AC50	Half maximal active concentration
BP Regulation	Biocidal Products Regulation
CAR	Competent Authority Report
CLP	Classification, Labelling and Packaging
CMR	Carcinogenic, Mutagenic, Reprotoxic
CoRAP	Community Rolling Action Plan
DAR	Draft Assessment Report
DG	Directorate General
E	Estrogenic pathway
EASIS	Endocrine Active Substances Information System
EATS	Estrogen, Androgen, Thyroid and Steroidogenesis
ECHA	European Chemicals Agency
EC50	Half maximal effective concentration
ED	Endocrine disruptor
EDSP	Endocrine Disruptor Screening Program
EFSA	European Food Safety Authority
EU	European Union
GD	Guidance Document
IC50	Half maximal inhibitory concentration
JRC	Joint Research Centre
MS	Member State
NOAEL	No Observed Adverse Effect Level
OECD	Organisation for Economic Co-operation and Development
PPP Regulation	Plant Protection Products Regulation
REACH	Registration, Evaluation, Authorisation and Restriction of CHemicals
S	Steroidogenesis pathway
SCCS	Scientific Committee on Consumer Safety
SIN	Substitute It Now
STOT-RE	Specific Target Organ Toxicity - Repeated Exposure
SVHC	Substance of Very High Concern
T	Thyroid pathway
TEDX	The Endocrine Disruptor eXchange
ToxCast	Database of *in vitro* assay data from US Environmental Protection Agency (EPA)
WFD	Water Framework Directive
WHO	World Health Organization
WoE	Weight of Evidence

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PART 5/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annex 4 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

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ANNEX 4

CHEMICAL SUBSTANCES SCREENED IN THE CONTEXT OF THE IMPACT ASSESSMENT ON CRITERIA TO IDENTIFY ENDOCRINE DISRUPTORS

Contents

1. INTRODUCTION

To support the impact assessment, a specific contract was signed in April 2015 under Framework Service Contract No SANCO/2012/02/011 with the aim of screening the available evidence on chemicals used in plant protection and/or biocidal products, as well as a selection of substances falling under the REACH Regulation[1] and the Cosmetic Products Regulation[2]. Some of these selected substances are also priority substances under the Water Framework Directive[3].

The identity (names and CAS-numbers) of the substances included in this exercise are provided in this Annex. This information was also published in December 2015 on the website of the European Commission[4]. Some chemicals fall within the scope of more than one legislative area and this is clearly indicated in the table below. The final list of substances may be subject to minor changes.

The screening was carried out in the context of an impact assessment to evaluate the impacts associated to options for criteria to identify endocrine disruptors under the regulations on plant protection products and biocidal products. The screening was based on available evidence (no additional testing) and needed to be carried out in a limited time. The screening methodology was developed for the purpose of the screening exercise. The results of the screening therefore do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

The selection of the chemicals for the impact assessment screening exercise was based on the following general principles but differed between the legislative areas as described further down:

1. the selection process should be transparent and objective;
2. availability of data is crucial for an assessment of endocrine properties. Therefore priority is given to chemicals for which data are available;
3. the selection should not lead to a bias in the assessment of the four options.

[1] Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency (OJ L 396, 30.12.2006, p. 1). Retrieved from: http://ec.europa.eu/health/endocrine_disruptors/docs/reach_1907_2006_regulation_en.pdf

[2] Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products (OJ L 342, 22.12.2009, p. 59). Retrieved from: http://ec.europa.eu/health/endocrine_disruptors/docs/cosmetic_1223_2009_regulation_en.pdf

[3] Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy (OJ L 327, 22.12.2000, p. 1). Retrieved from: http://ec.europa.eu/health/endocrine_disruptors/docs/wfd_200060ec_directive_en.pdf

[4] European Commission, DG SANTE, Endocrine disruptors – Impact Assessment. Available on: http://ec.europa.eu/health/endocrine_disruptors/impact_assessment/index_en.htm

2. CHEMICAL SUBSTANCES REGULATED UNDER THE PLANT PROTECTION PRODUCTS REGULATION AND THE BIOCIDAL PRODUCTS REGULATION

All relevant chemicals approved by 11 May 2015 at European level to be used in plant protection products and biocidal products were considered as a starting point.

The screening was then focused by excluding those substances that are considered to be out of scope. The step-wise rationale followed for excluding active substances from the screening is:

1. microorganisms (living organisms, no chemical substances);
2. basic substances, defined in Article 23 of Regulation (EC) No 1107/2009 as being substances of no concern and no inherent capacity to cause endocrine disrupting effects, and where the approval procedures follow particular rules;
3. low risk substances, defined in Annex II to Regulation (EC) 1107/2009 as, among others properties, not deemed to be an endocrine disruptor;
4. natural extracts, mixtures, or repellents;
5. attractants (pheromones) or plant hormones;
6. others (e.g. inert substances, salts, acids).

324 substances falling under the PPP Regulation and 95 substances falling under the BP Regulation were selected following this rationale. Among the 95 BP there are also some chemicals not yet approved but where the corresponding opinions were already adopted by the BP Committee of the European Chemical Agency (ECHA). 23 PPP and 3 BP were not selected following this rationale but appear on the list because they were substances screened during the earlier phase of the project.

3. CHEMICAL SUBSTANCES REGULATED UNDER THE REACH REGULATION

Substances were selected for the screening exercise according to the following step-wise rationale:

1. all substances on the Candidate List already identified as Substances of Very High Concern (SVHC) because of ED concerns under Art. 57(f);
2. all substances for which an SVHC opinion on the identification of the substance as SVHC due to its endocrine disrupting properties was provided by the Member State Committee at ECHA[5];
3. all substances on the Candidate list identified as SVHC because of reprotoxicity 1A/1B;
4. all substances listed in Annex XVII for restrictions due to an ED concern or because of having a harmonised classification as reprotoxic 1A/1B;
5. all substances placed on the community rolling action plan (CoRAP) due to ED concern.

[5] Member State Committee (MSC) Opinions on Substances of Very High Concern (SVHC). Retrieved from: http://echa.europa.eu/role-of-the-member-state-committee-in-the-authorisation-process/svhc-opinions-of-the-member-state-committee

149 REACH chemical substances were selected following this procedure. Further, 52 substances registered under REACH also appear on the list of screened chemicals but were selected following the rationales applied for other legislative frameworks (i.e. they are either PPP/BP or substances used in cosmetic products) or because they were substances screened during the earlier phase of the project.

4. CHEMICAL SUBSTANCES REGULATED UNDER THE COSMETIC PRODUCTS REGULATION

Substances used in cosmetic products were selected based on the following criteria:

1. Substances for which an opinion of the Scientific Committee on Consumer Safety (SCCS) was provided, which contained a discussion but not necessarily a conclusion on their endocrine disrupting potential;
2. Substances for which an SCCS opinion was provided due to the their potential or de facto classification as carcinogenic, mutagenic, or toxic for reproduction (CMR)1A/1B or CMR2 under the Classification, Labelling and Packaging (CLP) Regulation;
3. Substances not classified as CMR but for which SCCS expressed some concern on toxicity endpoints;
4. Substances for which concern was raised by stakeholders / Member States on potential endocrine disrupting properties;

45 chemical substances falling under the Cosmetic products regulation were selected following this procedure. A further 6 substances falling under the Cosmetic products regulation also appear on the list of screened chemicals because they were selected following the rationales applied for other legislative frameworks (i.e. they are either PPP/BP or REACH substances.)

5. CHEMICAL SUBSTANCES REGULATED UNDER THE WATER FRAMEWORK DIRECTIVE (WFD)

For the WFD, no specific selection criteria were applied to identify substances for the screening. However, some of the substances on the screening list, selected following the rationales applied for other legislative frameworks (i.e. PPP/BP, Cosmetics or REACH), are listed individually or fall under a group (e.g. lead and its compounds) in the list of priority substances under the WFD.

6. LIST OF CHEMICAL SUBSTANCES SCREENED IN THE CONTEXT OF THE IMPACT ASSESSMENT ON CRITERIA TO IDENTIFY ENDOCRINE DISRUPTORS (IN ALPHABETICAL ORDER) [6]

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
[Phthalato(2-)]dioxotrilead	69011-06-9				1	1*
1,2,3-trichloropropane	96-18-4				1	
1,2,4-trihydroxybenzene	533-73-3			1		
1,2-benzenedicarboxylic acid, di-C6-10-alkyl esters; 1,2-benzenedicarboxylic acid, mixed decyl and hexyl and octyl diesters with ≥ 0.3% of dihexyl phthalate (EC No. 201-559-5)	68515-51-5				1	
1,2-Benzenedicarboxylic acid, di-C6-8-branched alkyl esters, C7-rich	71888-89-6				1	
1,2-Benzenedicarboxylic acid, di-C7-11-branched and linear alkyl esters	68515-42-4				1	
1,2-Benzenedicarboxylic acid, dihexylester, branched and linear	68515-50-4				1	
1,2-Benzenedicarboxylic acid, dipentylester, branched and linear	84777-06-0				1	
1,2-bis(2-methoxyethoxy)ethane (TEGDME,triglyme)	112-49-2				1	
1,2-Diethoxyethane	629-14-1				1	
1,2-Dihydroxy-benzene	120-80-9			1	1*	
1,2-dimethoxyethane,ethylene glycol dimethyl ether (EGDME)	110-71-4				1	
1,4-Dimethylnaphthalene	571-58-4	1				
1-bromopropane (n-propyl bromide)	106-94-5				1	
1-Decanol	112-30-1	1			1*	
1-Methyl-2,6-diamino-benzene	823-40-5			1		
1-Methyl-cyclopropene	3100-04-7	1				
1-Naphthylacetamide (1-NAD)	86-86-2	1				
1-Naphthylacetic acid (1-NAA)	86-87-3	1				
1R-trans phenothrin	26046-85-5		1			
2-(2-butoxyethoxy)ethyl 6-propylpiperonyl ether	51-03-6				1	
2-(2-methoxyethoxy)ethanol	111-77-3			1	1*	
2,2,6,6-tetrabromo-4,4-isopropylidenediphenol	79-94-7				1	
2,2',6,6'-Tetrabromo-4,4'-isopropylidenediphenol, oligomeric reaction products with Propylene oxide and n-butyl glycidyl ether	-				1	

[6] The cells with an * refer to substances which were not identified following a selection rationale for a specific legislative framework but are on the list because they were selected following the rationales applied for other legislative frameworks or because they were substances screened during the earlier phase of the project.

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
2,2′,6,6′-Tetra-tert-butyl-4,4′-methylenediphenol	118-82-1				1	
2,2'-dimethyl-4,4'-methylenebis(cyclohexylamine)	6864-37-5				1	
2,4-D	94-75-7	1				
2,4-DB	94-82-6	1				
2,4-di-tert-butylphenol	96-76-4				1	
2,5-Dichlorobenzoic acid methylester	2905-69-3	1				
2-Amino-3-hydroxypyridine	16867-03-1			1		
2-amino-4-hydroxyethylaminoanisole sulfate	83763-48-8			1		
2-ethoxyethanol	110-80-5			1	1	
2-ethoxyethyl acetate	111-15-9			1	1	
2-ethylhexyl 10-ethyl-4,4-dioctyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate (DOTE)	15571-58-1				1	
2-Ethylhexyl-4-methoxycinnamate	5466-77-3			1	1	
2-Mercaptobenzothiazole	149-30-4			1	1*	
2-methoxyethanol	109-86-4			1	1	
2-methoxyethyl acetate	110-49-6			1		
2-Phenylphenol	90-43-7	1	1		1*	
3-amino-2,6-dimethylphenol	6994-64-5			1		
3-Benzylidene camphor	15087-24-8			1		
3-ethyl-2-methyl-2-(3-methylbutyl)-1,3-oxazolidine	143860-04-2				1	
3-methylpyrazole	1453-58-3				1	
4-(1,1,3,3-tetramethylbutyl)phenol	140-66-9				1	1*
4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated	-				1	
4,4'-isopropylidenediphenol (Bisphenol-A)	80-05-7				1	
4,4'-sulfonyldiphenol	80-09-1				1	
4,5-Dichloro-2-octylisothiazol-3(2H)-one	64359-81-5		1			
4-hydroxybenzoic acid	99-96-7				1	
4-Methylbenzylidene camphor	38102-62-4			1		
4-Nonylphenol, branched and linear	-			1	1	1*
4-Nonylphenol, branched and linear, ethoxylated	-				1	
4-tert-butylphenol	98-54-4				1	
6,6'-di-tert-butyl-4,4'-butylidenedi-m-cresol	85-60-9				1	
6,6'-di-tert-butyl-4,4'-thiodi-m-cresol	96-69-5				1	
6-Benzyladenine	1214-39-7	1				
8-Hydroxyquinoline incl. oxyquinoleine	148-24-3	1			1*	

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
Abamectin (aka avermectin)	71751-41-2	1	1			
Acequinocyl	57960-19-7	1				
Acetaldehyde	75-07-0			1	1*	
Acetamiprid	135410-20-7	1				
Acetic acid, lead salt, basic	51404-69-4				1	1*
Acibenzolar-S-methyl (benzothiadiazole)	135158-54-2	1				
Aclonifen	74070-46-5	1				1*
Acrinathrin	101007-06-1	1				
Acrolein	107-02-8		1		1*	
Alkyl (C12-16) dimethylbenzyl ammonium chloride; C 12-16-ADBAC	68424-85-1		1		1*	
alphachloralose	15879-93-3		1			
Alpha-Cypermethrin (aka alphamethrin)	67375-30-8	1	1			1*
Aluminium phosphide	20859-73-8	1	1			
Aluminium sulphate	10043-01-3	1*			1*	
Ametoctradin	865318-97-4	1				
Amidosulfuron	120923-37-7	1				
Aminopyralid	150114-71-9	1				
Amisulbrom	348635-87-0	1				
Amitrole (aminotriazole)	61-82-5	1				
Ammonium dichromate	7789-09-5				1	
Ammonium pentadecafluorooctanoate (APFO)	3825-26-1				1	
ammonium perchlorate	7790-98-9				1	
Ammonium thiocyanate	1762-95-4				1	
Ascorbic acid	50-81-7	1*				
Azadirachtin	11141-17-6	1				
Azimsulfuron	120162-55-2	1				
Azoxystrobin	131860-33-8	1				
Basic Copper carbonate: inorganic	12069-69-1		1		1*	
Beflubutamid	113614-08-7	1				
Benalaxyl	71626-11-4	1				
Benalaxyl-M	98243-83-5	1				
Bendiocarb	22781-23-3		1			
Benfluralin	1861-40-1	1				
Bensulfuron methyl	83055-99-6	1				
Bentazone	25057-89-0	1				
Benthiavalicarb	413615-35-7	1				
Benzo[a]pyrene	50-32-8				1	1*
Benzoic acid	65-85-0	1	1	1*	1*	
Benzophenone-3	131-57-7			1	1	
Benzotriazole	95-14-7				1	

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
Benzyl butyl phthalate (BBP)	85-68-7				1	
Beta-Cyfluthrin	68359-37-5	1				
Bifenazate	149877-41-8	1				
Bifenox	42576-02-3	1				1*
Bifenthrin	82657-04-3	1	1			
Bis (2-ethylhexyl)phthalate (DEHP)	117-81-7				1	1*
Bis(2-ethylhexyl) tetrabromophthalate	26040-51-7				1	
Bis(2-methoxyethyl) ether	111-96-6				1	
Bis(2-methoxyethyl) phthalate	117-82-8				1	
Bis(2-propylheptyl) phthalate	53306-54-0				1	
Bispyribac	125401-92-5	1				
Bixafen	581809-46-3	1				
Bordeaux mixture		1*				
Boric acid	10043-35-3		1	1	1	
Boric oxide: inorganic	1303-86-2		1		1	
Boscalid (formerly nicobifen)	188425-85-6	1				
Brodifacoum	56073-10-0		1			
Bromadiolone	28772-56-7	1	1			
Bromoacetic acid	79-08-3		1		1*	
Bromoxynil	1689-84-5	1				
Bromuconazole	116255-48-2	1				
Bupirimate	41483-43-6	1				
Buprofezin	69327-76-0	1				
C(M)IT/MIT	55965-84-9		1			
Cadmium chloride	10108-64-2				1	1*
Cadmium fluoride	7790-79-6				1	1*
Cadmium sulphate	10124-36-4				1	1*
Calcium phosphide	1305-99-3	1*				
Camphor benzalkonium methosulfate	52793-97-2			1		
Capric acid	334-48-5	1	1			
Caprylic acid	124-07-2	1	1		1*	
Captan	133-06-2	1				
Carbetamide	16118-49-3	1				
Carbon dioxide	124-38-9	1*	1*			
Carbon disulphide	75-15-0				1	
Carboxin	5234-68-4	1				
Carfentrazone-ethyl	128639-02-1	1				
Carvone	99-49-0	1				
Chlorantraniliprole	500008-45-7	1				
chlorfenapyr	122453-73-0		1			
Chloridazon (aka pyrazone)	1698-60-8	1				

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
Chlormequat	7003-89-6	1				
Chloroacetamide	79-07-2			1	1*	
Chloromethane	74-87-3				1	
Chlorophacinone	3691-35-8		1			
Chlorothalonil	1897-45-6	1				
Chlorotoluron	15545-48-9	1				
Chlorpropham	101-21-3	1				
Chlorpyrifos	2921-88-2	1				1*
Chlorpyrifos-methyl	5598-13-0	1				
Chlorsulfuron	64902-72-3	1				
Chromafenozide	143807-66-3	1				
cis-tricos-9-ene (Muscalure)	27519-02-4		1			
Clethodim	99129-21-2	1				
Clodinafop	114420-56-3	1				
Clofentezine	74115-24-5	1				
Clomazone	81777-89-1	1				
Clopyralid	1702-17-6	1				
Clothianidin	210880-92-5	1	1			
Cobalt dichloride	7646-79-9				1	
Cobalt(II) carbonate	513-79-1				1	
Cobalt(II) diacetate	71-48-7				1	
Cobalt(II) dinitrate	10141-05-6				1	
Cobalt(II) sulphate	10124-43-3				1	
Copper (II) oxide	1317-38-0		1		1*	
Copper hydroxide	20427-59-2	1	1		1*	
Copper pyrithione	14915-37-8		1			
Copper sulphate pentahydrate	7758-99-8		1			
Coumatetralyl	5836-29-3		1			
Creosote	8001-58-9		1			
Cu-HDO	312600-89-8		1			
Cyazofamid	120116-88-3	1				
Cycloxydim	101205-02-1	1				
Cyflufenamid	180409-60-3	1				
Cyflumetofen	400882-07-7	1				
Cyhalofop-butyl	122008-85-9	1				
Cymoxanil	57966-95-7	1				
Cypermethrin	52315-07-8	1	1			1*
Cyproconazole	94361-06-5	1	1			
Cyprodinil	121552-61-2	1				
Cyromazine	66215-27-8	1				
Daminozide	1596-84-5	1				
Dapsone	80-08-0				1	

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
Dazomet	533-74-4	1	1			
DCPP	3380-30-1		1		1*	
DDACarbonate	894406-76-9		1			
Decamethylcyclopentasiloxane	541-02-6			1	1*	
Deltamethrin	52918-63-5	1	1			
Denathonium benzoate	3734-33-6	1*				
Desmedipham	13684-56-5	1				
Dibutyl phthalate (DBP)	84-74-2				1	
Dibutyltin	-				1	
Dibutyltin dichloride (DBTC)	683-18-1				1	
Dicamba	1918-00-9	1				
dichlofluanid	1085-98-9		1			
Dichloromethane	75-09-2			1	1*	1*
Dichlorprop-P	15165-67-0	1				
Diclofop	51338-27-3	1				
Didecyldimethylammonium chloride; DDAC	7173-51-5		1		1*	
Diethofencarb	87130-20-9	1				
diethyl phthalate	84-66-2			1*	1	
Diethylene glycol monobutyl ether	111-90-0			1	1*	
Difenacoum	56073-07-5	1	1			
Difenoconazole	119446-68-3	1				
Difethialone	104653-34-1		1			
Diflubenzuron	35367-38-5	1	1			
Diflufenican	83164-33-4	1				
Dihexyl phthalate	84-75-3				1	
diisobutyl phthalate (DIBP)	84-69-5				1	
Diisopentylphthalate	605-50-5				1	
Dimethachlor	50563-36-5	1				
Dimethenamid-P	163515-14-8	1				
Dimethoate	60-51-5	1				
Dimethomorph	110488-70-5	1				
Dimethyl glutarate	1119-40-0				1	
Dimoxystrobin	149961-52-4	1				
Dinoseb (6-sec-butyl-2,4-dinitrophenol)	88-85-7				1	
Dinotefuran	165252-70-0		1			
dioctyltin oxide	870-08-6				1	
Dioxobis(stearato)trilead	12578-12-0				1	1*
Dipentyl phthalate (DPP)	131-18-0				1	
Diphenylether, octabromo derivative C12H2Br8O	-				1	
Diquat (dibromide)	2764-72-9	1				
Disodium octaborate tetrahydrate	12280-03-4		1			

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
Disodium phosphonate	13708-85-5	1*				
Disodium tetraborate decahydrate	1303-96-4		1			
Disodium tetraborate pentahydrate	12267-73-1		1		1	
Disodium tetraborate, anhydrous	12179-04-3				1	
Disodium tetraborate: inorganic or basic (food additive)	1330-43-4		1		1*	
Distillates (coal tar), naphthalene oils,naphthalene oil	84650-04-4				1	
Dithianon	3347-22-6	1				
Diuron	330-54-1	1			1	1*
Di-μ-oxo-di-n-butylstanniohydroxyborane/ Dibutyltin hydrogen borate C8H19BO3Sn (DBB)	75113-37-0				1	
Dodemorph	1593-77-7	1				
Dodine	112-65-2	1				
Emamectin	155569-91-8	1				
Epoxiconazole	133855-98-8	1				
Esfenvalerate	66230-04-4	1				
Ethephon	16672-87-0	1				
Ethofumesate	26225-79-6	1				
Ethoprophos	13194-48-4	1				
Ethyl butylacetylaminopropionate	52304-36-6		1			
Ethylene Glycol Monobutyl Ether	111-76-2			1	1*	
Etofenprox	80844-07-1	1	1			
Etoxazole	153233-91-1	1				
Etridiazole	2593-15-9	1				
Eugenol	97-53-0	1*			1*	
Famoxadone	131807-57-3	1				
Fatty acids, C16-18, lead salts	91031-62-8				1	1*
Fenamidone	161326-34-7	1				
Fenamiphos (aka phenamiphos)	22224-92-6	1				
Fenazaquin	120928-09-8	1				
Fenbuconazole	114369-43-6	1				
Fenhexamid	126833-17-8	1				
Fenoxaprop-P	113158-40-0	1				
Fenoxycarb	72490-01-8	1	1			
Fenpropidin	67306-00-7	1				
Fenpropimorph	67564-91-4	1	1			
Fenpyrazamine	473798-59-3	1				
Fenpyroximate	134098-61-6	1				
Ferric phosphate	10045-86-0	1*			1*	
Fipronil	120068-37-3	1	1			
Flazasulfuron	104040-78-0	1				

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
Flocoumafen	90035-08-8		1			
Flonicamid (IKI-220)	158062-67-0	1				
Florasulam	145701-23-1	1				
Fluazifop-P	83066-88-0	1			1*	
Fluazinam	79622-59-6	1				
Flubendiamide	272451-65-7	1				
Fludioxonil	131341-86-1	1				
Flufenacet (formerly fluthiamide)	142459-58-3	1				
flufenoxuron	101463-69-8		1			
Flumioxazin	103361-09-7	1				
Fluometuron	2164-17-2	1				
Fluopicolide	239110-15-7	1				
Fluopyram	658066-35-4	1				
Fluoxastrobin	361377-29-9	1				
Flupyrsulfuron-methyl (DPX KE 459)	144740-54-5	1				
Fluquinconazole	136426-54-5	1				
Flurochloridone	61213-25-0	1				
Fluroxypyr	69377-81-7	1				
Flurtamone	96525-23-4	1				
Flutolanil	66332-96-5	1				
Flutriafol	76674-21-0	1				
Fluxapyroxad	907204-31-3	1				
Folpet	133-07-3	1	1			
Foramsulfuron	173159-57-4	1				
Forchlorfenuron	68157-60-8	1				
Formamide	75-12-7				1	
Formetanate	22259-30-9	1				
Fosetyl	39148-24-8	1				
Fosthiazate	98886-44-3	1				
Fuberidazole	3878-19-1	1				
Furfural	98-01-1			1	1*	
Gamma-cyhalothrin	76703-62-3	1				
Geraniol	106-24-1	1*			1*	
Glufosinate	51276-47-2	1				
Glutaraldehyde	111-30-8		1		1*	
Glyphosate (incl trimesium aka sulfosate)	1071-83-6	1				
Halosulfuron methyl	100784-20-1	1				
Haloxyfop-P (Haloxyfop-R)	95977-29-0	1				
Heptamaloxyloglucan	870721-81-6	1				
Hexaflumuron	86479-06-3		1			
Hexythiazox	78587-05-0	1				

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
Hydrochloric acid	7647-01-0		1		1*	
hydrogen cyanide	74-90-8		1		1*	
Hydrogen peroxide	7722-84-1		1		1*	
Hydroxyethyl-3,4-methylenedioxyaniline HCl	94158-14-2			1		
Hydroxyethyl-p-phenylenediamine sulfate	93841-25-9			1		
Hymexazol	10004-44-1	1				
Imazalil (aka enilconazole)	35554-44-0	1				
Imazamox	114311-32-9	1				
Imazaquin	81335-37-7	1				
Imazosulfuron	122548-33-8	1				
Imidacloprid	138261-41-3	1	1			
Imidazolidine-2-thione (2-imidazoline-2-thiol)	96-45-7				1	
Indolylbutyric acid	133-32-4	1				
Indoxacarb	144171-61-9	1				
Indoxacarb (enantiomeric reaction mass S:R 75:25)	173584-44-6		1			
Iodine	7553-56-2		1		1*	
Iodosulfuron	185119-76-0	1				
IPBC	55406-53-6		1	1*		
Ipconazole	125225-28-7	1				
Iprodione	36734-19-7	1				
Iprovalicarb	140923-17-7	1				
Isopentyl-p-Methoxycinnamate	71617-10-2			1	1	
Isoproturon	34123-59-6	1				1*
Isopyrazam	881685-58-1	1				
Isoxaben	82558-50-7	1				
Isoxaflutole	141112-29-0	1				
K-HDO	66603-10-9		1			
Kojic Acid	501-30-4			1		
Kresoxim-methyl	143390-89-0	1				
lambda-Cyhalothrin	91465-08-6	1	1			
Laminarin	9008-22-4	1				
Lauric acid	143-07-7	1*	1*		1*	
Lead bis(tetrafluoroborate)	13814-96-5				1	1*
Lead chromate	7758-97-6				1	1*
Lead chromate molybdate sulphate red (C.I. Pigment Red 104)	12656-85-8				1	1*
Lead cyanamidate	20837-86-9				1	1*
Lead di(acetate)	301-04-2				1	1*
Lead diazide, Lead azide	13424-46-9				1	1*
Lead dinitrate	10099-74-8				1	1*
Lead dipicrate	6477-64-1				1	1*

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
Lead hydrogen arsenate	7784-40-9				1	1*
Lead monoxide (lead oxide)	1317-36-8				1	1*
Lead oxide sulfate	12036-76-9				1	1*
Lead styphnate	15245-44-0				1	1*
Lead sulfochromate yellow (C.I. Pigment Yellow 34)	1344-37-2				1	1*
Lead titanium trioxide	12060-00-3				1	1*
Lead titanium zirconium oxide	12626-81-2				1	1*
Lead(II) bis(methanesulfonate)	17570-76-2				1	1*
Lenacil	2164-08-1	1				
Limestone	1317-65-3	1*				
Linuron	330-55-2	1				
Low temperature tar oil, alkaline,extract residues (coal), low temperature coal tar alkaline	122384-78-5				1	
Lufenuron	103055-07-8	1				
Magnesium phosphide	12057-74-8	1	1			
Malathion	121-75-5	1				
Maleic hydrazide	123-33-1	1				
Mancozeb	8018-01-7	1				
Mandipropamid	374726-62-2	1				
Maneb	12427-38-2	1				
MBM	5625-90-1		1			
MCPA	94-74-6	1				
MCPB	94-81-5	1				
Mecoprop	93-65-2	1				
Mecoprop-P	16484-77-8	1			1*	
Medetomidine	86347-14-0		1			
Mepanipyrim	110235-47-7	1				
Mepiquat	15302-91-7	1				
Meptyldinocap	6119-92-2	1				
Mercury	7439-97-6				1	1*
Mesosulfuron	400852-66-6	1				
Mesotrione	104206-82-8	1				
Metaflumizone	139968-49-3	1				
Metalaxyl	57837-19-1	1				
Metalaxyl-M	70630-17-0	1				
Metaldehyde	108-62-3	1				
Metam (incl. -potassium and -sodium)	144-54-7	1				
Metamitron	41394-05-2	1				
Metazachlor	67129-08-2	1				
Metconazole	125116-23-6	1				
Methomyl	16752-77-5	1				

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
Methoxyacetic acid	625-45-6				1	
Methoxyfenozide	161050-58-4	1				
Methyl 4-hydroxybenzoate	99-76-3				1	
Methyl decanoate	110-42-9	1			1*	
Methyl nonyl ketone	112-12-9	1*	1*			
Methyl octanoate	111-11-5	1			1*	
Metiram	9006-42-2	1				
Metobromuron	3060-89-7	1				
Metofluthrin	240494-71-7		1			
Metosulam	139528-85-1	1				
Metrafenone	220899-03-6	1				
Metribuzin	21087-64-9	1				
Metsulfuron-methyl	74223-64-6	1				
Milbemectin	51596-10-2	1				
MIT	2682-20-4		1	1*		
Musk Ketone	81-14-1			1		
Musk Xylene	81-15-2			1		
Myclobutanil	88671-89-0	1				
N,N-diethyl-meta-toluamide	134-62-3		1			
N,N-dimethylacetamide	127-19-5				1	
N,N-dimethylformamide	68-12-2				1	
Napropamide	15299-99-7	1				
Nicosulfuron	111991-09-4	1				
Nitrobenzene	98-95-3				1*	
Nitrogen	7727-37-9		1			
N-Methyl-2-pyrrolidone	872-50-4			1	1	
N-methylacetamide	79-16-3				1	
N-pentyl-isopentylphthalate	776297-69-9				1	
N-Phenyl-P-Phenylenediamine	101-54-2			1	1*	
n-Tetradecylacetate		1				
o-Aminophenol	95-55-6			1	1*	
Octabenzone	1843-05-6				1	
Octamethyl cyclotetrasiloxane	556-67-2			1	1*	
Oligomerisation and alkylation reaction products of 2-phenylpropene and phenol [Previously registered as Phenol, methylstyrenated - EC N. 270-966-8 and CAS N. 68512-30-1]	-				1	
Orange lead (lead tetroxide)	1314-41-6				1	1*
Oryzalin	19044-88-3	1				
Oxadiazon	19666-30-9	1				
Oxamyl	23135-22-0	1				
Oxasulfuron	144651-06-9	1				

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
Oxyfluorfen	42874-03-3	1				
p-(1,1-dimethylpropyl)phenol	80-46-6				1	
Paclobutrazol	76738-62-0	1				
p-aminophenol	123-30-8			1	1*	
Parabens				1		
Paraformaldehyde	30525-89-4			1		
p-cresol	106-44-5				1	
Pelargonic acid	112-05-0	1*	1		1*	
Penconazole	66246-88-6	1				
Pencycuron	66063-05-6	1				
Pendimethalin	40487-42-1	1				
Penflufen	494793-67-8	1				
Penoxsulam	219714-96-2	1				
Pentadecafluorooctanoic acid (PFOA)	335-67-1				1	
Pentalead tetraoxide sulphate	12065-90-6				1	1*
Penthiopyrad	183675-82-3	1				
Permethrin	52645-53-1		1			
Pethoxamid	106700-29-2	1				
Phenmedipham	13684-63-4	1				
phenol, styrenated,reaction mass of 2,4,6-tris(1-phenyl-ethyl)phenol and Bis(1-phenylethyl) phenol	61788-44-1				1	
Phenolphthalein				1		
Phosmet	732-11-6	1				
Picloram	1918-02-1	1				
Picolinafen	137641-05-5	1				
Picoxystrobin	117428-22-5	1				
Pirimicarb	23103-98-2	1				
Pirimiphos-methyl	29232-93-7	1				
p-METHYLAMINOPHENOL sulphate	1936-57-8			1		
Polyhexamethylene biguanide hydrochloride	27083-27-8			1		
Polyvinylpyrrolidone iodine	25655-41-8		1			
Potassium dichromate	7778-50-9				1	
Potassium sorbate	24634-61-5		1		1*	
p-phenylenediamine	106-50-3			1	1*	
Prochloraz	67747-09-5	1				
Profoxydim	139001-49-3	1				
Prohexadione	127277-53-6	1				
Propamocarb	24579-73-5	1				
Propan-2-ol	67-63-0		1		1*	
Propaquizafop	111479-05-1	1				
Propargite	2312-35-8				1	

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
Propiconazole	60207-90-1	1	1			
Propineb	12071-83-9	1				
Propoxycarbazone	145026-81-9	1				
propyl 4-hydroxybenzoate	94-13-3				1	
Propyzamide	23950-58-5	1				
Proquinazid	189278-12-4	1				
Prosulfocarb	52888-80-9	1				
Prosulfuron	94125-34-5	1				
Prothioconazole	178928-70-6	1				
Pymetrozine	123312-89-0	1				
Pyraclostrobin	175013-18-0	1				
Pyraflufen-ethyl	129630-19-9	1				
Pyrethrins	121-21-1	1				
Pyridaben	96489-71-3	1				
Pyridalyl	179101-81-6	1				
Pyridate	55512-33-9	1				
Pyrimethanil	53112-28-0	1				
Pyriofenone	688046-61-9	1				
Pyriproxyfen	95737-68-1	1	1			
Pyrochlore, antimony lead yellow	8012-00-8				1	1*
Pyroxsulam	422556-08-9	1				
Quaternium-15 (cis-isomer)	51229-78-8			1		
Quinmerac	90717-03-6	1				
Quinoclamine	2797-51-5	1				
Quinoxyfen	124495-18-7	1				1*
Quizalofop-P	94051-08-8	1				
Quizalofop-P-ethyl	100646-51-3	1				
Quizalofop-P-tefuryl	119738-06-6	1				
reaction mass of 1-(1,2,3,4,5,6,7,8-octahydro-2,3,8,8-tetramethyl-2-naphthyl)ethan-1-one and 1-(1,2,3,4,6,7,8,8a-octahydro-2,3,8,8-tetramethyl-2-naphthyl)ethan-1-one and 1-(1,2,3,5,6,7,8,8a-octahydro-2,3,8,8-tetramethyl-2-naphthyl)ethan-1-one	-				1	
reaction mass of 2-ethylhexyl 10-ethyl-4,4-dioctyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate and 2-ethylhexyl 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-octyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate (reaction mass of DOTE and MOTE)	-				1	
Reaction product: bisphenol-A-(epichlorhydrin),epoxy resin	25068-38-6				1	

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
(number average molecular weight ≤ 700)						
Repellents by smell of animal or plant origin/ sheep fat	98999-15-6	1*				
Repellents by smell of animal or plant origin/ tall oil crude	8002-26-4	1*				
Repellents by smell of animal or plant origin/ tall oil pitch	8016-81-7	1*				
Resorcinol	108-46-3			1*	1	
Rimsulfuron (aka renriduron)	122931-48-0	1				
Sea-algae extract (formerly sea-algae extract and seaweeds)	Not applicable	1*				
Sedaxane	874967-67-6	1				
Silicic acid (H2Si2O5), barium salt (1:1), lead-doped,	68784-75-8				1	
Silicic acid, lead salt	11120-22-2				1	1*
Silthiofam	175217-20-6	1				
Sintofen (aka Cintofen)	130561-48-7	1				
S-Methoprene	65733-16-6		1			
S-Metolachlor	178961-20-1	1				
Sodium 5-nitroguaiacolate	67233-85-6	1				
Sodium chromate	7775-11-3				1	
Sodium dichromate	10588-01-9				1	
Sodium o-nitrophenolate	824-39-5	1				
Sodium perborate,perboric acid, sodium salt	-				1	
sodium perchlorate	7601-89-0				1	
Sodium peroxometaborate	7632-04-4				1	
Sodium p-nitrophenolate	824-78-2	1				
Spinetoram	187166-15-0	1				
Spinosad	168316-95-8	1	1			
Spirodiclofen	148477-71-8	1				
Spiromesifen	283594-90-1	1				
Spirotetramat	203313-25-1	1				
Spiroxamine	118134-30-8	1				
Sucrose	57-50-1	1*				
Sulcotrione	99105-77-8	1				
Sulfosulfuron	141776-32-1	1				
Sulfurous acid, lead salt, dibasic	62229-08-7				1	1*
Sulfuryl fluoride	2699-79-8	1	1			
Tar acids, coal, crude,crude phenols	65996-85-2				1	
tau-Fluvalinate	102851-06-9	1				
Tebuconazole	107534-96-3	1	1			
Tebufenozide	112410-23-8	1				
Tebufenpyrad	119168-77-3	1				

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
Teflubenzuron	83121-18-0	1				
Tefluthrin	79538-32-2	1				
Tembotrione	335104-84-2	1				
Tepraloxydim	149979-41-9	1				
Terbuthylazine	5915-41-3	1				
Tert-butyl methyl ether	1634-04-4				1	
tert-butyl-4-methoxyphenol	25013-16-5				1	
Tetraconazole	112281-77-3	1				
Tetraethyllead	78-00-2				1	1*
Tetralead trioxide sulphate	12202-17-4				1	1*
Thiabendazole	148-79-8	1	1			
Thiacloprid	111988-49-9	1	1			
Thiamethoxam	153719-23-4	1	1			
Thiencarbazone	317815-83-1	1				
Thifensulfuron-methyl	79277-27-3	1				
Thiophanate-methyl	23564-05-8	1				
Thiram	137-26-8	1			1	
Thymol	89-83-8	1*			1*	
Tolclofos-methyl	57018-04-9	1				
toluene-2,5-diamine sulfate	615-50-9			1	1*	
tolylfluanid	731-27-1		1			
Tralkoxydim	87820-88-0	1				
Tralopyril	122454-29-9		1			
Transfluthrin	118712-89-3		1			
Triadimenol	55219-65-3	1				
Tri-allate	2303-17-5	1				
Triasulfuron	82097-50-5	1				
Triazoxide	72459-58-6	1				
Tribasic copper sulfate	1333-22-8	1*				
Tribenuron (aka metometuron)	106040-48-6	1				
Tributyltin compounds	-				1	1*
Triclopyr	55335-06-3	1				
Triclosan	3380-34-5			1*	1	
Trifloxystrobin	141517-21-7	1				
Triflumizole	68694-11-1	1				
Triflumuron	64628-44-0	1	1			
Triflusulfuron	135990-29-3	1				
Trilead bis(carbonate) dihydroxide	1319-46-6				1	1*
Trilead diarsenate	3687-31-8				1	1*
Trilead dioxide phosphonate	12141-20-7				1	1*
Trimethylamine hydrochloride	593-81-7	1			1*	
Trinexapac (aka cimetacarb ethyl)	143294-89-7	1				

Chemical Name	CAS	Plant Protection Products	Biocidal Products	Cosmetics	REACH	Water Framework Directive
Triphenyl phosphate	115-86-6				1	
Triphenyl phosphite	101-02-0				1	
Triphenyltin	-				1	
Tris(2-chloroethyl)phosphate	115-96-8				1	
Triticonazole	131983-72-7	1				
Tritosulfuron	142469-14-5	1				
Trixylyl phosphate	25155-23-1				1	
Urea	57-13-6	1*			1*	
Valifenalate (formerly Valiphenal)	283159-90-0	1				
Warfarin	81-81-2		1		1*	
Warfarin sodium	129-06-6		1			
zeta-Cypermethrin	1315501-18-8	1				
Zinc phosphide	1314-84-7	1*				
Zineb	12122-67-7		1			
Ziram	137-30-4	1			1	
Zoxamide	156052-68-5	1				

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PART 6/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annex 5 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

{COM(2016) 350 final}
{SWD(2016) 212 final}

ANNEX 5

CHEMICAL SUBSTANCES USED IN PPP OR BP, IDENTIFIED AS ENDOCRINE DISRUPTORS UNDER EACH OF THE 4 OPTIONS

Contents

The present screening was performed in the framework of a study contracted by the Commission and carried out in the context of an impact assessment to evaluate the impacts associated to options for criteria to identify endocrine disruptors under the regulations on plant protection products and biocidal products. The screening was based on available evidence (no additional testing) and needed to be carried out in a limited time. The screening methodology was developed for the purpose of the screening exercise. The results of the screening therefore do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

1. INTRODUCTION

An external contractor under supervision of the Joint Research Center (JRC), European Commission) screened the available evidence of approximately 600 chemicals (listed in Annex 4) with a method developed by the JRC and summarised in Annex 3. The screening started in May 2015 and sequentially covered active substances used in plant protection products (PPP) and biocidal products (BP), as well as a selection of substances falling under REACH Regulation, the cosmetic products Regulation and the Water Framework Directive (WFD).

The new criteria to identify endocrine disruptors (EDs) are requested by the legislation on PPP and BP and will be applicable to these two sectors. This is why this impact assessment (IA) focuses on these two sectors. However, it is acknowledged that the new criteria may also have repercussions on other EU legislation containing specific provisions regarding EDs (for example REACH and the WFD). Therefore, the screening is carried out also on a selection of substances falling under REACH Regulation, the Cosmetic Products Regulation and the WFD.

The work is expected to last until end of May 2016. Results for active substances used in PPP and BP were available by February 2016 and are reported below, while the screening of the chemicals falling under REACH, the cosmetics products Regulation and WFD was still on-going when this report was drafted.

The results for substances used in PPP and BP constitute the basis for this IA and give an estimation of which substances are expected to fall under each of the four options for the criteria to identify EDs, as outlined in the roadmap. The screening results do not substitute evaluations of individual substances to be carried out under the respective chemical legislations and do not pre-empt the regulatory conclusions that may eventually be drawn.

The contractor was selected following public procurement rules using the Framework Contract (FWC) SANCO/2012/02/011 (Specific Contract SANTE/2015/E3/001). The contractor is bound by conflict of interest and confidentiality rules.

The methodology, the results of the screening, and the contractor's details will be published once the screening is finalised, which is expected by end June 2016.

The results of the screening on PPP and BP were based on the extensive data sets available in the approval/renewal dossiers, plus several studies from the public scientific literature stored in EU and international databases. Most of these studies were considered in the screening. Due to time constraints, a minority of them (most from US-EPA EDSP and ToxCast ER model databases and some from EU EASIS database) could not be included in the screening by February 2016 and were therefore not considered in the results used for this IA. These additional data were anyhow considered in a refinement of the results that will be published in the final study report expected by end June 2016.

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

2. SCREENING RESULTS FOR ACTIVE SUBSTANCES USED IN PPP

A total of 324 active substances used as PPP were screened. The selection of the chemicals for the IA screening exercise is explained in Annex 4. As of January 1, 2016, there are 482 substances approved in the EU market; 147 fungicides, 123 herbicides, 98 insecticides, and 114 other type of pesticides (Figure 1).

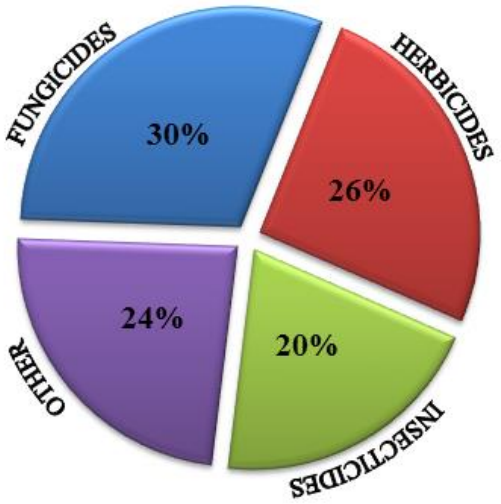

Figure 1. Approved active substances to be used in PPP in the EU, by 01/01/2016.

The screened active substances identified as potential EDs under each of the options are summarised in Figure 3 and listed in Table 2 (Option 1, Option 2, Option 3 Category I, Option 4). Table 3 also gives the chemical class according to Annex III in Regulation (EC) No 1185/2009 (Regulation on pesticides statistics)[1].

The results of the screening were filtered for other "cut off" criteria:

1. none of the substances identified as potential ED were classified or to be classified as M1 nor persistent in the environment. Substances persistent in the environment were identified using the results of the study reported in "Ad-hoc study to support the initial establishment of the list of candidates for substitution as required in Article 80(7) of Regulation (EC) No 1107/2009"[2] .

[1] Pesticides are generally divided into three broad groups; insecticides, herbicides and fungicides. To further refine the categorisation, pesticides can be divided into chemical classes, as done in Regulation EC No 1185/2009. This may be of importance if most or all substances within the same chemical class will be banned, because then the likelihood of finding an appropriate substitute to fight a certain pest decreases.

[2] Arcadia International (2013). Ad-hoc study to support the initial establishment of the list of candidates for substitution as required in Article 80(7) of Regulation (EC) No 1107/2009. Framework Contract for evaluation and evaluation related services - Lot 3: Food Chain. Final Report, retrieved from: http://ec.europa.eu/food/plant/pesticides/approval_active_substances/docs/cfs_final_report_072013_en.pdf.

2. substances which are classified or to be classified as C1, or R1 were flagged and excluded from the analysis of the impacts in the different policy areas (in particular agriculture and trade). In this way, substances which are already having regulatory consequences under Regulation (EC) No 1107/2009 under consideration of other "cut off" criteria are not double counted (Figure 2 and Table 3).

The screening of chemical substances used in PPP or BP resulted in the same number of active substances identified as potential EDs under Option 2 and Option 3 Category I, while the number of substances identified under Option 4 is a subset of these. Option 1 (interim criteria) identifies almost twice as many substances than Option 2 or Option 3 Category I, but only a small overlap (5 substances) exists between them, see table 2 for more details.

A total of 37 substances are identified under Option 1 as potential ED, but are not overlapping with the substances identified under Options 2, 3 Category I, or 4. Consequently they are considered to be **false positives** because they are identified as potential EDs under Option 1 without appearing to have ED properties according to Options 2, 3 and 4 (Table 1). This is because the approach followed for Option 1 and Options 2, 3 Category I, and 4 differ: while the interim criteria are based on potential categorisation of substances as suspected of being carcinogenic (C2) or suspected of being toxic for reproduction (R2), Options 2 to 4 are based on implementation of the WHO definition of EDs (adverse effects, mode of action and causal link).

The results also show that Option 1 (interim criteria) did not identify all active substances that were considered ED under Options 2, 3 Category I, or 4. These 21 substances are **false negatives** because substances identified as potential ED using the WHO definition are not identified under Option 1 (Table 1).

A graphic illustration of the overlap between the options can be seen in Figure 4. The figure shows that all substances identified by Option 4 represent a subset of the substances identified under Option 2 (equivalent to those under Option 3 Category I). It also clear that most of the substances identified under Option 1 do not overlap with those identified under Option 2, 3 Category I, and 4 (thus being either false negatives or false positives as explained above). Finally, all substances falling under the cut-off criteria overlap with substances under Option 1, while only a subset of them overlaps with substances under Option 2, 3 Cat I and 4.

Option 3 introduces the concept of additional categories, which would have no direct regulatory consequences. The substances identified under Option 3 Category I, Category II and Category III are reported in Table 4.

Additional information available on:
http://ec.europa.eu/food/plant/pesticides/approval_active_substances/index_en.htm

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

Table 1. False positive and false negatives identified for Option 1 by the screening.

	PPP	BP
False positives (identified under Option 1 but not under Options 2 to 4)	37	13
False negatives (identified under Options 2 to 4 but not under Option 1)	21	2

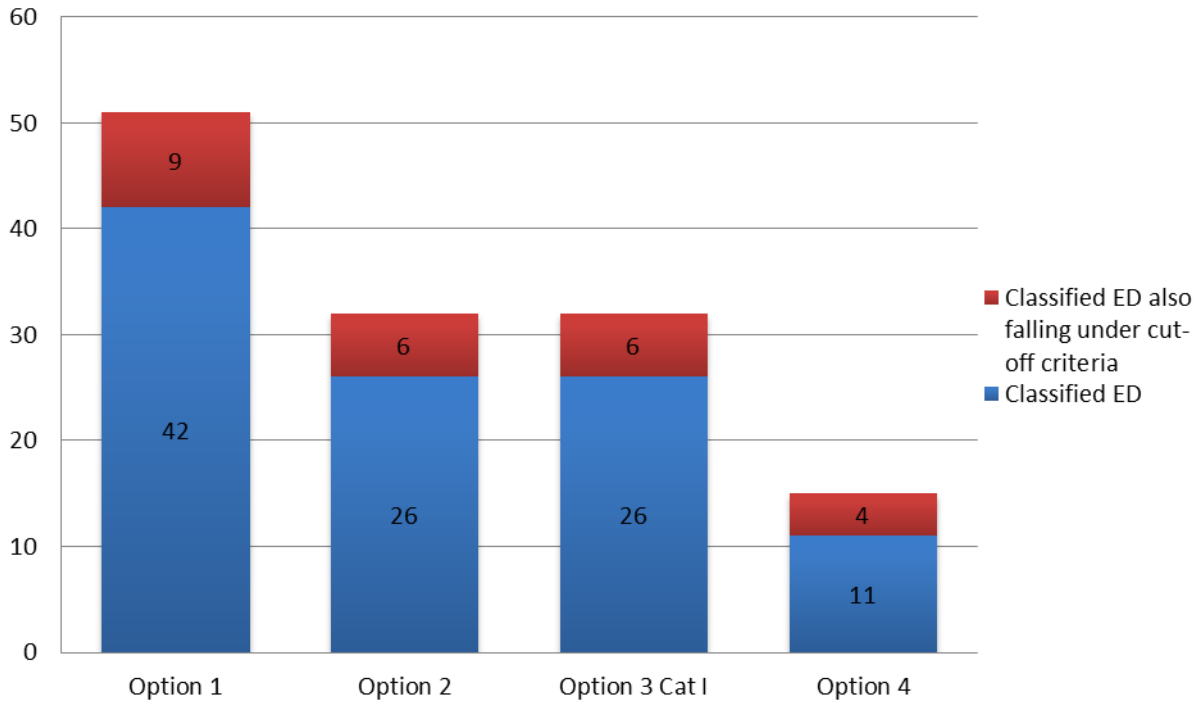

Figure 2. Number of active substances used in PPP identified as potential EDs under each of the four options: Option 1, Option 2, Option 3 Category I, Option 4. Substances identified as potential ED and also classified as C1 or R1 are reported separately in this figure.

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

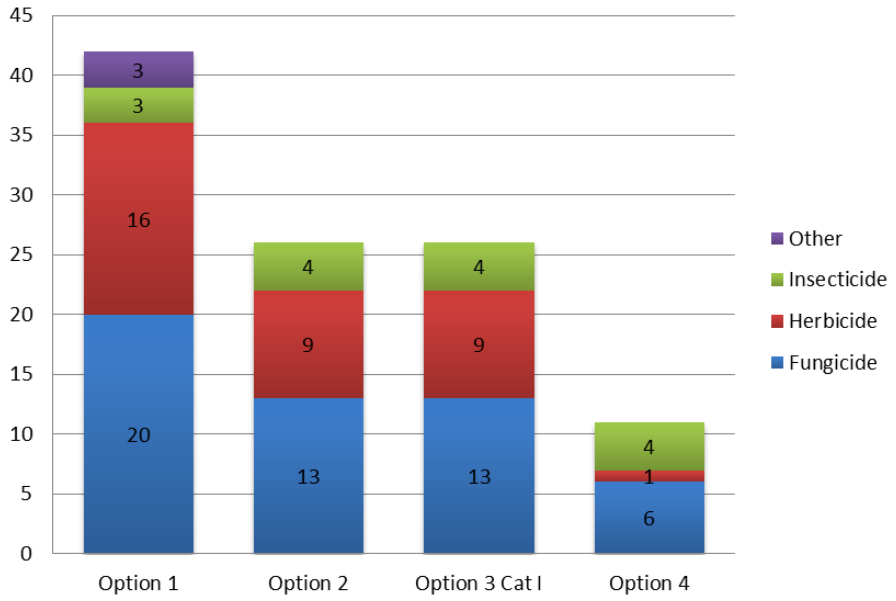

Figure 3. Number of substances classified as potential ED by PPP major group excluding substances that are classified as C1 or R1.

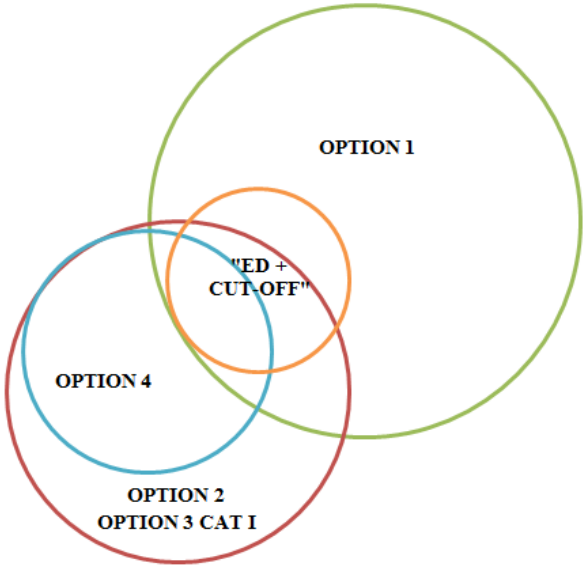

Figure 4. Overlap of active substances used as PPP screened in the framework of this IA and identified as potential ED under the four options: Option 1, Option 2, Option 3 Category I, and Option 4. The circle "ED + cut off" represents substances that are identified as potential ED and also classified as C1 or R1 and therefore falling under the cut-off criteria in the PPP Regulation.

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

Table 2. Active substances used in PPP identified as potential ED during the screening study (substances identified as potential ED and classified as C1 or R1 are excluded)

Option 1 (total 42)	Option 2 and Option 3 Cat I (total 26)	Option 4 (total 11)
1-Naphthylacetamide	2,4-D	8-hydroxyquinoline
1-Naphthylacetic acid	8-hydroxyquinoline	Cypermethrin
8-hydroxyquinoline	Boscalid	Fenamidone
Abamectin	Cypermethrin	Flubendiamide
Benthiavalicarb	Desmedipham	Malathion
Bromoxynil	Fenamidone	Mancozeb
Captan	Flubendiamide	Metiram
Chlorotoluron	Iprodione	Pendimethalin
Cycloxydim	Lenacil	Spirodiclofen
Cymoxanil	Malathion	Tetraconazole
Dazomet	Mancozeb	Ziram
Dimoxystrobin	Maneb	
Fenbuconazole	Metiram	
Fenpropimorph	Myclobutanil	
Fluazifop-P-butyl	Oxadiazon	
Fluazinam	Pendimethalin	
Flupyrsulfuron-methyl	Propyzamide	
Halosulfuron methyl	Spirodiclofen	
Hymexazol	Tebuconazole	
Indolylbutyric acid	Tepraloxydim	
Ipconazole	Tetraconazole	
Isoproturon	Thiophanate-methyl	
Isopyrazam	Thiram	
Isoxaflutole	Tralkoxydim	
Maneb	Triflusulfuron	
Metam	Ziram	
Metconazole		
Metribuzin		
Myclobutanil		
Prochloraz		
Profoxydim		
Prothioconazole		
Pymetrozine		
Quinoclamine		
Quizalfop-P		
Spirotetramat		
Spiroxamine		
Tebuconazole		
Tembotrione		
Tepraloxydim		
Thifensulfuron-methyl		
Triadimenol		

Table 3. Active substances used as PPP identified as potential EDs under each of the four options: Option 1, Option 2 and Option 3 Category I, Option 4. Substances that are classified as C1 or R1 are identified and reported in the column "ED + cut off".

Note: A cell containing a "1" indicates that the substance was identified as potential ED under the respective option. An empty cell indicates that the substance was NOT identified as ED under the respective option. False positives are substances identified under Option 1, but not under Option 2 and Option 3 Category I (e.g. Abamectin). False negatives are those substances identified under Option 2 and Option 3 Category I but not identified under Option 1 (e.g., Malathion).

	Substance	Option 1	Option 2 + Option 3 Cat I	Option 4	"ED + cut-off "	Chemical class
INSECTICIDE	**Abamectin**	**1**				INSECTICIDES PRODUCED BY FERMENTATION
	Malathion		**1**	**1**		ORGANOPHOSPHORUS INSECTICIDES
	Flubendiamide		**1**	**1**		PYRAZOLE (PHENYL-) INSECTICIDES
	Cypermethrin		**1**	**1**		PYRETHROID INSECTICIDES
	Pymetrozine (A)	**1**				PYRIDINE INSECTICIDES
	Thiacloprid	**1**			**1**	PYRIDYLMETHYLAMINE INSECTICIDES
	Spirodiclofen		**1**	**1**		TETRONIC ACID INSECTICIDES
	Spirotetramat	**1**				UNCLASSIFIED INSECTICIDES-ACARICIDES
FUNGICIDE	**Cymoxanil**	**1**				ALIPHATIC NITROGEN FUNGICIDES
	Boscalid		**1**			AMIDE FUNGICIDES
	Prochloraz	**1**				AMIDE FUNGICIDES
	Isopyrazam	**1**				ANILIDE FUNGICIDES
	Thiophanate-methyl		**1**			BENZIMIDAZOLE FUNGICIDES
	Benthiavalicarb	**1**				CARBAMATE FUNGICIDES
	Cyproconazole	**1**	**1**	**1**	**1**	CONAZOLE FUNGICIDES
	Epoxiconazole	**1**	**1**	**1**	**1**	CONAZOLE FUNGICIDES
	Fenbuconazole	**1**				CONAZOLE FUNGICIDES
	Ipconazole	**1**				CONAZOLE FUNGICIDES
	Metconazole	**1**				CONAZOLE FUNGICIDES
	Myclobutanil	**1**	**1**			CONAZOLE FUNGICIDES
	Prothioconazole	**1**				CONAZOLE FUNGICIDES
	Tebuconazole	**1**	**1**			CONAZOLE FUNGICIDES
	Tetraconazole		**1**	**1**		CONAZOLE FUNGICIDES
	Triadimenol	**1**				CONAZOLE FUNGICIDES
	Triflumizole	**1**	**1**	**1**	**1**	CONAZOLE FUNGICIDES
	Iprodione		**1**			DICARBOXIMIDE FUNGICIDES
	Fluazinam	**1**				DINITROANILINE FUNGICIDES
	Mancozeb		**1**	**1**		DITHIOCARBAMATE FUNGICIDES
	Maneb	**1**	**1**			DITHIOCARBAMATE FUNGICIDES
	Metiram		**1**	**1**		DITHIOCARBAMATE FUNGICIDES
	Thiram		**1**			DITHIOCARBAMATE FUNGICIDES
	Ziram		**1**	**1**		DITHIOCARBAMATE FUNGICIDES
	Fenamidone		**1**	**1**		IMIDAZOLE FUNGICIDES
	Fenpropimorph	**1**				MORPHOLINE FUNGICIDES
	Metam	**1**				OTHER SOIL STERILANTS
	Hymexazol	**1**				OXAZOLE FUNGICIDES

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

	Substance	Option 1	Option 2 + Option 3 Cat I	Option 4	"ED + cut-off "	Chemical class
	Captan	**1**				PHTHALIMIDE FUNGICIDES
	8-hydroxyquinoline	**1**	**1**	**1**		QUINOLINE FUNGICIDES
	Dimoxystrobin	**1**				STROBILURINE FUNGICIDES
	Spiroxamine	**1**				UNCLASSIFIED FUNGICIDES
HERBICIDE	**Propyzamide**		**1**			AMIDE HERBICIDES
	Halosulfuron methyl	**1**				ANILIDE HERBICIDES
	Fluazifop-P-butyl	**1**				ARYLOXYPHENOXY- PROPIONIC HERBICIDES
	Quizalofop	**1**				ARYLOXYPHENOXY- PROPIONIC HERBICIDES
	Desmedipham		**1**			BIS-CARBAMATE HERBICIDES
	Carbetamide	**1**			**1**	CARBAMATE HERBICIDES
	Cycloxydim	**1**				CYCLOHEXANEDIONE HERBICIDES
	Tepraloxydim**	**1**	**1**			CYCLOHEXANEDIONE HERBICIDES
	Tralkoxydim		**1**			CYCLOHEXANEDIONE HERBICIDES
	Pendimethalin		**1**	**1**		DINITROANILINE HERBICIDES
	Profoxydim	**1**				DINITROANILINE HERBICIDES
	Isoxaflutole	**1**				ISOXAZOLE HERBICIDES
	Bromoxynil	**1**				NITRILE HERBICIDES
	Dazomet	**1**				OTHER SOIL STERILANTS
	2,4-D		**1**			PHENOXY HERBICIDES
	Flupyrsulfuron-methyl	**1**				SULFONYLUREA HERBICIDES
	Thifensulfuron-methyl	**1**				SULFONYLUREA HERBICIDES
	Triflusulfuron		**1**			SULFONYLUREA HERBICIDES
	Metribuzin	**1**				TRIAZINONE HERBICIDES
	Amitrole	**1**	**1**	**1**	**1**	TRIAZOLE HERBICIDES
	Tembotrione	**1**				TRIKETONE HERBICIDES
	Flurochloridone	**1**	**1**		**1**	UNCLASSIFIED HERBICIDES
	Oxadiazon		**1**			UNCLASSIFIED HERBICIDES
	Quinoclamine	**1**				UNCLASSIFIED HERBICIDES
	Lenacil		**1**			URACIL HERBICIDES
	Isoproturon	**1**				UREA HERBICIDES
	Linuron	**1**	**1**		**1**	UREA HERBICIDES
	Chlorotoluron	**1**				UREA HERBICIDES
OTHER	**1-Naphthylacetamide**	**1**				OTHER PHYSIOLOGICAL PLANT GROWTH REGULATORS
	1-Naphthylacetic acid	**1**				OTHER PHYSIOLOGICAL PLANT GROWTH REGULATORS
	Indolylbutyric acid	**1**				OTHER PHYSIOLOGICAL PLANT GROWTH REGULATORS
	Difenacoum	**1**			**1**	RODENTICIDES

** Tepraloxydim non-approved on the 31/05/2015

Table 4. Active substances used in PPP identified under each of the categories of Option 3 during the screening of substances (substances identified under Category I, II, or III and also classified as C1 or R1, or persistent are included in the table and flagged with an asterisk).

Cat I (32)	Cat II (84)		Cat III (46)
2,4-D	1-Naphthylacetamide	Ipconazole	Azoxystrobin
8-Hydroxyquinoline	1-Naphthylacetic acid	Isoproturon	Benfluralin
Amitrole*	2,4-DB	Isoxaflutole	Beta-Cyfluthrin
Boscalid	Abamectin	lambda-Cyhalothrin	Bifenox
Cypermethrin	Acrinathrin	Meptyldinocap	Bupirimate
Cyproconazole*	Azadirachtin	Metaldehyde	Captan
Desmedipham	Azimsulfuron	Metazachlor	Carfentrazone-ethyl
Epoxiconazole*	Benthiavalicarb	Methoxyfenozide	Chlorpyrifos
Fenamidone	Bifenthrin	Oryzalin	Clofentezine
Flubendiamide	Bixafen	Oxasulfuron	Clomazone
Flurochloridone*	Bromoxynil	Paclobutrazol	Cyazofamid
Iprodione	Bromuconazole	Penflufen	Cyhalofop-butyl
Lenacil	Buprofezin	Penthiopyrad	Cyprodinil
Linuron*	Carbetamide	Pethoxamid	Daminozide
Malathion	Carboxin	Phenmedipham	Difenoconazole
Mancozeb	Chlorothalonil	Picolinafen	Diuron
Maneb	Chlorpropham	Prochloraz	Etofenprox
Metiram	Chlorpyrifos-methyl	Profoxydim	Famoxadone
Myclobutanil	Chlorsulfuron	Prohexadione	Fenoxaprop-P
Oxadiazon	Clethodim	Propaquizafop	Fenoxycarb
Pendimethalin	Clodinafop	Propiconazole	Fludioxonil
Propyzamide	Clothianidin	Propineb	Flumioxazin*
Spirodiclofen	Cycloxydim	Proquinazid	Fluoxastrobin
Tebuconazole	Cyflumetofen	Prosulfuron	Fluroxypyr
Tepraloxydim	Cymoxanil	Prothioconazole	Flutolanil
Tetraconazole	Dazomet	Pymetrozine	Folpet
Thiophanate-methyl	Deltamethrin	Pyraflufen-ethyl	Forchlorfenuron
Thiram	Dicamba	Pyridaben	Haloxyfop-P
Tralkoxydim	Diclofop	Pyridalyl	Hexythiazox
Triflumizole*	Diethofencarb	Pyriproxyfen	Imazalil
Triflusulfuron	Difenacoum*	Quizalofop-P-ethyl	Imidacloprid
Ziram	Diflufenican	Quizalofop-P-tefuryl	Isoxaben
	Dimethoate	Rimsulfuron	MCPA
	Dimethomorph	Sedaxane	MCPB
	Esfenvalerate	Silthiofam	Mecoprop
	Etoxazole	Spiromesifen	Mecoprop-P
	Etridiazole	Spirotetramat	Methyl octanoate
	Fenazaquin	Spiroxamine	Oxamyl
	Fenbuconazole	Tembotrione	Oxyfluorfen
	Fenhexamid	Terbuthylazine	Penconazole
	Fipronil	Thiabendazole	Phosmet
	Flonicamid	Thiacloprid*	Picoxystrobin
	Fluazifop-P	Thiamethoxam	Pirimiphos-methyl
	Fluazinam	Thifensulfuron-methyl	Propamocarb
	Flufenacet	Triadimenol	Pyraclostrobin
	Glyphosate	Triticonazole	Pyrimethanil
	Hymexazol	Tritosulfuron	tau-Fluvalinate
	Indolylbutyric acid	Valifenalate	Tefluthrin
			Tolclofos-methyl
			Tribenuron
			Trifloxystrobin
			Zoxamide

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

3. SCREENING RESULTS FOR ACTIVE SUBSTANCES USED IN BP

A total of 98 active substances contained in BP or used in treated articles were screened. Only the substances of which sufficient information was available, i.e. active substances that were approved at EU level or where an opinion of the BP Committee of ECHA was available, were screened.

Active substances and BP are approved or authorised for 22 product types. Therefore the total number of active substances per product type is of relevance. In total 700 active substance and product type combinations are approved or under review of which 266, 320, 95 and 19 for disinfectants, preservatives, pest control, and other, respectively.

A significant number of these active subsatnces is currently under review. In this review programme the existing active substances that were on the market on 14 May 2000, and are supported by companies, are included. These substances will be assessed in the review programme and, if they fulfill the required conditions, approved in accordance with a working schedule linked to groups of product types. Each year, up to 2024, about 50 dossiers will be examined.

The number and type of substances screened is directly linked to the set up of the review working programme. This implies that the screening is not representative for the active substances/product types distribution currently available on the market. For example, only 17% of the active substances used in disinfectants are screened in comparison with 52% of the pest control substances (see Figure 5). This is caused by the priority given for pest control substances in the review programme of active substances. Therefore, any result of the screening should be very cautiously interpreted for the potential impact on all product types on the market as it is not possible to judge how representative the screening results are within and across the product groups.

The screened substances identified as potential EDs under each of the options are listed in Table 5 (Option 1, Option 2 and Option 3 Category I, and Option 4).

Substances identified as potential ED under each of the options considered for the screening may also fall under the so called "cut-off criteria" mentioned in Section 2 of this Annex[3], or fulfilling the exclusion criteria (Article 5(1) of the BP Regulation[4]). The substances fulfilling these criteria are listed in Table 6; in the same table the substances identified as potential EDs and being used in both PPP and BP are also indicated.

[3] This refers to the substances also approved for use in PPP.

[4] Article 5(1) of BP Regulation: CMR, PBT, vPvB or having endocrine-disrupting properties (C=carcinogen category 1A or 1B; M= mutagen category 1A or 1B; R=toxic for reproduction category 1A or 1B; substances meet the criteria for being Persistent Bioaccumulative and Toxic or very Persistent and very Biocaccumulative according to Annex XIII to Regulation (EC) No 1907/2006).

Option 3 introduces the concept of additional categories. The substances identified under Option 3 in the Category I, Category II and Category III are reported in Table 6. For Categories I, II and III, 5, 26 and 8 substances were identified respectively.

In total 16 biocidal substances were identified as potential ED under Option 1, five substances under Option 2 and 3 Category I, and three substances under Option 4. The number of false positives and false negatives show the same trend for BP as for PPP. A total of 13 substances are identified under Option 1 for BP but not under Option 2 and 3 Cat I (false positives). The interim criteria failed to identify two substances that have endocrine modes of actions (false negatives) that were identified as potential EDs under Option 2 and 3 Cat I.

From Table 6 it becomes clear that of the substances identified as potential ED under Option 2, Option 3 Category I and Option 4, one (Cyproconazole) is currently fulfilling the exclusion criteria. However, taking into account the screening cannot be considered representative for the active substances/product types currently available on the market, it is challenging to extrapolate this result to all BP substances.

Further, iodine (used as disinfectant) is identified as potential ED under Options 2 and 3 Category I. Iodine is a physiologically essential element and needed for maintaining hormone homeostasis. It is required for the synthesis of the thyroid hormones, which control metabolism and play an important role in reproduction, growth and development. This means that both iodine deficiency as well as excess iodine can affect thyroid hormone levels and is to be considered as an endocrine effect. However, as essential element it differs from typical xenobiotic substances, which are not needed for the functioning of the human or animal body. ECHA stated in the assessment report[5] on iodine that the concept of endocrine disruption is not meaningful for essential elements as iodine.

[5] Assessment report on iodine, available on the section of ECHA website providing information on biocidal active substances: http://echa.europa.eu/web/guest/information-on-chemicals/biocidal-active-substances.

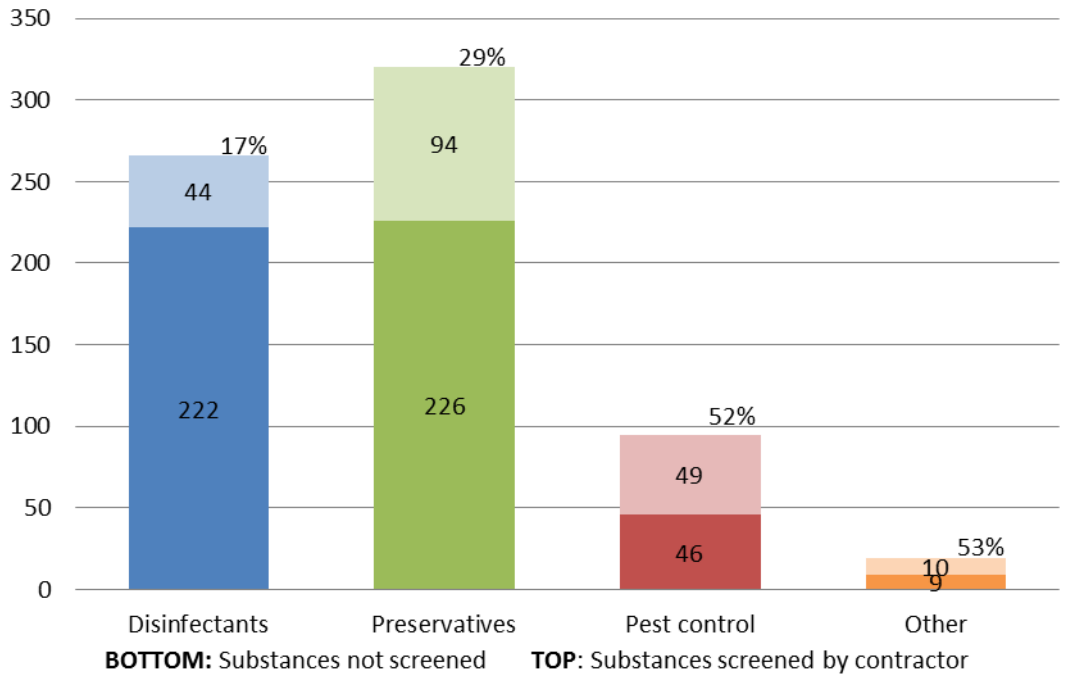

Figure 5. Number of biocidal active substances arranged by major group of product types, included (bottom) and not included (top) in the screening.

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

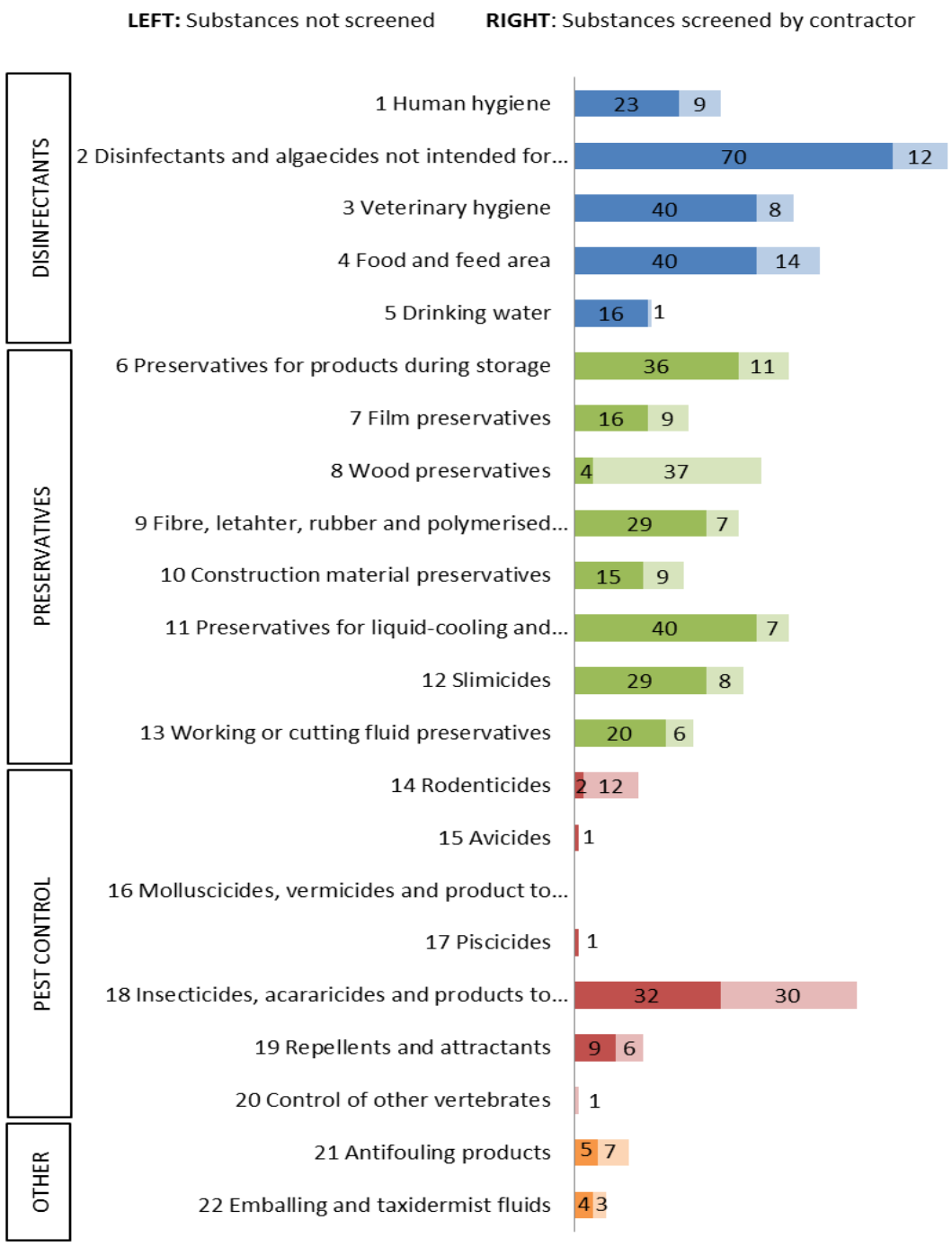

Figure 6. Number of biocidal active substances arranged by product type included and not included in the screening.

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

Table 5. Biocidal active substances identified under Options 1, Option 2 and 3 Cat I, and Option 4 as potential EDs.

Option 1 (16)	Option 2 and Option 3 Cat I (5)	Option 4 (2)
Abamectin (aka avermectin)	Cypermethrin	Cypermethrin
Boric acid	Cyproconazole	Cyproconazole
Boric oxide	Iodine	Zineb
Copper pyrithione	Tebuconazole	
Creosote	Zineb	
Cyproconazole		
Dazomet		
Difenacoum		
Disodium octaborate tetrahydrate		
Disodium tetraborate		
Disodium tetraborate decahydrate		
Disodium tetraborate pentahydrate		
Fenpropimorph		
Tebuconazole		
Thiacloprid		
Zineb		

Table 6. Biocidal active substances identified as potential EDs under the three categories of Option 3.

Option 3 Cat I (5)	Option 3 Cat II (26)	Option 3 Cat III (8)
Cypermethrin	4,5-Dichloro-2-octylisothiazol-3(2H)-one	1R-trans phenothrin
Cyproconazole	Abamectin (aka avermectin)	Chlorophacinone
Iodine	Bifenthrin	DDACarbonate
Tebuconazole	Boric acid	Didecyldimethylammonium chloride; DDAC
Zineb	Boric oxide	Etofenprox
	Clothianidin	Fenoxycarb
	Copper pyrithione	Folpet
	Dazomet	Imidacloprid
	DCPP	
	Deltamethrin	
	Dichlofluanid	
	Difenacoum	
	Disodium octaborate tetrahydrate	
	Disodium tetraborate	
	Disodium tetraborate decahydrate	
	Disodium tetraborate pentahydrate	
	Fipronil	
	Glutaraldehyde	
	Hydrogen cyanide	
	Lambda-Cyhalothrin	
	Permethrin	
	Propan-2-ol	
	Propiconazole	
	Pyriproxyfen	
	Thiabendazole	
	Thiamethoxam	

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

Table 7. Biocidal active substances identified as potential EDs under option 1, option 2 and option 3 Cat I, and option 4 and the associated product types.

Note: A cell containing a "1" indicates that the substance was identified as potential ED under the respective option. An empty cell indicates that the substance was NOT identified as potential ED under the respective option. False positives are substances identified under Option 1, but not under Option 2 and Option 3 Category I (e.g. Abamectin). False negatives are those substances identified under Option 2 and Option 3 Category I but not identified under Option 1 (e.g., Malathion).

	Substance	Option 1	Option 2 and Option 3 Cat I	Option 4	Cut-off PPP	BP Exclusion criteria	Product Type No	Main group of product types
BIOCIDES AND PESTICIDES	Abamectin (aka avermectin)	1					18	PEST CONTROL
	Cypermethrin		1	1			8; 18	PRESERVATIVES; PEST CONTROL
	Cyproconazole	1	1	1	1	1	8	PRESERVATIVES
	Dazomet	1					6; 8; 12	PRESERVATIVES
	Difenacoum	1			1	1	14	PEST CONTROL
	Fenpropimorph	1					8	PRESERVATIVES
	Tebuconazole	1	1				7; 8; 10	PRESERVATIVES
	Thiacloprid	1			1	1	8	PRESERVATIVES
BIOCIDES	Boric acid	1				1	8	PRESERVATIVES
	Boric oxide	1				1	8	PRESERVATIVES
	Copper pyrithione	1					21	OTHER BIOCIDAL PRODUCTS
	Creosote	1				1	8	PRESERVATIVES
	Disodium octaborate tetrahydrate	1				1	8	PRESERVATIVES
	Disodium tetraborate	1				1	8	PRESERVATIVES
	Disodium tetraborate decahydrate	1				1	8	PRESERVATIVES
	Disodium tetraborate pentahydrate	1				1	8	PRESERVATIVES
	Iodine		1				1; 3; 4; 22	DISINFECTANTS. OTHER
	Zineb	1	1	1			21	OTHER BIOCIDAL PRODUCTS
	TOTAL	**16**	**5**	**3**	**3**	**10**		

Table 8. Biocidal active substances identified as potential EDs under the three categories of Option 3, the associated product types, the applicability of cut-off values for PPP and the exclusion[6] as included in BP Regulation[7].

	Substance	Option 3 Cat I	Option 3 Cat II	Option 3 Cat III	Cut-off PPP	BP Exclusion criteria	Product Type No	Main group
BIOCIDES AND PESTICIDES	Abamectin (aka avermectin)		1				18	PEST CONTROL
	Bifenthrin		1				8	PRESERVATIVES
	Clothianidin		1				8; 18	PRESERVATIVES; PEST CONTROL
	Cypermethrin	1					8; 18	PRESERVATIVES; PEST CONTROL
	Cyproconazole	1			1	1	8	PRESERVATIVES
	Dazomet		1				6; 8; 12	PRESERVATIVES
	Deltamethrin		1				18	PEST CONTROL
	Difenacoum		1		1	1	14	PEST CONTROL
	Etofenprox			1			8; 18	PRESERVATIVES; PEST CONTROL
	Fenoxycarb			1			8	PRESERVATIVES
	Fipronil		1				18	PEST CONTROL
	Folpet			1			6; 7; 9	PRESERVATIVES
	Imidacloprid			1			18	PEST CONTROL
	Lambda-Cyhalothrin		1				18	PEST CONTROL
	Propiconazole		1				7; 8; 9	PRESERVATIVES
	Pyriproxyfen		1				18	PEST CONTROL
	Tebuconazole	1					7; 8; 10	PRESERVATIVES
	Thiabendazole		1		1		7; 8; 9; 10	PRESERVATIVES
	Thiamethoxam		1				8,18	PRESERVATIVES; PEST CONTROL

[6] Article 5 of BP Regulation: CMR, PBT, vPvB or ED (C=carcinogen Category IA or 1B; M= mutagen category 1A or 1B; R=toxic for reproduction category 1A or 1B; Persistent Bioaccumulative Toxic or vPvB according to Annex XIII to Regulation (EC) No 1907/2006).

[7] In addition to exclusion criteria the BP Regulation provides that active substances should be designated as candidate for substitution if they have intrinsic hazardous properties. Article 10(1) of the BP Regulation stipulates the criteria for designating a substance as a candidate for substitution

	Substance	Option 3 Cat I	Option 3 Cat II	Option 3 Cat III	Cut-off PPP	BP Exclusion criteria	Product Type No	Main group
BIOCIDES	1R-trans phenothrin			1			18	PEST CONTROL
	4,5-Dichloro-2-octylisothiazol-3(2H)-one (DCOIT)		1				7; 8; 9; 10; 11; 21	PRESERVATIVES; OTHER BIOCIDAL PRODUCTS
	Boric acid		1			1	8	PRESERVATIVES
	Boric oxide		1			1	8	PRESERVATIVES
	Chlorophacinone			1		1	14	PEST CONTROL
	Copper pyrithione		1				21	OTHER BIOCIDAL PRODUCTS
	DCPP		1				1; 2; 4	DISINFECTANTS
	DDACarbonate			1			8	PRESERVATIVES
	Dichlofluanid		1				7; 8; 21	PRESERVATIVES; OTHER BIOCIDAL PRODUCTS
	Didecyldimethylammonium chloride; DDAC			1			1; 2; 3; 4; 6; 8; 10; 11; 12	PRESERVATIVES; DISINFECTANTS
	Disodium octaborate tetrahydrate		1			1	8	PRESERVATIVES
	Disodium tetraborate		1			1	8	PRESERVATIVES
	Disodium tetraborate decahydrate		1			1	8	PRESERVATIVES
	Disodium tetraborate pentahydrate		1			1	8	PRESERVATIVES
	Glutaraldehyde		1				1; 2; 3; 4; 6; 11; 12; 13	DISINFECTANTS; PRESERVATIVES
	Hydrogen cyanide		1				8; 14; 18	PRESERVATIVES; PEST CONTROL
	Iodine	1					1; 3; 4; 22	DISINFECTANTS. OTHER
	Permethrin		1				8; 18	PRESERVATIVES; PEST CONTROL
	Propan-2-ol		1				1; 2; 4	DISINFECTANTS
	Zineb	1					21	OTHER BIOCIDAL PRODUCTS
	TOTAL	**5**	**26**	**8**	**3**	**9**		

4. CONCLUSIONS

The results presented in this Annex show that it was possible to screen the evidence available for PPP and BP chemicals with the aim to estimate which substances would fall under different options for the criteria to identify EDs.[8] This was possible not only for Option 1 (interim criteria under PPP and BP legislation), but also for the other three options which are based on the WHO definition (Options 2, 3 and 4). This means that it is possible to use scientific evidence available on EDs (test methods and results) and interpret it for an estimate on whether they may be identified as EDs.

Criteria under options 2, 3 and 4 are based on the widely agreed WHO/IPCS definition of an ED[9]. The WHO/IPCS definition is characterised by three elements: a chemical can be defined an ED; 1) if it shows an adverse effect in an intact organism (generally from in vivo animal testing); 2) if it is able to interfere with the endocrine/hormonal system (mechanistic data show the substance can act via an endocrine/hormonal mode of action); and 3) if a plausible link can be established between the endocrine mode of action and the adverse effect observed for the substance.

OECD test methods are available for four of the various endocrine modalities: the androgen (A), the oestrogen (E), the thyroid (T) and the (S) steroidogenesis modalities (often referred to as EATS modalities) (OECD 2012[10]; EFSA 2013[11]). Therefore, the present screening was limited to the available evidence related to modes of actions along these four modalities (see also Annex 3).[12] Similarly, the evidence available could only be assessed for vertebrate wildlife species, because the endocrine system of invertebrates is not well understood and test capable of discriminating adverse effects by an endocrine mode of action are not yet available.

[8] The screening study also includes screening of substances falling under REACH, Cosmetics Regulation, or Water Framework Directive (see Annex 4). The results of the screening of these substances were neither available nor relevant in the context of this impact assessment report. They will be available once the report of the screening study will be published.

[9] WHO/IPCS. 2002. Definition of an Endocrine Disruptor: an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations.

[10] OECD Guidance Document On Standardised Test Guidelines For Evaluating Chemicals For Endocrine Disruption Series on Testing and Assessment No. 150, ENV/JM/MONO(2012)22. Retrieved from: http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2012)22&doclanguage=en

[11] EFSA Scientific Committee; Scientific Opinion on the hazard assessment of endocrine disruptors: scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing effects mediated by these substances on human health and the environment. EFSA Journal 2013;11(3):31323. doi: 10.2903/j.efsa.2013.3132.

[12] A detailed description of the methodology applied in the screening will be published at the same time the Commission would propose draft measures to specify scientific criteria for the determination of endocrine-disrupting properties.

OECD Guidance[13] was used to interpret results on adverse effect and mechanistic data related to endocrine disruption. A decision tree based on information taken from the OECD GD 150[9] was used to decide whether or not enough evidence is available to categorise a substance as a potential ED (and if relevant as ED Cat I, II or III). In addition, as mentioned in Annex 3 to this Report - where the methodology applied to this screening is described - a limited weight of evidence approach based on expert judgement was necessary to evaluate the evidence available and ultimately decide whether or not a substance can be identified as a potential ED (or, if relevant, as potential ED Category II or III under Option 3). It is stressed that the weight of evidence approach could only be used to a limited extent compared to standard regulatory assessment because of the time constraints and the level of expertise of the present project.

This limited weight of evidence approach used was based, among others, on the following considerations:

a) the magnitude and nature of the adverse effects;

b) the pattern and coherence of adverse effects observed at different doses within and between studies of a similar design and across different species;

c) the weight of certain studies with respect to others: e.g. long term/chronic/repeated-dose studies versus short term/acute studies; *in vivo* tests versus *in vitro* tests; studies with clear study-design versus poorly detailed studies;

d) the biological plausibility of a causal relationship between the induced endocrine activity and the adverse effect(s);

e) the presence of overt toxicity together with the potential ED-related effects;

f) the data available on the human relevance of the effects and mode of action observed.

Thus, for instance, an isolated effect of low magnitude in one species not observed in other studies of similar design with the same species (provided the effect had been measured) would have lower weight than a case where a clear pattern of effects was seen across a number of studies and in more than one species. As this largely depends on expert judgement, this part could not be codified into the decision tree. When potential ED-related effects were observed in the presence of overt toxicity, these effects were not considered to be informative of an endocrine mode of action.

As mentioned above, some additional data could only be considered at a late stage of the screening and could therefore not be included in the results used for the IA. These additional data may refine to a limited extent the final results, in that a few substances have changed categorisation: some became identified as potential EDs, while they were

[13] OECD Work Related to Endocrine Disrupters, available on: http://www.oecd.org/env/ehs/testing/oecdworkrelatedtoendocrinedisrupters.htm

not before; others became unclassified or potential EDs Cat II or III, while they were potential EDs Cat I before. For instance, using new data from EDSP/EASIS databases and/or from the ToxCast ER prediction model, the following substances were identified as potential EDs under Option 2 and 3 Category I: flutolanil, prochloraz, pyriproxyfen, 2-phenylphenol, propiconazole, metalaxyl. For prochloraz the categorisation is elevated because of data relevant for both human health and wildlife, while for the other five substances the updated categorisation is related to data relevant for wildlife only (fish/amphibian) data. The refined results will be published in the final report of the screening, which is expected to be published by end June 2016.

The fact that additional data can affect the outcome of the screening shows how availability of experimental data can influence the conclusions with respect to the identification of a substance as an ED. To this respect, PPP and BP are based on pre-market approval ("positive list") which relies on data-rich dossiers. This pre-market approval system described above is considered as one of the strictest worldwide and the data requirements are very detailed and require extensive in vivo testing.

On the other hand, in the relatively new field of endocrine disruption, test methods to detect an endocrine mode of action have been recently developed. When these test methods are internationally validated (e.g.at OECD level), the data requirements for PPP[14] and BP[15] are updated. Studies from the public literature can provide additional weight to the body of evidence.

The screening results for PPP and BP provided in this IA - together with those refined in the final screening report to be published by end June 2016 - have a degree of uncertainty associated to any assessment in a complex field like the one of endocrine disruption. This uncertainty is determined by several factors, including the expert judgement involved in each decision, the availability of scientific evidence on the various chemicals, the developments in test methods and guidance to interpret their results.

[14] European Commission, DG SANTE. EU Legislation on PPP, available on: http://ec.europa.eu/food/plant/pesticides/legislation/index_en.htm

[15] ECHA Guidance on biocides legislation, available on: http://echa.europa.eu/guidance-documents/guidance-on-biocides-legislation

The results of the screening performed in the framework of a study contracted by the Commission do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation.

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Brussels, 15.6.2016
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PART 7/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annex 6 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

{COM(2016) 350 final}
{SWD(2016) 212 final}

ANNEX 6

ANALYTICAL METHOD USED TO COMPARE AND RANK THE OPTIONS: THE MULTI-CRITERIA ANALYSIS

Contents

This Annex focuses on the assessment of potential impacts, which build on the results of the screening study explained in Annexes 3 to 5. The results of the screening do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation. The methods and results presented in this Annex are to be interpreted as an estimation of the potential impacts.

The MCAs results are not concluding on any preferred option for setting scientific criteria to identify endocrine disruptors, but aim at providing additional information to decision makers with regards to the potential impacts expected when implementing the criteria, after those would have been selected on the basis of science (two MCAs were performed: Options 1 to 4 under the current regulatory context, and Options A compared to Options B and C).

At a preliminary stage of the impact assessment it was anticipated that Option C should be discarded, nevertheless it was maintained for the analysis of the impacts for methodological reasons (see Section 4.2.3 of the main report and Annexes 6 and 7). Option C only applies to the PPP Regulation.

1. INTRODUCTION

In order to compare and rank the options considered in the course of this impact assessment (IA), the methods presented in the Tool #55 of the Better Regulation Guidelines ("Useful analytical methods to compare options or assess performance") were analysed and compared with respect to the following dimensions: availability of evidence/data and appropriateness of each method for assessing the key impacts listed in the Tool #16 of the Better Regulation Guidelines ("Identification/screening of impacts") that are important for this IA.

2. SELECTION OF THE METHOD

1.1. Analysis of availability of evidence and data

The analysis of the data and evidence showed that the data were insufficient, partial or not sufficiently robust for assessing the impacts on agriculture, trade, human health and environment.

In particular:

- For agricultural/trade impacts, basic data are either not available, not ready, or not easy to use (e.g. information on uses of active substances per crop and per pest is patchy; yield decreases in crop production due to the absence of a plant protection product - crucial for any estimation of impacts - can only be based on significant assumptions; extrapolation from case studies based on few Member States to the whole EU will be difficult due to e.g. differences in climate conditions; extrapolation from the impacts related to the non-approval of one active substance to the non-approval of several active substances is technically complex and entails difficulties for the comparison of the options; some agronomic impacts cannot be quantified in any case for example due to resistance to target organisms).
- For health impacts, no active substance identified in the options can be linked directly to a disease due to general lack of scientific studies proving such links. Therefore, any quantification regarding health costs is controversial and any approach to estimate health impacts will differ from that chosen to calculate the agriculture/trade impacts creating a strong imbalance between the assessments of the areas. Further, due to the already high protection of health in the plant protection products (PPP) and biocidal products (BP) legislations (no use of substances that pose a serious health or environmental concern would be authorised), a comparison between Option A and Option B (approaches to regulatory decision making) would be difficult.
- For environmental impacts, assessing the impacts on biodiversity/ecosystems is even more difficult than impacts on human health (e.g. in the study of DG ENV[1] on benefits of chemical legislation, assessments can only be done based on a few case studies).

Also, a sufficient number of representative and reliable case studies to be used in assessing the impacts in all areas were not available.

[1] RPA et al. 2015. Study on the Calculation of the Benefits of Chemical Legislation on Human Health and the Environment, Draft final report for DG Environment, December 2015, Loddon, Norfolk, UK

1.2. Analysis of analytical methods

The selection of the analytical method started by considering the methods listed in the Better Regulation Guidelines' Tool #55: Cost Benefit Analysis (CBA), Least Cost Analysis (LCA), Multi-Criteria Analysis (MCA), Cost-Effectiveness Analysis (CEA), Counterfactual Analysis, and SWOT Analysis.

Cost-Benefit Analysis, Least Cost Analysis and Cost-Effectiveness Analysis were discarded as potential methods because robust assumptions for quantifying and monetizing the impacts were not available.

The Counterfactual analysis was also discarded as it is an analytical method that is more appropriate for evaluations as it looks at what would have happened in the absence of an intervention.

The SWOT analysis was also discarded as it is not an analytical method per se, but it is used to identify Strengths, Weaknesses, Opportunities and Threats in relation to a project/organisation.

In light of the availability of evidence/data and suitability of the methods presented in the Tool #55 of the Better Regulation Guidelines, the Multi-Criteria Analysis was considered the most appropriate method because:

- it is useful when impacts cannot be fully quantified or monetised;
- it allows impacts to be reconciled with policy objectives;
- it can capture distributional impacts (e.g. in terms of stakeholder types);
- it enables to judge the pros and cons of options along the MCA-criteria chosen for the comparison;
- it allows the selected MCA-criteria to determine the results obtained by assigning weights to them.

The Multi-Criteria Analysis has also many advantages over informal judgement unsupported by proper and robust analysis:

- the choice of objectives and MCA-criteria are open to analysis and to change if they are felt to be inappropriate. The objectives and MCA-criteria were discussed by the Impact Assessment Steering Group (IASG);
- performance scores and weights are explicit and are developed according to established techniques. They can easily be amended if necessary;
- a sensitivity analysis can be easily performed, highlighting how the weights assigned to MCA-criteria influence the final result;
- as scores and weights are used, it provides an audit trail.

3. THE MULTI-CRITERIA ANALYSIS

A key step in determining the MCA-methodology to be applied was to assess whether trade-offs between different MCA-criteria were acceptable, considering that some public decisions admit such trade-offs.

Admitting trade-offs would imply that good performance on one MCA-criterion can, in principle, compensate for weaker performance on another; however there may be some circumstances, for example, where ethical, health or environmental issues are central, where trade-offs of this type are not acceptable. If it is not acceptable to consider trade-offs between MCA-criteria, then a non-compensatory MCA should be employed.

After assessing the appropriateness of a compensatory MCA-method vs. a non-compensatory MCA-method, it was concluded that the non-compensatory methods should be followed in the course of this IA in view of the following elements:

1. *Performance assessment of options based on relative performance.* The performance of the options was evaluated based on relative performance. In order to be able to compensate correctly it is necessary to determine the actual performance of an option, and then transpose it in a standardised measurement unit so that compensation can be performed. However, in the current situation it is not possible to determine actual performance; it is only possible to specify if one option is performing better or worse than another, without being able to determine with a sufficient accuracy the magnitude of the difference between the two options. Being in the impossibility to determine accurately how much better or how much worse an option is performing on a certain MCA-criterion; it is considered inappropriate in this case to compensate performance, as such compensation would be rather arbitrary.
2. *Unacceptable trade-offs between MCA-criteria.* It was determined that in the case of this IA it is not acceptable to allow trade-offs between MCA-criteria. For example, in the case of a compensatory method, if an option is performing weak on a certain MCA-criterion, this can be offset by a very strong performance on another MCA-criterion. As a concrete example, a weak performance on environment related MCA-criteria can be totally offset by an excellent performance on trade related MCA-criteria. However, the purpose of this IA is to determine the option that is performing well on the most MCA-criteria and not offset bad performance by excellent performance, especially when the actual performance of the option cannot be determined (as mentioned in the previous point).

Before carrying-out the MCA, it is fundamental to consider what the main purpose of the intervention and the options to be compared are.

The methodology was illustrated to the members of the IASG at the meetings on January 19 and February 1, 2016.

1.3. Main purpose of the intervention

As described in Section 3 of the main IA report, the comparison of the options should consider how each is contributing to the attainment of the main policy objectives:

- General objective within the Treaty, as they are the legal basis for both the PPP and BP Regulations:
    - ensuring a high level of protection to human health and the environment;
    - strengthening the functioning of the internal market

In addition, for the PPP Regulation the two objectives mentioned above should be considered while improving agricultural production (see Article 1 of Regulation (EC) No 1107/2009).

The compliance with international obligations, notably under the Sanitary and Phyto-sanitary (SPS) and Technical Barriers to Trade (TBT) Agreements in the World Trade Organisation are also important considerations.

- Specific objective for PPP and BP Regulations:
    - providing for legal clarity, predictability and coherence in the identification of endocrine disruptors (ED);
    - providing for scientific ED-criteria that are operational in terms of regulatory decision-making;
    - offering possibility to apply these ED-criteria across both the PPP and BP Regulations.

1.4. The options to be compared

As described in Section 4 of the IA report, the following options were compared:

Aspect I: Setting scientific criteria to identify EDs

- ***Option 1:*** *No policy change (baseline).* No criteria are specified and the interim criteria set in the PPP and BP Regulations continue to apply.
- ***Option 2****: WHO/IPCS definition to identify endocrine disruptors.*
- ***Option 3****: WHO/IPCS definition to identify endocrine disruptors and introduction of additional categories based on the different strength of evidence for fulfilling the WHO/IPCS definition.*
- ***Option 4****: WHO/IPCS definition to identify endocrine disruptors and inclusion of potency as element of hazard characterization.*

Aspect II: Implementation of the ED criteria / approach to regulatory decision making

- ***Option A****: No policy change (Baseline).* The regulatory consequences under the PPP and BP Regulations remain unchanged and therefore different between them.
- ***Option B****: Adjustment of the PPP derogations in light of current scientific knowledge*

- ***Option C**: Alignment of the PPP with the BP Regulation by introducing further socio-economic considerations.*

4. STEPS OF THE MULTI-CRITERIA ANALYSIS

The full application of multi-criteria analysis was based on the procedure described in the Tool #57 of the Better Regulation Guidelines ("Multi-Criteria Analysis") and followed several steps:

1. identify the "dimensions" where significant impact of the options is expected and define MCA criteria corresponding to the dimensions in order to compare key impacts of the options;
2. describe the expected performance of each option against the MCA-criteria and 'score' the options,
3. 'weighting': assign weights for each of the MCA-criteria to reflect their relative importance to the decision. The weighting was carried out through a sensitivity analysis, as explained in the following pages
4. combine the weights and scores for each of the options;
5. examining the results.

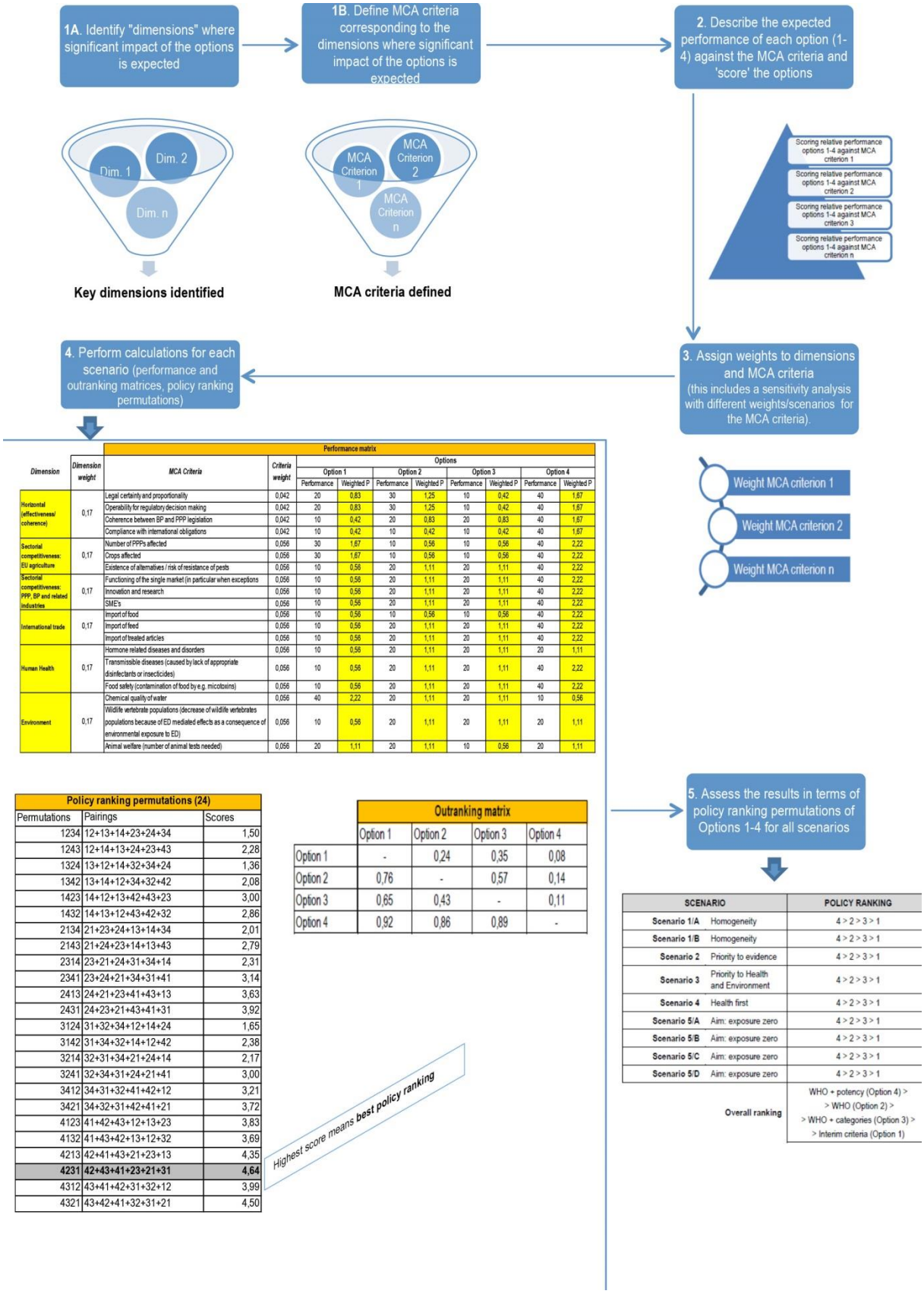
The MCA was carried out in a step-wise approach, as there were two sets of options (for aspect I and aspect II):

- Step 1: the MCA methodology will be applied to Options 1 to 4.
- Step 2: the MCA methodology will be applied to Options A to C.

The same MCA parameters (MCA-criteria, weights, performance assessment methods, etc.) were employed for both steps. The step-wise approach was selected rather than an approach comparing combined options for two major reasons:

1. The step-wise approach simplifies the already very complex analysis. Analysing the combined options would bring even more complexity into the analysis, increasing the difficulty level and potentially reducing the comprehensibility of the results to a larger audience.
2. The step-wise approach facilitates the ranking of the options for each MCA-criterion and enables for a clearer justification of the ranking order.

A graphical representation of the MCA-methodology applied is provided in Figure 1.



Dimension	Dimension weight	MCA Criteria	Criteria weight	Options							
				Option 1		Option 2		Option 3		Option 4	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Horizontal (effectiveness/ coherence)	0,17	Legal certainty and proportionality	0,042	20	0,83	30	1,25	10	0,42	40	1,67
		Operability for regulatory decision making	0,042	20	0,83	30	1,25	10	0,42	40	1,67
		Coherence between BP and PPP legislation	0,042	10	0,42	20	0,83	20	0,83	40	1,67
		Compliance with international obligations	0,042	10	0,42	10	0,42	10	0,42	40	1,67
Sectorial competitiveness: EU agriculture	0,17	Number of PPPs affected	0,056	30	1,67	10	0,56	10	0,56	40	2,22
		Crops affected	0,056	30	1,67	10	0,56	10	0,56	40	2,22
		Existence of alternatives / risk of resistance of pests	0,056	10	0,56	20	1,11	20	1,11	40	2,22
Sectorial competitiveness: PPP, BP and related industries	0,17	Functioning of the single market (in particular when exceptions	0,056	10	0,56	20	1,11	20	1,11	40	2,22
		Innovation and research	0,056	10	0,56	20	1,11	20	1,11	40	2,22
		SME's	0,056	10	0,56	20	1,11	20	1,11	40	2,22
International trade	0,17	Import of food	0,056	10	0,56	10	0,56	10	0,56	40	2,22
		Import of feed	0,056	10	0,56	20	1,11	20	1,11	40	2,22
		Import of treated articles	0,056	10	0,56	20	1,11	20	1,11	40	2,22
Human Health	0,17	Hormone related diseases and disorders	0,056	10	0,56	20	1,11	20	1,11	20	1,11
		Transmissible diseases (caused by lack of appropriate disinfectants or insecticides)	0,056	10	0,56	20	1,11	20	1,11	40	2,22
		Food safety (contamination of food by e.g. micotoxins)	0,056	10	0,56	20	1,11	20	1,11	40	2,22
Environment	0,17	Chemical quality of water	0,056	40	2,22	20	1,11	20	1,11	10	0,56
		Wildlife vertebrate populations (decrease of wildlife vertebrates populations because of ED mediated effects as a consequence of environmental exposure to ED)	0,056	10	0,56	20	1,11	20	1,11	20	1,11
		Animal welfare (number of animal tests needed)	0,056	20	1,11	20	1,11	10	0,56	20	1,11

Policy ranking permutations (24)		
Permutations	Pairings	Scores
1234	12+13+14+23+24+34	1,50
1243	12+14+13+24+23+43	2,28
1324	13+12+14+32+34+24	1,36
1342	13+14+12+34+32+42	2,08
1423	14+12+13+42+43+23	3,00
1432	14+13+12+43+42+32	2,86
2134	21+23+24+13+14+34	2,01
2143	21+24+23+14+13+43	2,79
2314	23+21+24+31+34+14	2,31
2341	23+24+21+34+31+41	3,14
2413	24+21+23+41+43+13	3,63
2431	24+23+21+43+41+31	3,92
3124	31+32+34+12+14+24	1,65
3142	31+34+32+14+12+42	2,38
3214	32+31+34+21+24+14	2,17
3241	32+34+31+24+21+41	3,00
3412	34+31+32+41+42+12	3,21
3421	34+32+31+42+41+21	3,72
4123	41+42+43+12+13+23	3,83
4132	41+43+42+13+12+32	3,69
4213	42+41+43+21+23+13	4,35
4231	**42+43+41+23+21+31**	**4,64**
4312	43+41+42+31+32+12	3,99
4321	43+42+41+32+31+21	4,50

Outranking matrix				
	Option 1	Option 2	Option 3	Option 4
Option 1	-	0,24	0,35	0,08
Option 2	0,76	-	0,57	0,14
Option 3	0,65	0,43	-	0,11
Option 4	0,92	0,86	0,89	-

SCENARIO		POLICY RANKING
Scenario 1/A	Homogeneity	4 > 2 > 3 > 1
Scenario 1/B	Homogeneity	4 > 2 > 3 > 1
Scenario 2	Priority to evidence	4 > 2 > 3 > 1
Scenario 3	Priority to Health and Environment	4 > 2 > 3 > 1
Scenario 4	Health first	4 > 2 > 3 > 1
Scenario 5/A	Aim: exposure zero	4 > 2 > 3 > 1
Scenario 5/B	Aim: exposure zero	4 > 2 > 3 > 1
Scenario 5/C	Aim: exposure zero	4 > 2 > 3 > 1
Scenario 5/D	Aim: exposure zero	4 > 2 > 3 > 1
Overall ranking		WHO + potency (Option 4) > > WHO (Option 2) > > WHO + categories (Option 3) > > Interim criteria (Option 1)

Figure 1. Exemplary steps of the MCA applied in this IA for options 1 to 4. A similar process was followed for options A to C.

1.5. Identifying the MCA-criteria to compare key impacts of the options

The MCA-criteria are means of assessing the performance of the options; hence they need to be operational. A judgment needs to specify how well each option meets the objectives expressed by the MCA-criteria. In practice, a question that was borne in mind in developing the set of MCA-criteria was "Is it possible in practice to assess how well an option performs on these MCA-criteria?"

It is worth noting that the number of MCA-criteria should be kept as low as is consistent with making a well-founded decision. There is no 'rule' to guide this judgment and it certainly varies from application to application.

During the development of these MCA-criteria, the following principles were considered:

1. *Observing the Better Regulation Guidelines.* In designing the MCA-criteria, the requirements of Tool 8 of the Better Regulation Guidelines have been considered, meaning the aspects related to option effectiveness, efficiency and coherence.
   a. *Link with the objectives (effectiveness).* MCA-criteria were considered in relation to the objectives to be attained in order to facilitate the judgement on how the options will contribute to the achievement of the objectives set.
   b. *Areas with significant impacts (efficiency).* The MCA-criteria cover the areas that were considered to experience significant impacts in order to compare such effects between the various options and determine how efficiently the options are performing. In deciding which the key economic, social and environmental impacts are, Tool #16 – "Identification/screening of impacts" was employed.
   c. *Consistency with other EU legislation (coherence).* MCA-criteria give consideration to international treaties (like WTO and Codex Alimentarius) that the EU needs to observe or the coherence between PPP and BP legislation.
2. *Availability of evidence.* One of the most important considerations in the selection of MCA-criteria was the availability of quantifiable or qualitative information/data. It is acknowledged that the degree of granularity of available data would vary between the various areas, with some fields benefiting from more detailed statistics, while others being characterised by the prevalence of qualitative data.

Before finalising the choice of criteria of this MCA, they were assessed against a range of qualities:

1. completeness: this aspect considered whether all important criteria were included;
2. redundancy: this aspect considered whether there were criteria which were unnecessary. If in the process of fine-tuning it was discovered that MCA-criteria that mean the same thing have been defined in different ways, this represents a case of redundancy and one MCA-criterion will be discarded;
3. operationality: this aspect considered whether each option could have been judged against each MCA-criterion based on the available evidence;

4. mutual independence of preferences: this aspect considered whether preference scores for the options on one MCA-criterion could have been assigned without knowing what the options' preference scores were on any other criteria. If the answer is yes, then this MCA-criterion is preference independent of the others. If in the process of option ranking, it is discovered that MCA-criteria are dependent, they will be combined, to the extent possible, in order to eliminate dependence

Table 1. Potential impacts and the corresponding dimensions and criteria used in the MCA

Impacts		Dimensions and MCA-criteria	
EFFECTIVENESS & COHERENCE		**EFFECTIVENESS & COHERENCE**	
		Legal certainty and proportionality:	degree to which legal certainty is ensured
		Operability for regulatory decision making:	additional efforts required to public authorities and applicants resulting from implementing derogations and a revision of categories
		Coherence between BP and PPP legislation:	
		Compliance with international obligations of the EU:	compliance with international obligations of the EU (WTO and Codex Alimentarius)
EFFICIENCY	Economic	**SECTORIAL COMPETITIVENESS: EU AGRICULTURE**	
		Number of PPP affected:	number of PPP authorised at national level that will be affected as a consequence of the non-approval of active substances identified as EDs
		Crops affected:	number of crops affected by the non-approval of active substances identified as ED
		Existence of alternatives / risk of resistance of pests:	number of PPP alternatives existing for each crop, under consideration that the risk of appearance of resistance in pests is related to a lower number of available PPP
		SECTORIAL COMPETITIVENESS: PPP, BP AND RELATED INDUSTRIES	
		Functioning of the single market:	Functioning of the single market, in particular when exceptions apply
		Innovation and research:	increase of innovation, research, and technical development in PPP and BP industry, pesticide application industry, food industry, others
		SME's:	Burden to SMEs
		INTERNATIONAL TRADE	
		Import of food:	imports of food potentially affected by lowering the Maximum Residue Levels (MRLs) at the Limit of Quantification - LoQ (technical zero)
		Import of feed:	imports of feed potentially affected by lowering the Maximum Residue Levels (MRLs) at the Limit of Quantification - LoQ (technical zero)
		Import of treated articles:	imports of goods which may be affected as a consequence of implementing the BP Regulation in relation to treated articles
	Social	**HUMAN HEALTH**	
		Hormone related diseases and disorders:	health risks potentially related to hormonal modalities (EATS)
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides:	Health risks caused by lack of appropriate disinfectants (e.g. in hospital settings) or insecticides (e.g. mosquito borne public health treats)
		Food safety:	risk of contamination of food (e.g. by mycotoxins)
	Environment	**ENVIRONMENT**	
		Chemical quality of water:	contamination of ground, surface, and drinking water with ED used as PPP or BP
		Wildlife vertebrate populations:	decrease of wildlife vertebrate populations because of ED mediated effects (e.g. reproduction, sex ratio) as a consequence of environmental exposure to ED
		Animal welfare:	number of animal tests needed

Finally, the MCA-criteria defined were then cross-checked with the Public Consultation Report to ensure that important areas mentioned by stakeholders have not been missed. Furthermore, the MCA-criteria were discussed with the members of the IASG at the meeting of 1st February 2016.

In addition to the MCA-criteria included in the table, serious consideration has been given also to other potential MCA-criteria. Nevertheless, following an analysis of the evidence available it was decided that the quantitative and qualitative findings are not sufficiently robust in order to provide a solid basis for properly ranking the options' performance.

The final result of considering the different aspects mentioned before is illustrated in Table 1.

1.6. Describing the expected performance of each option against the MCA-criteria and scoring the options

Considering the limitations encountered in obtaining fully quantifiable data that would allow the determination of the absolute performance of each option, the options are assessed based on their relative performance. More precisely, it is specified how each option is performing in relation to the other options. In consequence, the options are ranked on a scale. The ranking only indicates if an option has a stronger or a weaker performance than another option, but it does not represent the extent to which an option is performing better/worse than another. Strongest performance means the highest positive impact or the lowest negative impact. Lowest performance means the lowest positive impact or the highest negative impact.

The r*elative performance* of the policy option was evaluated with respect to each MCA-criterion based on the results of the screening, illustrated in Annex 5, and further available specific evidence. The evaluation of the options (indicated as, e.g. B>A>C, meaning B performing better than A, which is performing better than C) and the consideration of the respective additional evidence is detailed in the respective Annexes:

- Achievement of effectiveness and coherence (Annex 8)
- Human Health-Hormone related diseases and disorders (Annex 9)
- Human Health-Transmissible diseases and food safety (Annex 10)
- Environment (Annex 11)
- Sectorial competitiveness: EU agriculture (Annex 12 and 13)
- Sectorial competitiveness: Plant Protection Products, Biocidal Products and related industries (Annex 14)
- International Trade (Annex 15)

For the MCA-calculations, the ranking of the options was entered as an *ordinal scale*. Each value on the ordinal scale has an ordered relationship to every other value on the scale. The values assigned to options performance have no inherent numerical value with respect to magnitude. The least performing option will be assigned a value of 10, with the next options being assigned values in intervals of 10. The size of the interval was selected at 10 only to facilitate calculations. It has no impact on the results. For example, B>A>C, which means that B performs better than A which performs better than C was coded in the MCA-calculations as follows: Option B performs the best and receives a score of 30, Option A is second best and receives a score of 20, and Option C is the worst performing and receives a score of 10.

The differences in values on the scale do not represent differences in strengths of performance. It cannot be inferred that an option scored with 30 is 3 times better than an

option scored with 10. The only inference that can be made is that one option performs better than another on that particular MCA-criterion. Therefore, only a relative judgement can be made, comparing differences in consequences between options, without determining the exact magnitude of those differences.

For ranking the options, the following elements were considered:

1. *"Direction" is not looked at separately*. In Tool #57 of the Better Regulation Guidelines – Multi-Criteria Analysis, it is foreseen that for each MCA-criterion a "direction" will be indicated, whereas "option performance" is only looking at the magnitude of the performance, without considering if it is a negative or a positive impact. Considering that the IA is looking at relative and not absolute performance, the ranking of the options already takes into account the direction of the MCA-criteria. Therefore "direction" will not be considered separately, but only in connection with performance in order to allow for proper ranking of the options. An option that indicates a lower negative impact or a higher positive impact will always rank better than another option that indicates a higher negative impact or a lower positive impact.
2. *Equal performance.* For options that score equally on a certain MCA-criterion, the lower end of the range will be selected to show their performance. This does not exert any influence in the ordering of the options or in the MCA calculations considering that the values do not represent magnitude, they only represent the order. For example, assuming that the four options perform in this order: Option 1 is the best, Option 2 and Option 3 follow, and Option 4 is the worst, the values on the ranking scale would be the following: 40 for Option 1; 20 each for Option 2 and Option 3; 10 for Option 4. Different methods of ranking equal options were also considered – taking the middle point (assigning 25 each to Option 2 and Option 3) or taking the higher value (assigning 30 each to Option 2 and Option 3). However, this does not influence the results in any way because this is an ordinal scale where the values only indicate the order and not the magnitude. Therefore, no matter which method would have been selected, the final result would have remained unchanged.
3. *Dominating and dominated options*. If one of the options has a consistently strong performance (ranks equally to other options on certain MCA-criteria, but performs better than all other options on the rest of the MCA-criteria) or a consistently low performance (ranks equally to a specific option on certain MCA-criteria and on the rest of the MCA-criteria it ranks consistently worse), it will be maintained in the analysis as the purpose of the assessment is not to determine which is the best or worst option, but to consider all options in the analysis and understand how they perform in relation to each other.

1.7. Weighting and sensitivity analysis

According to Tool 57 of the Better Regulation Toolbox, the standard approach in applying the MCA methodology would require first to assign weights to each MCA-criteria, then perform the analysis, obtain the results, and finally carry out a sensitivity analysis.

In fact, it is a recommendation of Tool 57 to complement this type of MCA with sensitivity analysis to determine the robustness of the final ranking to the assumption about the weights given to each MCA-criterion. The Better Regulation Guidelines document supports this approach in section 2.5.3 – "Assessment of most significant impacts" where it recommends that when an assumption is particularly important or uncertain, sensitivity analysis should be used to check whether changing it would lead to significantly different results.

However, a slightly modified approach was followed in the course of this MCA to consider the particularities of this IA. Therefore, the methodology was adapted in order to take into account that, unless making a value judgement e, it was not possible to establish the relative importance of each MCA-criterion/dimension (i.e. horizontal, health, environment, agriculture, trade, etc.) with respect to the other MCA-criteria/dimension.

For this reason, the weighting was carried out through a sensitivity analysis; after identifying the MCA-criteria for each area of impacts (i.e. dimension), the options were compared under four main scenarios (with 2 sub-scenarios being also considered) in order to ascertain how different weights could have affected the overall ordering of the options (sensitivity analysis). A 5^{th} scenario was included in addition, based on two of the previously described scenarios. This scenario 5 includes 4 sub-scenarios which consider a more protective analysis of the options (performance) based on hazard regulatory decision making instead of risk, and also a higher weight on the dimensions of human health and environment.

The following elements were considered in assigning the weights to the different MCA-criteria:

1. *Evidence robustness*. If the available evidence used to assess option performance for the respective MCA-criterion is not considered sufficient or robust enough, the weight of the respective MCA-criterion could be lowered
2. *Equal performance.* If the options have very similar performance levels for a certain MCA-criterion (for example several options register equal performance), the weight of the respective MCA-criterion could be lowered as the MCA-criterion is not instrumental in analysing differences between the options. Nevertheless, if the respective MCA-criterion was considered to be very important, its weight was not adjusted based on this principle.

   If for a certain MCA-criterion all options of aspect I receive equal scores, then the respective MCA-criterion will be maintained if options of aspect II rank differently. The reverse is also valid.
3. *Fulfilment of legal obligations.* If a certain MCA-criterion is very important to the fulfilment of legal obligations (for example obligations assumed in the Treaties or other legal acts, such as the protection of health by application of the precautionary principle), the weight of the respective MCA-criterion could be increased.

The scenarios considered are summarised as follows:

- **SCENARIO 1 - HOMOGENITY:** under this scenario, equal weights were assigned to all dimensions (i.e. impacts) considered: achievement of effectiveness and coherence; sectorial competitiveness: EU agriculture; sectorial competitiveness: PPP, BP and related industries; international trade; human health; environment. For the weights of the MCA-criteria within each dimension, two sub-scenarios were considered:
  - 1/A: within each dimension, equal weights were assigned to each MCA-criterion;
  - 1/B: within each dimension, higher weights were assigned to those MCA-criteria for which the availability of data/evidence was considered to be higher, while equal weights were assigned to those MCA-criteria for which data/evidence available was thought to be insufficient to discriminate. The overall availability of evidence was expressed as a value which resulted from the analysis included in the respective annexes.
- **SCENARIO 2 - PRIORITY TO EVIDENCE:** under this scenario, different weights were assigned to the dimensions depending on the overall availability of data/evidence for the respective dimensions. Within each dimension, higher weights were assigned to those MCA-criteria for which the availability of data/evidence was considered to be higher, while equal weights were assigned to those MCA-criteria for which data/evidence available was thought to be insufficient to discriminate. The overall availability of evidence was expressed as a value which resulted from the analysis included in the respective annexes.
- **SCENARIO 3 – PRIORITY TO HEALTH AND ENVIRONMENT:** under this scenario, equal weights were assigned to the dimensions Health and Environment, in light of the precautionary principle set out in article 191 of the Treaty on the Functioning of the EU[2]. Decreasing weights were assigned to the remaining dimensions depending on the overall availability of data/evidence. Within each dimension, higher weights were assigned to those MCA-criteria for which the availability of data/evidence was considered to be higher, while equal weights were assigned to those MCA-criteria for which data/evidence available was thought to be insufficient to discriminate. The overall availability of evidence was expressed as a value which resulted from the analysis included in the respective annexes.
- **SCENARIO 4 - HEALTH FIRST:** under this scenario, the highest weight was assigned to the dimension Health. The remaining dimensions were assigned a weight dependent on the overall availability of data/evidence. Within each dimension, higher weights were assigned to those MCA-criteria for which the availability of data/evidence was considered to be higher, while equal weights were assigned to those MCA-criteria for which data/evidence available was thought to be insufficient to discriminate. The overall availability of evidence was expressed as a value which resulted from the analysis included in the respective annexes.

[2] Retrieved from: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=URISERV%3Al32042

- **SCENARIO 5 – AIM: EXPOSURE ZERO:** this scenario considers scenarios 3 (priority to health and environment) and 4 (Health first) as a starting point to examine what would be the effect for the policy ranking of the options considering a regulatory decision making which aims at reducing exposure to chemicals as completely as possible and as a consequence is based on hazard and does not consider risk assessment[3]. It then examines what would be the effect for the policy ranking of the options considered if the initial weight assigned to Health is increased. The resulting 4 sub-scenarios are described as follows:
  - 5/A: as scenario 3 + Hazard based decision making;
  - 5/B: as scenario 3 + Hazard based decision making + increase of the weight assigned to Health (from 0,20 to 0,40) at the expenses of the other dimensions excluding Environment. Further, 50% of the overall weight for Human Health (0,40) was assigned to the MCA-criterion "hormone related diseases and disorders" and the remaining 50% was split equally between the other two MCA-criteria of the dimension Human Health. In all other scenarios considered, equal weights were assigned to the Human Health MCA-criteria as data/evidence available was considered to be insufficient to discriminate among them. This scenario is consequently giving the highest weight to ED related issues on human health (20%) and environment (13.4%), amounting to 33.4 % of the total weight.
  - 5/C: as scenario 4 + Hazard based decision making;
  - 5/D: as scenario 4 + Hazard based decision making + an increase of the weight assigned to Health (from 0,25 to 0,40) at the expenses of the other dimensions.

Table 2 provides an overview of the weights corresponding to each scenario, as well as the assessment of the overall availability of data/evidence.

[3] Taking into account hazard based regulatory decision making for the approval of chemicals translates into a change of the relative performance for the following MCA criteria linked directly to ED effects: Hormone related diseases and disorders; Wildlife vertebrate populations and Chemical quality of water.

Table 2. Overview of weights assigned to the MCA criteria according to the different scenarios (sensitivity analysis).

			SCENARIO 1 HOMOGENITY		SCENARIO 2 PRIORITY TO EVIDENCE	SCENARIO 3 PRIORITY TO HEALTH AND ENVIRONMENT	SCENARIO 4 HEALTH FIRST	SCENARIO 5 AIM: EXPOSURE ZERO				Qualitative assessment of evidence
			A	B				A	B	C	D	
IMPACTS		Dimensions and MCA-criteria[4]	Weight	Weight	Weight	Weight	Weight	Weight	Weight	Weight	Weight	
EFFECTIVENESS & COHERENCE		**Effectiveness & coherence**	**0,167**	**0,167**	**0,18**	**0,16**	**0,16**	**0,16**	**0,11**	**0,16**	**0,13**	
		Legal certainty and proportionality	0,042	0,033	0,036	0,032	0,032	0,032	0,022	0,032	0,026	0,20
		Operability for regulatory decision making	0,042	0,033	0,036	0,032	0,032	0,032	0,022	0,032	0,026	0,20
		Coherence between BP and PPP legislation	0,042	0,050	0,054	0,048	0,048	0,048	0,033	0,048	0,039	0,30
		Compliance with international obligations of the EU	0,042	0,050	0,054	0,048	0,048	0,048	0,033	0,048	0,039	0,30
EFFICIENCY	Economic	**Sectorial competitiveness: EU agriculture**	**0,167**	**0,167**	**0,21**	**0,17**	**0,19**	**0,17**	**0,12**	**0,19**	**0,16**	
		Number of PPPs affected	0,056	0,083	0,105	0,085	0,095	0,085	0,060	0,095	0,080	0,50
		Crops affected	0,056	0,050	0,063	0,051	0,057	0,051	0,036	0,057	0,048	0,30
		Existence of alternatives / risk of resistance of pests	0,056	0,033	0,042	0,034	0,038	0,034	0,024	0,038	0,032	0,20
		Sectorial competitiveness: PPP, BP and related industries	**0,167**	**0,167**	**0,12**	**0,09**	**0,08**	**0,09**	**0,04**	**0,08**	**0,05**	
		Functioning of the single market	0,056	0,056	0,040	0,030	0,027	0,030	0,013	0,027	0,017	0,33
		Innovation and research	0,056	0,056	0,040	0,030	0,027	0,030	0,013	0,027	0,017	0,33
		SME's	0,056	0,056	0,040	0,030	0,027	0,030	0,013	0,027	0,017	0,33
		International trade	**0,167**	**0,167**	**0,22**	**0,180**	**0,20**	**0,180**	**0,13**	**0,20**	**0,17**	
		Import of food	0,056	0,058	0,077	0,063	0,070	0,063	0,046	0,070	0,060	0,35
		Import of feed	0,056	0,058	0,077	0,063	0,070	0,063	0,046	0,070	0,060	0,35
		Import of treated articles	0,056	0,050	0,066	0,054	0,060	0,054	0,039	0,060	0,051	0,30
	Social	**Human Health**	**0,167**	**0,167**	**0,13**	**0,20**	**0,25**	**0,20**	**0,40**	**0,25**	**0,40**	
		Hormone related diseases and disorders	0,056	0,056	0,043	0,067	0,083	0,067	0,20	0,083	0,133	0,33 [5]
		Food safety	0,056	0,056	0,043	0,067	0,083	0,067	0,10	0,083	0,133	0,33
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,056	0,056	0,043	0,067	0,083	0,067	0,10	0,083	0,133	0,33
	Environment	**Environment**	**0,167**	**0,167**	**0,14**	**0,20**	**0,12**	**0,20**	**0,20**	**0,12**	**0,09**	
		Chemical quality of water	0,056	0,056	0,047	0,067	0,040	0,067	0,067	0,040	0,030	0,33
		Wildlife vertebrate populations	0,056	0,056	0,047	0,067	0,040	0,067	0,067	0,040	0,030	0,33
		Animal welfare	0,056	0,056	0,047	0,067	0,040	0,067	0,067	0,040	0,030	0,33

[4] Note that some criteria names have been abbreviated. See table 1 for complete titles for the criteria.

[5] Scenario 5/B, assigns 50% of the overall weight for Human Health (0,40) to "hormone related diseases and disorders" and split the remaining 50% equally between the other two MCA-criteria of Human Health. In all other scenarios, equal weights are assigned to these 3 MCA-criteria as data/evidence available was considered insufficient to discriminate among them. This scenario is thus giving the highest weight to ED related issues on human health (20%) and environment (13.4%).

1.8. Combining the weights and the scores for each of the options

Multiplication of the performance and weight gives a weighted performance which allows each policy option to be compared and ranked with respect to each MCA-criterion.

An outranking matrix[6], summarising how one option compares against another for all possible pairs of policy options, was built.

For a given pair of options (say Option A and Option B), the weightings for each MCA-criterion are summed but only for those MCA-criteria where the first option is determined to be better than the second. This sum provides an element (A-B) of the outranking matrix. Only the weightings are added. It makes no difference how much better each option is in respect to another.

In case of equally performing options, two methods were considered for the calculation of the outranking matrix:

- *discarding the ties.* The sum of the element (A-B) of the outranking matrix will include only the weights where Option A is better than Option B. In case they performing equally on a certain MCA-criterion, the weight of the respective MCA-criterion is not added to the sum. This prevents the outranking matrix from being perfectly symmetrical; however this has no impact on the final result.
- *divide the MCA-criterion weight equally between the pairs of options.* The sum of the element (A-B) of the outranking matrix will include the weights where Option A is better than Option B, and only half of the weights for the MCA-criteria on which Option A and Option B are equally performing. This results in the outranking matrix being perfectly symmetrical.

Both methods were discussed and tested with JRC and the final result remains unchanged, no matter which method is used. For the purpose of this IA the second method was used.

For scoring the pairs of ordered options, numerous[7] ways to rank the policy options which must be "scored" using the outranking matrix are available. For example, in the case of three policy options A, B, and C, there are 3! (i.e. 6) different possible rankings (ABC, ACB, BAC, BCA, CAB, and CBA). These are scored by summing the elements from the outranking matrix for each policy pair which make up a given ranking of the policy options (i.e. for the ranking ABC, the policy pairs are AB, AC and BC).

1.9. Analysis of the results

The analyses of the results obtained through the MCA are illustrated in Annex 7.

[6] The outranking matrix is a square 4 x 4 matrix for step 1 when options 1-4 are compared and it is a square 3 x 3 matrix for step 2 when options A-C are compared.

[7] There are 4! (factorial) = 24 possible combinations for step 1 when options 1-4 are compared and 3! (factorial) = 6 possible combinations for step 2 when options A-C are compared.

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PART 8/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annex 7 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

{COM(2016) 350 final}
{SWD(2016) 212 final}

ANNEX 7

THE MULTI-CRITERIA ANALYSIS: RESULTS

Contents

This Annex focuses on the assessment of potential impacts, which build on the results of the screening study explained in Annexes 3 to 5. The results of the screening do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation. The methods and results presented in this Annex are to be interpreted as an estimation of the potential impacts.

The MCAs results are not concluding on any preferred option for setting scientific criteria to identify endocrine disruptors, but aim at providing additional information to decision makers with regards to the potential impacts expected when implementing the criteria, after those would have been selected on the basis of science (two MCAs were performed: Options 1 to 4 under the current regulatory context, and Options A compared to Options B and C).

At a preliminary stage of the impact assessment it was anticipated that Option C should be discarded, nevertheless it was maintained for the analysis of the impacts for methodological reasons (see Section 4.2.3 of the main report and Annexes 6 and 7). Option C only applies to the PPP Regulation.

1. INTRODUCTION

As set out in Annex 6, a Multi Criteria Analysis (MCA) was performed to compare Options 1 to 4 (Aspect I, EU criteria to identify endocrine disruptors (EDs)) and Options A to C (Aspect II, Approaches to regulatory decision making).

The options were compared under different scenarios in order to ascertain how different weights could have affected the overall ordering of the options:

1. **SCENARIO 1 - HOMOGENITY**: equal weights were assigned to all dimensions. For the weights of the MCA-criteria within each dimension, two sub-scenarios were considered:

   i) **1/A:** within each dimension, equal weights were assigned to each MCA-criterion;

   ii) **1/B:** within each dimension, higher weights were assigned to those MCA-criteria for which the availability of data/evidence was considered to be higher, while equal weights were assigned to those MCA-criteria for which data/evidence available was thought to be insufficient to discriminate.

2. **SCENARIO 2 - PRIORITY TO EVIDENCE:** different weights were assigned to the dimensions depending on the overall availability of data/evidence. Within each dimension, higher weights were assigned to those MCA-criteria for which the availability of data/evidence was considered to be higher, while equal weights were assigned to those MCA-criteria for which data/evidence available was thought to be insufficient to discriminate.

3. **SCENARIO 3 – PRIORITY TO HEALTH AND ENVIRONMENT:** equal weights were assigned to the dimensions Health and Environment, in light of the precautionary principle set out in article 191 of the Treaty on the Functioning of the EU. Decreasing weights were assigned to the remaining dimensions depending on the overall availability of data/evidence. Within each dimension, higher weights were assigned to those MCA-criteria for which the availability of data/evidence was considered to be higher, while equal weights were assigned to those MCA-criteria for which data/evidence available was thought to be insufficient to discriminate.

4. **SCENARIO 4 - HEALTH FIRST:** the highest weight was assigned to the dimension Health. The remaining dimensions were assigned a weight dependent on the overall availability of data/evidence. Within each dimension, higher weights were assigned to those MCA-criteria for which the availability of data/evidence was considered to be higher, while equal weights were assigned to those MCA-criteria for which data/evidence available was thought to be insufficient to discriminate.

5. **SCENARIO 5 – AIM: EXPOSURE ZERO:** this scenario examines what would be the effect considering a regulatory decision making which aims at completely reducing exposure to chemicals and as a consequence is based on hazard and does not consider risk assessment. Scenarios 3 (priority to health and environment) and 4 (Health first) were used as starting points. Additionally, sub scenarios were developed

which increase the weight assigned to Health. The resulting 4 sub-scenarios are described as follows:

i) **5/A:** as scenario 3 + Hazard based decision making;

ii) **5/B:** as scenario 3 + Hazard based decision making + increase of the weight assigned to Health (from 0,20 to 0,40) at the expenses of the other dimensions excluding Environment. Further, 50% of the overall weight for Human Health (0,40) was assigned to the criterion "hormone related diseases and disorders" and the remaining 50% was split equally between the other two MCA-criteria of the dimension Human Health (in all other scenarios considered, equal weights were assigned to the Human Health MCA-criteria as data/evidence available was considered to be insufficient to discriminate among them). This scenario is consequently giving the highest weight to ED related issues on human health (20%) and environment (13.4%), amounting to 33.4 % of the total weight.

iii) **5/C:** as scenario 4 + Hazard based decision making;

iv) **5/D:** as scenario 4 + Hazard based decision making + an increase of the weight assigned to Health (from 0,25 to 0,40) at the expenses of the other dimensions.

For the purpose of the sensitivity analysis, additional simulations were run under Scenario 5/B (Aim: exposure zero) in order to evaluate when the policy ranking of the options would change.

In this annex, the tabular results are presented:

- overview of weights assigned to the MCA criteria and dimensions according to the different scenarios considered (sensitivity analysis, Table 1);
- performance of the options 1,2,3 and 4, and options A, B, and C.
- weighted performance matrices (multiplication of the performance and weights), giving composite quantities which allow each policy option to be compared and ranked for each criterion (Sections 2 and 3);
- outranking matrices and policy ranking permutations. Outranking matrices summarise how each option compared against another for all possible pairs of policy options. Policy ranking permutations allow selecting the policy options which maximise pair-wise agreement - and minimise disagreement (Sections 4 and 5);
- summary overview of the results (Section 6).

Table 1. Overview of weights assigned to the MCA criteria according to the different scenarios (sensitivity analysis)

			SCENARIO 1 HOMOGENITY		SCENARIO 2 PRIORITY TO EVIDENCE	SCENARIO 3 PRIORITY TO HEALTH AND ENVIRONMENT	SCENARIO 4 HEALTH FIRST	SCENARIO 5 AIM: EXPOSURE ZERO				Qualitative assessment of evidence
			A	B				A	B	C	D	
IMPACTS		Dimensions and criteria[1]	Weight	Weight	Weight	Weight	Weight	Weight	Weight	Weight	Weight	
EFFECTIVENESS & COHERENCE		**Effectiveness & coherence**	**0,167**	**0,167**	**0,18**	**0,16**	**0,16**	**0,16**	**0,11**	**0,16**	**0,13**	
		Legal certainty and proportionality	0,042	0,033	0,036	0,032	0,032	0,032	0,022	0,032	0,026	0,20
		Operability for regulatory decision making	0,042	0,033	0,036	0,032	0,032	0,032	0,022	0,032	0,026	0,20
		Coherence between BP and PPP legislation	0,042	0,050	0,054	0,048	0,048	0,048	0,033	0,048	0,039	0,30
		Compliance with international obligations of the EU	0,042	0,050	0,054	0,048	0,048	0,048	0,033	0,048	0,039	0,30
EFFICIENCY	Economic	**Sectorial competitiveness: EU agriculture**	**0,167**	**0,167**	**0,21**	**0,17**	**0,19**	**0,17**	**0,12**	**0,19**	**0,16**	
		Number of PPP affected	0,056	0,083	0,105	0,085	0,095	0,085	0,060	0,095	0,080	0,50
		Crops affected	0,056	0,050	0,063	0,051	0,057	0,051	0,036	0,057	0,048	0,30
		Existence of alternatives / risk of resistance of pests	0,056	0,033	0,042	0,034	0,038	0,034	0,024	0,038	0,032	0,20
		Sectorial competitiveness: PPP, BP and related industries	**0,167**	**0,167**	**0,12**	**0,09**	**0,08**	**0,09**	**0,04**	**0,08**	**0,05**	
		Functioning of the single market	0,056	0,056	0,040	0,030	0,027	0,030	0,013	0,027	0,017	0,33
		Innovation and research	0,056	0,056	0,040	0,030	0,027	0,030	0,013	0,027	0,017	0,33
		SME's	0,056	0,056	0,040	0,030	0,027	0,030	0,013	0,027	0,017	0,33
		International trade	**0,167**	**0,167**	**0,22**	**0,180**	**0,20**	**0,180**	**0,13**	**0,20**	**0,17**	
		Import of food	0,056	0,058	0,077	0,063	0,070	0,063	0,046	0,070	0,060	0,35
		Import of feed	0,056	0,058	0,077	0,063	0,070	0,063	0,046	0,070	0,060	0,35
		Import of treated articles	0,056	0,050	0,066	0,054	0,060	0,054	0,039	0,060	0,051	0,30
	Social	**Human Health**	**0,167**	**0,167**	**0,13**	**0,20**	**0,25**	**0,20**	**0,40**	**0,25**	**0,40**	
		Hormone related diseases and disorders	0,056	0,056	0,043	0,067	0,083	0,067	0,20	0,083	0,133	0,33 [2]
		Food safety	0,056	0,056	0,043	0,067	0,083	0,067	0,10	0,083	0,133	0,33
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,056	0,056	0,043	0,067	0,083	0,067	0,10	0,083	0,133	0,33
	Environment	**Environment**	**0,167**	**0,167**	**0,14**	**0,20**	**0,12**	**0,20**	**0,20**	**0,12**	**0,09**	
		Chemical quality of water	0,056	0,056	0,047	0,067	0,040	0,067	0,067	0,040	0,030	0,33
		Wildlife vertebrate populations	0,056	0,056	0,047	0,067	0,040	0,067	0,067	0,040	0,030	0,33
		Animal welfare	0,056	0,056	0,047	0,067	0,040	0,067	0,067	0,040	0,030	0,33

[1] Note that some criteria names have been abbreviated. See Table 1 in Annex 6 or Table 3 in the main report for complete titles for the criteria.

[2] Scenario 5/B, assigns 50% of the overall weight for Human Health (0,40) to "hormone related diseases and disorders" and split the remaining 50% equally between the other two MCA-criteria of Human Health. In all other scenarios, equal weights are assigned to these 3 MCA-criteria as data/evidence available was considered insufficient to discriminate among them. This scenario is thus giving the highest weight to ED related issues on human health (20%) and environment (13.4%).

Table 2. Performance of Option 1, 2, 3 and 4.

PERFORMANCE OF OPTION 1, 2, 3, AND 4									
		Dimensions/Criteria	*Best performing*				*Worst performing*		
			40		*30*		*20*		*10*
	Horizontal	**Horizontal (effectiveness/coherence)**							
Effectiveness		Legal certainty and proportionality	4	>	2	>	1	>	3
		Operability for regulatory decision making	4	>	2	>	1	>	3
Coherence		Coherence between BP and PPP legislation	4	>	2	/	3	>	1
		Compliance with international obligations	4	>	2	/	3	/	1
Efficiency	Economic	**Sectorial competitiveness: EU agriculture**							
		Number of PPPs affected	4	>	1	>	2	/	3
		Crops affected	4	>	1	>	2	/	3
		Existence of alternatives/risk of resistance of pests	4	>	2	/	3	>	1
		Sectorial competitiveness: PPP, BP and related industries							
		Functioning of the single market	4	>	2	/	3	>	1
		Innovation and research	4	>	2	/	3	>	1
		SME's	4	>	2	/	3	>	1
		International trade							
		Import of food	4	>	1	/	2	/	3
		Import of feed	4	>	2	/	3	>	1
		Import of treated articles	4	>	2	/	3	>	1
	Social	**Human Health**							
		Hormone related chronic diseases	2	/	3	/	4	>	1
		Hormone related chronic diseases [exposure zero]	*2*	*/*	*3*	*>*	*4*	*>*	*1*
		Transmissible diseases	4	>	2	/	3	>	1
		Food safety	4	>	2	/	3	>	1
	Environmental	**Environment**							
		Chemical quality of water	1	>	2	/	3	>	4
		Wildlife vertebrate populations	2	/	3	/	4	>	1
		Wildlife vertebrate populations [exposure zero]	*2*	*/*	*3*	*>*	*4*	*>*	*1*
		Animal welfare	1	/	2	/	4	>	3

Table 3. Performance of Option A, B and C.

PERFORMANCE OF OPTION A, B, AND C							
		Dimensions/Criteria	*Best performing*				*Worst performing*
			30		*20*		*10*
	Horizontal	**Horizontal (effectiveness/coherence)**					
Effectiveness		Legal certainty and proportionality	C	>	B	>	A
		Operability for regulatory decision making	C	>	B	>	A
Coherence		Coherence between BP and PPP legislation	C	>	B	>	A
		Compliance with international obligations	B	/	C	>	A
Efficiency	Economic	**Sectorial competitiveness: EU agriculture**					
		Number of PPPs affected	C	>	B	>	A
		Crops affected	C	>	B	>	A
		Existence of alternatives/risk of resistance of pests	C	>	B	>	A
		Sectorial competitiveness: PPP, BP and related industries					
		Functioning of the single market	C	>	B	>	A
		Innovation and research	C	>	B	>	A
		SME's	C	>	B	>	A
		International trade					
		Import of food	C	/	B	>	A
		Import of feed	C	/	B	>	A
		Import of treated articles	non applicable for BP				
	Social	**Human Health**					
		Hormone related chronic diseases	A	/	B	>	C
		Hormone related chronic diseases [exposure zero]	*A*	>	*B*	>	*C*
		Transmissible diseases	non applicable for BP				
		Food safety	C	>	B	>	A
	Environmental	**Environment**					
		Chemical quality of water	A	/	B	>	C
		Chemical quality of water [exposure zero]	*A*	>	*B*	>	*C*
		Wildlife vertebrate populations	A	/	B	>	C
		Wildlife vertebrate populations [exposure zero]	*A*	>	*B*	>	*C*
		Animal welfare	A	/	B	/	C

2. WEIGHTED PERFORMANCE MATRICES: ASPECT I - SETTING SCIENTIFIC CRITERIA TO IDENTIFY EDS

1.1. Table 4 and 5. Scenario 1 - Homogeneity

Table 4. Sub scenario 1/A

Dimension	Dimension weight	SCENARIO 1/A - HOMOGENITY									
		Criteria	Criteria weight	Options							
				Option 1		Option 2		Option 3		Option 4	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,17	Legal certainty and proportionality	0,042	20	0,83	30	1,25	10	0,42	40	1,67
		Operability for regulatory decision making	0,042	20	0,83	30	1,25	10	0,42	40	1,67
		Coherence between BP and PPP legislation	0,042	10	0,42	20	0,83	20	0,83	40	1,67
		Compliance with international obligations of the EU	0,042	10	0,42	10	0,42	10	0,42	40	1,67
Sectorial competitiveness: EU agriculture	0,17	Number of PPP affected	0,056	30	1,67	10	0,56	10	0,56	40	2,22
		Crops affected	0,056	30	1,67	10	0,56	10	0,56	40	2,22
		Existence of alternatives / risk of resistance of pests	0,056	10	0,56	20	1,11	20	1,11	40	2,22
Sectorial competitiveness: PPP, BP and related industries	0,17	Functioning of the single market	0,056	10	0,56	20	1,11	20	1,11	40	2,22
		Innovation and research	0,056	10	0,56	20	1,11	20	1,11	40	2,22
		SME's	0,056	10	0,56	20	1,11	20	1,11	40	2,22
International trade	0,17	Import of food	0,056	10	0,56	10	0,56	10	0,56	40	2,22
		Import of feed	0,056	10	0,56	20	1,11	20	1,11	40	2,22
		Import of treated articles	0,056	10	0,56	20	1,11	20	1,11	40	2,22
Human Health	0,17	Hormone related diseases and disorders	0,056	10	0,56	20	1,11	20	1,11	20	1,11
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,056	10	0,56	20	1,11	20	1,11	40	2,22
		Food safety	0,056	10	0,56	20	1,11	20	1,11	40	2,22
Environment	0,17	Chemical quality of water	0,056	40	2,22	20	1,11	20	1,11	10	0,56
		Wildlife vertebrate populations	0,056	10	0,56	20	1,11	20	1,11	20	1,11
		Animal welfare	0,056	20	1,11	20	1,11	10	0,56	20	1,11

Table 5. Sub scenario 1/B

Dimension	Dimension weight	Criteria	Criteria weight	SCENARIO 1/B - HOMOGENITY							
				Options							
				Option 1		Option 2		Option 3		Option 4	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,17	Legal certainty and proportionality	0,033	20	0,67	30	1,00	10	0,33	40	1,33
		Operability for regulatory decision making	0,033	20	0,67	30	1,00	10	0,33	40	1,33
		Coherence between BP and PPP legislation	0,050	10	0,50	20	1,00	20	1,00	40	2,00
		Compliance with international obligations of the EU	0,050	10	0,50	10	0,50	10	0,50	40	2,00
Sectorial competitiveness: EU agriculture	0,17	Number of PPP affected	0,083	30	2,50	10	0,83	10	0,83	40	3,33
		Crops affected	0,050	30	1,50	10	0,50	10	0,50	40	2,00
		Existence of alternatives / risk of resistance of pests	0,033	10	0,33	20	0,67	20	0,67	40	1,33
Sectorial competitiveness: PPP, BP and related industries	0,17	Functioning of the single market	0,056	10	0,56	20	1,11	20	1,11	40	2,22
		Innovation and research	0,056	10	0,56	20	1,11	20	1,11	40	2,22
		SME's	0,056	10	0,56	20	1,11	20	1,11	40	2,22
International trade	0,17	Import of food	0,058	10	0,58	10	0,58	10	0,58	40	2,33
		Import of feed	0,058	10	0,58	20	1,17	20	1,17	40	2,33
		Import of treated articles	0,050	10	0,50	20	1,00	20	1,00	40	2,00
Human Health	0,17	Hormone related diseases and disorders	0,056	10	0,56	20	1,11	20	1,11	20	1,11
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,056	10	0,56	20	1,11	20	1,11	40	2,22
		Food safety	0,056	10	0,56	20	1,11	20	1,11	40	2,22
Environment	0,17	Chemical quality of water	0,056	40	2,22	20	1,11	20	1,11	10	0,56
		Wildlife vertebrate populations	0,056	10	0,56	20	1,11	20	1,11	20	1,11
		Animal welfare	0,056	20	1,11	20	1,11	10	0,56	20	1,11

1.2. Table 6. Scenario 2 - Priority to evidence

Dimension	Dimension weight	Criteria	Criteria weight	SCENARIO 2 - PRIORITY TO EVIDENCE							
				Options							
				Option 1		Option 2		Option 3		Option 4	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,18	Legal certainty and proportionality	0,036	20	0,72	30	1,08	10	0,36	40	1,44
		Operability for regulatory decision making	0,036	20	0,72	30	1,08	10	0,36	40	1,44
		Coherence between BP and PPP legislation	0,054	10	0,54	20	1,08	20	1,08	40	2,16
		Compliance with international obligations of the EU	0,054	10	0,54	10	0,54	10	0,54	40	2,16
Sectorial competitiveness: EU agriculture	0,21	Number of PPP affected	0,105	30	3,15	10	1,05	10	1,05	40	4,20
		Crops affected	0,063	30	1,89	10	0,63	10	0,63	40	2,52
		Existence of alternatives / risk of resistance of pests	0,042	10	0,42	20	0,84	20	0,84	40	1,68
Sectorial competitiveness: PPP, BP and related industries	0,12	Functioning of the single market	0,040	10	0,40	20	0,80	20	0,80	40	1,60
		Innovation and research	0,040	10	0,40	20	0,80	20	0,80	40	1,60
		SME's	0,040	10	0,40	20	0,80	20	0,80	40	1,60
International trade	0,22	Import of food	0,077	10	0,77	10	0,77	10	0,77	40	3,08
		Import of feed	0,077	10	0,77	20	1,54	20	1,54	40	3,08
		Import of treated articles	0,066	10	0,66	20	1,32	20	1,32	40	2,64
Human Health	0,13	Hormone related diseases and disorders	0,043	10	0,43	20	0,87	20	0,87	20	0,87
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,043	10	0,43	20	0,87	20	0,87	40	1,73
		Food safety	0,043	10	0,43	20	0,87	20	0,87	40	1,73
Environment	0,14	Chemical quality of water	0,047	40	1,87	20	0,93	20	0,93	10	0,47
		Wildlife vertebrate populations	0,047	10	0,47	20	0,93	20	0,93	20	0,93
		Animal welfare	0,047	20	0,93	20	0,93	10	0,47	20	0,93

1.3. Table 7. Scenario 3 - Priority to health and environment

Dimension	Dimension weight	Criteria	Criteria weight	SCENARIO 3 - PRIORITY TO HEALTH and ENVIRONMENT							
				Options							
				Option 1		Option 2		Option 3		Option 4	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,16	Legal certainty and proportionality	0,032	20	0,64	30	0,96	10	0,32	40	1,28
		Operability for regulatory decision making	0,032	20	0,64	30	0,96	10	0,32	40	1,28
		Coherence between BP and PPP legislation	0,048	10	0,48	20	0,96	20	0,96	40	1,92
		Compliance with international obligations of the EU	0,048	10	0,48	10	0,48	10	0,48	40	1,92
Sectorial competitiveness: EU agriculture	0,17	Number of PPP affected	0,085	30	2,55	10	0,85	10	0,85	40	3,40
		Crops affected	0,051	30	1,53	10	0,51	10	0,51	40	2,04
		Existence of alternatives / risk of resistance of pests	0,034	10	0,34	20	0,68	20	0,68	40	1,36
Sectorial competitiveness: PPP, BP and related industries	0,09	Functioning of the single market	0,030	10	0,30	20	0,60	20	0,60	40	1,20
		Innovation and research	0,030	10	0,30	20	0,60	20	0,60	40	1,20
		SME's	0,030	10	0,30	20	0,60	20	0,60	40	1,20
International trade	0,18	Import of food	0,063	10	0,63	10	0,63	10	0,63	40	2,52
		Import of feed	0,063	10	0,63	20	1,26	20	1,26	40	2,52
		Import of treated articles	0,054	10	0,54	20	1,08	20	1,08	40	2,16
Human Health	0,20	Hormone related diseases and disorders	0,067	10	0,67	20	1,33	20	1,33	20	1,33
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,067	10	0,67	20	1,33	20	1,33	40	2,67
		Food safety	0,067	10	0,67	20	1,33	20	1,33	40	2,67
Environment	0,20	Chemical quality of water	0,067	40	2,67	20	1,33	20	1,33	10	0,67
		Wildlife vertebrate populations	0,067	10	0,67	20	1,33	20	1,33	20	1,33
		Animal welfare	0,067	20	1,33	20	1,33	10	0,67	20	1,33

1.4. Table 8. Scenario 4 - Health first

Dimension	Dimension weight	Criteria	Criteria weight	SCENARIO 4 - HEALTH FIRST							
				Options							
				Option 1		Option 2		Option 3		Option 4	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,16	Legal certainty and proportionality	0,032	20	0,64	30	0,96	10	0,32	40	1,28
		Operability for regulatory decision making	0,032	20	0,64	30	0,96	10	0,32	40	1,28
		Coherence between BP and PPP legislation	0,048	10	0,48	20	0,96	20	0,96	40	1,92
		Compliance with international obligations of the EU	0,048	10	0,48	10	0,48	10	0,48	40	1,92
Sectorial competitiveness: EU agriculture	0,19	Number of PPP affected	0,095	30	2,85	10	0,95	10	0,95	40	3,80
		Crops affected	0,057	30	1,71	10	0,57	10	0,57	40	2,28
		Existence of alternatives / risk of resistance of pests	0,038	10	0,38	20	0,76	20	0,76	40	1,52
Sectorial competitiveness: PPP, BP and related industries	0,08	Functioning of the single market	0,027	10	0,27	20	0,53	20	0,53	40	1,07
		Innovation and research	0,027	10	0,27	20	0,53	20	0,53	40	1,07
		SME's	0,027	10	0,27	20	0,53	20	0,53	40	1,07
International trade	0,20	Import of food	0,070	10	0,70	10	0,70	10	0,70	40	2,80
		Import of feed	0,070	10	0,70	20	1,40	20	1,40	40	2,80
		Import of treated articles	0,060	10	0,60	20	1,20	20	1,20	40	2,40
Human Health	0,25	Hormone related diseases and disorders	0,083	10	0,83	20	1,67	20	1,67	20	1,67
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,083	10	0,83	20	1,67	20	1,67	40	3,33
		Food safety	0,083	10	0,83	20	1,67	20	1,67	40	3,33
Environment	0,12	Chemical quality of water	0,040	40	1,60	20	0,80	20	0,80	10	0,40
		Wildlife vertebrate populations	0,040	10	0,40	20	0,80	20	0,80	20	0,80
		Animal welfare	0,040	20	0,80	20	0,80	10	0,40	20	0,80

1.5. Table 9 to 11. Scenario 5 - Aim: exposure zero

Table 9. Sub scenario 5/A[3]

Dimension	Dimension weight	Criteria	Criteria weight	SCENARIO 5/A - AIM: EXPOSURE ZERO							
				Options							
				Option 1		Option 2		Option 3		Option 4	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,16	Legal certainty and proportionality	0,032	20	0,64	30	0,96	10	0,32	40	1,28
		Operability for regulatory decision making	0,032	20	0,64	30	0,96	10	0,32	40	1,28
		Coherence between BP and PPP legislation	0,048	10	0,48	20	0,96	20	0,96	40	1,92
		Compliance with international obligations of the EU	0,048	10	0,48	10	0,48	10	0,48	40	1,92
Sectorial competitiveness: EU agriculture	0,17	Number of PPP affected	0,085	30	2,55	10	0,85	10	0,85	40	3,40
		Crops affected	0,051	30	1,53	10	0,51	10	0,51	40	2,04
		Existence of alternatives / risk of resistance of pests	0,034	10	0,34	20	0,68	20	0,68	40	1,36
Sectorial competitiveness: PPP, BP and related industries	0,09	Functioning of the single market	0,030	10	0,30	20	0,60	20	0,60	40	1,20
		Innovation and research	0,030	10	0,30	20	0,60	20	0,60	40	1,20
		SME's	0,030	10	0,30	20	0,60	20	0,60	40	1,20
International trade	0,18	Import of food	0,063	10	0,63	10	0,63	10	0,63	40	2,52
		Import of feed	0,063	10	0,63	20	1,26	20	1,26	40	2,52
		Import of treated articles	0,054	10	0,54	20	1,08	20	1,08	40	2,16
Human Health	0,20	Hormone related diseases and disorders	0,067	10	0,67	30	2,00	30	2,00	20	1,33
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,067	10	0,67	20	1,33	20	1,33	40	2,67
		Food safety	0,067	10	0,67	20	1,33	20	1,33	40	2,67
Environment	0,20	Chemical quality of water	0,067	40	2,67	20	1,33	20	1,33	10	0,67
		Wildlife vertebrate populations	0,067	10	0,67	30	2,00	30	2,00	20	1,33
		Animal welfare	0,067	20	1,33	20	1,33	10	0,67	20	1,33

[3] This sub scenario corresponds to Scenario 3 (precautionary principle) but considers hazard, which translates into a different relative performance of options 2 and 3 with respect to the following MCA criteria linked directly to ED effects: hormone related diseases and disorders, and wildlife vertebrate populations (highlighted in grey)

Table 10. Sub scenario 5/B[4]

Dimension	Dimension weight	SCENARIO 5/B - AIM: EXPOSURE ZERO Criteria	Criteria weight	Options Option 1		Option 2		Option 3		Option 4	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,11	Legal certainty and proportionality	0,022	20	0,44	30	0,66	10	0,22	40	0,88
		Operability for regulatory decision making	0,022	20	0,44	30	0,66	10	0,22	40	0,88
		Coherence between BP and PPP legislation	0,033	10	0,33	20	0,66	20	0,66	40	1,32
		Compliance with international obligations of the EU	0,033	10	0,33	10	0,33	10	0,33	40	1,32
Sectorial competitiveness: EU agriculture	0,12	Number of PPP affected	0,060	30	1,80	10	0,60	10	0,60	40	2,40
		Crops affected	0,036	30	1,08	10	0,36	10	0,36	40	1,44
		Existence of alternatives / risk of resistance of pests	0,024	10	0,24	20	0,48	20	0,48	40	0,96
Sectorial competitiveness: PPP, BP and related industries	0,04	Functioning of the single market	0,013	10	0,13	20	0,27	20	0,27	40	0,53
		Innovation and research	0,013	10	0,13	20	0,27	20	0,27	40	0,53
		SME's	0,013	10	0,13	20	0,27	20	0,27	40	0,53
International trade	0,13	Import of food	0,046	10	0,46	10	0,46	10	0,46	40	1,82
		Import of feed	0,046	10	0,46	20	0,91	20	0,91	40	1,82
		Import of treated articles	0,039	10	0,39	20	0,78	20	0,78	40	1,56
Human Health	0,40	Hormone related diseases and disorders	0,200	10	2,00	30	6,00	30	6,00	20	4,00
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,100	10	1,00	20	2,00	20	2,00	40	4,00
		Food safety	0,100	10	1,00	20	2,00	20	2,00	40	4,00
Environment	0,20	Chemical quality of water	0,067	40	2,67	20	1,33	20	1,33	10	0,67
		Wildlife vertebrate populations	0,067	10	0,67	30	2,00	30	2,00	20	1,33
		Animal welfare	0,067	20	1,33	20	1,33	10	0,67	20	1,33

[4] This sub scenario builds on 5A which considers hazard, and translates into a different relative performance of options 2 and 3 with respect to the following MCA criteria, linked directly to ED effects: hormone related diseases and disorders, and wildlife vertebrate populations (highlighted in grey). In addition, it increases the weight for Human Health (from 0,20 to 0,40) at the expenses of the other dimensions excluding Environment.

Table 11. Sub scenario 5/C[5]

Dimension	Dimension weight	SCENARIO 5/C - AIM: EXPOSURE ZERO Criteria	Criteria weight	Options Option 1		Option 2		Option 3		Option 4	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,16	Legal certainty and proportionality	0,032	20	0,64	30	0,96	10	0,32	40	1,28
		Operability for regulatory decision making	0,032	20	0,64	30	0,96	10	0,32	40	1,28
		Coherence between BP and PPP legislation	0,048	10	0,48	20	0,96	20	0,96	40	1,92
		Compliance with international obligations of the EU	0,048	10	0,48	10	0,48	10	0,48	40	1,92
Sectorial competitiveness: EU agriculture	0,19	Number of PPP affected	0,095	30	2,85	10	0,95	10	0,95	40	3,80
		Crops affected	0,057	30	1,71	10	0,57	10	0,57	40	2,28
		Existence of alternatives / risk of resistance of pests	0,038	10	0,38	20	0,76	20	0,76	40	1,52
Sectorial competitiveness: PPP, BP and related industries	0,08	Functioning of the single market	0,027	10	0,27	20	0,53	20	0,53	40	1,07
		Innovation and research	0,027	10	0,27	20	0,53	20	0,53	40	1,07
		SME's	0,027	10	0,27	20	0,53	20	0,53	40	1,07
International trade	0,20	Import of food	0,070	10	0,70	10	0,70	10	0,70	40	2,80
		Import of feed	0,070	10	0,70	20	1,40	20	1,40	40	2,80
		Import of treated articles	0,060	10	0,60	20	1,20	20	1,20	40	2,40
Human Health	0,25	Hormone related diseases and disorders	0,083	10	0,83	30	2,50	30	2,50	20	1,67
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,083	10	0,83	20	1,67	20	1,67	40	3,33
		Food safety	0,083	10	0,83	20	1,67	20	1,67	40	3,33
Environment	0,12	Chemical quality of water	0,040	40	1,60	20	0,80	20	0,80	10	0,40
		Wildlife vertebrate populations	0,040	10	0,40	30	1,20	30	1,20	20	0,80
		Animal welfare	0,040	20	0,80	20	0,80	10	0,40	20	0,80

[5] This sub scenario corresponds to Scenario 4 (health first) but considers hazard, which translates into a different relative performance of options 2 and 3 with respect to the following MCA criteria, linked directly to ED effects: hormone related diseases and disorders, and wildlife vertebrate populations (highlighted in grey).

Table 12. Sub scenario 5/D[6]

Dimension	Dimension weight	SCENARIO 5/D - AIM: EXPOSURE ZERO Criteria	Criteria weight	Options Option 1		Option 2		Option 3		Option 4	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,13	Legal certainty and proportionality	0,026	20	0,52	30	0,78	10	0,26	40	1,04
		Operability for regulatory decision making	0,026	20	0,52	30	0,78	10	0,26	40	1,04
		Coherence between BP and PPP legislation	0,039	10	0,39	20	0,78	20	0,78	40	1,56
		Compliance with international obligations of the EU	0,039	10	0,39	10	0,39	10	0,39	40	1,56
Sectorial competitiveness: EU agriculture	0,16	Number of PPP affected	0,080	30	2,40	10	0,80	10	0,80	40	3,20
		Crops affected	0,048	30	1,44	10	0,48	10	0,48	40	1,92
		Existence of alternatives / risk of resistance of pests	0,032	10	0,32	20	0,64	20	0,64	40	1,28
Sectorial competitiveness: PPP, BP and related industries	0,05	Functioning of the single market	0,017	10	0,17	20	0,33	20	0,33	40	0,67
		Innovation and research	0,017	10	0,17	20	0,33	20	0,33	40	0,67
		SME's	0,017	10	0,17	20	0,33	20	0,33	40	0,67
International trade	0,17	Import of food	0,060	10	0,60	10	0,60	10	0,60	40	2,38
		Import of feed	0,060	10	0,60	20	1,19	20	1,19	40	2,38
		Import of treated articles	0,051	10	0,51	20	1,02	20	1,02	40	2,04
Human Health	0,40	Hormone related diseases and disorders	0,133	10	1,33	30	4,00	30	4,00	20	2,67
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,133	10	1,33	20	2,67	20	2,67	40	5,33
		Food safety	0,133	10	1,33	20	2,67	20	2,67	40	5,33
Environment	0,09	Chemical quality of water	0,030	40	1,20	20	0,60	20	0,60	10	0,30
		Wildlife vertebrate populations	0,030	10	0,30	30	0,90	30	0,90	20	0,60
		Animal welfare	0,030	20	0,60	20	0,60	10	0,30	20	0,60

[6] This sub scenario builds on 5C, which considers hazard, and translates into a different relative performance of options 2 and 3 with respect to the following MCA criteria linked directly to ED effects: hormone related diseases and disorders, and wildlife vertebrate populations (highlighted in grey). In addition, it increases the weight for Human Health (from 0,25 to 0,40) while decreasing the weights for all other dimensions.

3. WEIGHTED PERFORMANCE MATRICES: ASPECT II - IMPLEMENTATION OF THE ED CRITERIA / APPROACH TO REGULATORY DECISION MAKING

1.6. Table 13 and 14. Scenario 1 - Homogeneity

Table 13. Sub scenario 1/A

		SCENARIO 1/A - HOMOGENITY							
Dimension	*Dimension weight*	*Criteria*	*Criteria weight*	Options					
				Option A		Option B		Option C	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,17	Legal certainty and proportionality	0,042	10	0,42	20	0,83	30	1,25
		Operability for regulatory decision making	0,042	10	0,42	20	0,83	30	1,25
		Coherence between BP and PPP legislation	0,042	10	0,42	20	0,83	30	1,25
		Compliance with international obligations of the EU	0,042	10	0,42	20	0,83	20	0,83
Sectorial competitiveness: EU agriculture	0,17	Number of PPP affected	0,056	10	0,56	20	1,11	30	1,67
		Crops affected	0,056	10	0,56	20	1,11	30	1,67
		Existence of alternatives / risk of resistance of pests	0,056	10	0,56	20	1,11	30	1,67
Sectorial competitiveness: PPP, BP and related industries	0,17	Functioning of the single market	0,056	10	0,56	20	1,11	30	1,67
		Innovation and research	0,056	10	0,56	20	1,11	30	1,67
		SME's	0,056	10	0,56	20	1,11	30	1,67
International trade	0,17	Import of food	0,056	10	0,56	20	1,11	20	1,11
		Import of feed	0,056	10	0,56	20	1,11	20	1,11
		Import of treated articles	0,056	10	0,56	10	0,56	10	0,56
Human Health	0,17	Hormone related diseases and disorders	0,056	20	1,11	20	1,11	10	0,56
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,056	10	0,56	10	0,56	10	0,56
		Food safety	0,056	10	0,56	20	1,11	30	1,67
Environment	0,17	Chemical quality of water	0,056	20	1,11	20	1,11	10	0,56
		Wildlife vertebrate populations	0,056	20	1,11	20	1,11	10	0,56
		Animal welfare	0,056	10	0,56	10	0,56	10	0,56

Table 14. Sub scenario 1/B

Dimension	Dimension weight	Criteria	Criteria weight	SCENARIO 1/B - HOMOGENITY					
				Options					
				Option A		Option B		Option C	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,17	Legal certainty and proportionality	0,033	10	0,33	20	0,67	30	1,00
		Operability for regulatory decision making	0,033	10	0,33	20	0,67	30	1,00
		Coherence between BP and PPP legislation	0,050	10	0,50	20	1,00	30	1,50
		Compliance with international obligations of the EU	0,050	10	0,50	20	1,00	20	1,00
Sectorial competitiveness: EU agriculture	0,17	Number of PPP affected	0,083	10	0,83	20	1,67	30	2,50
		Crops affected	0,050	10	0,50	20	1,00	30	1,50
		Existence of alternatives / risk of resistance of pests	0,033	10	0,33	20	0,67	30	1,00
Sectorial competitiveness: PPP, BP and related industries	0,17	Functioning of the single market	0,056	10	0,56	20	1,11	30	1,67
		Innovation and research	0,056	10	0,56	20	1,11	30	1,67
		SME's	0,056	10	0,56	20	1,11	30	1,67
International trade	0,17	Import of food	0,058	10	0,58	20	1,17	20	1,17
		Import of feed	0,058	10	0,58	20	1,17	20	1,17
		Import of treated articles	0,050	10	0,50	10	0,50	10	0,50
Human Health	0,17	Hormone related diseases and disorders	0,056	20	1,11	20	1,11	10	0,56
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,056	10	0,56	10	0,56	10	0,56
		Food safety	0,056	10	0,56	20	1,11	30	1,67
Environment	0,17	Chemical quality of water	0,056	20	1,11	20	1,11	10	0,56
		Wildlife vertebrate populations	0,056	20	1,11	20	1,11	10	0,56
		Animal welfare	0,056	10	0,56	10	0,56	10	0,56

1.7. Tabel 15. Scenario 2 - Priority to evidence

Dimension	Dimension weight	Criteria	Criteria weight	SCENARIO 2 - PRIORITY TO EVIDENCE					
				Options					
				Option A		Option B		Option C	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,18	Legal certainty and proportionality	0,036	10	0,36	20	0,72	30	1,08
		Operability for regulatory decision making	0,036	10	0,36	20	0,72	30	1,08
		Coherence between BP and PPP legislation	0,054	10	0,54	20	1,08	30	1,62
		Compliance with international obligations of the EU	0,054	10	0,54	20	1,08	20	1,08
Sectorial competitiveness: EU agriculture	0,21	Number of PPP affected	0,105	10	1,05	20	2,10	30	3,15
		Crops affected	0,063	10	0,63	20	1,26	30	1,89
		Existence of alternatives / risk of resistance of pests	0,042	10	0,42	20	0,84	30	1,26
Sectorial competitiveness: PPP, BP and related industries	0,12	Functioning of the single market	0,040	10	0,40	20	0,80	30	1,20
		Innovation and research	0,040	10	0,40	20	0,80	30	1,20
		SME's	0,040	10	0,40	20	0,80	30	1,20
International trade	0,22	Import of food	0,077	10	0,77	20	1,54	20	1,54
		Import of feed	0,077	10	0,77	20	1,54	20	1,54
		Import of treated articles	0,066	10	0,66	10	0,66	10	0,66
Human Health	0,13	Hormone related diseases and disorders	0,043	20	0,87	20	0,87	10	0,43
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,043	10	0,43	10	0,43	10	0,43
		Food safety	0,043	10	0,43	20	0,87	30	1,30
Environment	0,14	Chemical quality of water	0,047	20	0,93	20	0,93	10	0,47
		Wildlife vertebrate populations	0,047	20	0,93	20	0,93	10	0,47
		Animal welfare	0,047	10	0,47	10	0,47	10	0,47

1.8. Table 16. Scenario 3 - Priority to health and environment

Dimension	Dimension weight	SCENARIO 3 - PRIORITY TO HEALTH and ENVIRONMENT Criteria	Criteria weight	Options Option A		Option B		Option C	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,16	Legal certainty and proportionality	0,032	10	0,32	20	0,64	30	0,96
		Operability for regulatory decision making	0,032	10	0,32	20	0,64	30	0,96
		Coherence between BP and PPP legislation	0,048	10	0,48	20	0,96	30	1,44
		Compliance with international obligations of the EU	0,048	10	0,48	20	0,96	20	0,96
Sectorial competitiveness: EU agriculture	0,17	Number of PPP affected	0,085	10	0,85	20	1,70	30	2,55
		Crops affected	0,051	10	0,51	20	1,02	30	1,53
		Existence of alternatives / risk of resistance of pests	0,034	10	0,34	20	0,68	30	1,02
Sectorial competitiveness: PPP, BP and related industries	0,09	Functioning of the single market	0,030	10	0,30	20	0,60	30	0,90
		Innovation and research	0,030	10	0,30	20	0,60	30	0,90
		SME's	0,030	10	0,30	20	0,60	30	0,90
International trade	0,18	Import of food	0,063	10	0,63	20	1,26	20	1,26
		Import of feed	0,063	10	0,63	20	1,26	20	1,26
		Import of treated articles	0,054	10	0,54	10	0,54	10	0,54
Human Health	0,20	Hormone related diseases and disorders	0,067	20	1,33	20	1,33	10	0,67
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,067	10	0,67	10	0,67	10	0,67
		Food safety	0,067	10	0,67	20	1,33	30	2,00
Environment	0,20	Chemical quality of water	0,067	20	1,33	20	1,33	10	0,67
		Wildlife vertebrate populations	0,067	20	1,33	20	1,33	10	0,67
		Animal welfare	0,067	10	0,67	10	0,67	10	0,67

1.9. Table 17. Scenario 4 - Health first

Dimension	Dimension weight	Criteria	Criteria weight	SCENARIO 4 - HEALTH FIRST					
				Options					
				Option A		Option B		Option C	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,16	Legal certainty and proportionality	0,032	10	0,32	20	0,64	30	0,96
		Operability for regulatory decision making	0,032	10	0,32	20	0,64	30	0,96
		Coherence between BP and PPP legislation	0,048	10	0,48	20	0,96	30	1,44
		Compliance with international obligations of the EU	0,048	10	0,48	20	0,96	20	0,96
Sectorial competitiveness: EU agriculture	0,19	Number of PPP affected	0,095	10	0,95	20	1,90	30	2,85
		Crops affected	0,057	10	0,57	20	1,14	30	1,71
		Existence of alternatives / risk of resistance of pests	0,038	10	0,38	20	0,76	30	1,14
Sectorial competitiveness: PPP, BP and related industries	0,08	Functioning of the single market	0,027	10	0,27	20	0,53	30	0,80
		Innovation and research	0,027	10	0,27	20	0,53	30	0,80
		SME's	0,027	10	0,27	20	0,53	30	0,80
International trade	0,20	Import of food	0,070	10	0,70	20	1,40	20	1,40
		Import of feed	0,070	10	0,70	20	1,40	20	1,40
		Import of treated articles	0,060	10	0,60	10	0,60	10	0,60
Human Health	0,25	Hormone related diseases and disorders	0,083	20	1,67	20	1,67	10	0,83
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,083	10	0,83	10	0,83	10	0,83
		Food safety	0,083	10	0,83	20	1,67	30	2,50
Environment	0,12	Chemical quality of water	0,040	20	0,80	20	0,80	10	0,40
		Wildlife vertebrate populations	0,040	20	0,80	20	0,80	10	0,40
		Animal welfare	0,040	10	0,40	10	0,40	10	0,40

1.10. Table 18 to 21. Scenario 5 - Aim: exposure zero

Table 18. Sub scenario 5/A[7]

Dimension	Dimension weight	SCENARIO 5/A - AIM: EXPOSURE ZERO Criteria	Criteria weight	Options Option A		Option B		Option C	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,16	Legal certainty and proportionality	0,032	10	0,32	20	0,64	30	0,96
		Operability for regulatory decision making	0,032	10	0,32	20	0,64	30	0,96
		Coherence between BP and PPP legislation	0,048	10	0,48	20	0,96	30	1,44
		Compliance with international obligations of the EU	0,048	10	0,48	20	0,96	20	0,96
Sectorial competitiveness: EU agriculture	0,17	Number of PPP affected	0,085	10	0,85	20	1,70	30	2,55
		Crops affected	0,051	10	0,51	20	1,02	30	1,53
		Existence of alternatives / risk of resistance of pests	0,034	10	0,34	20	0,68	30	1,02
Sectorial competitiveness: PPP, BP and	0,09	Functioning of the single market	0,030	10	0,30	20	0,60	30	0,90
		Innovation and research	0,030	10	0,30	20	0,60	30	0,90
		SME's	0,030	10	0,30	20	0,60	30	0,90
International trade	0,18	Import of food	0,063	10	0,63	20	1,26	20	1,26
		Import of feed	0,063	10	0,63	20	1,26	20	1,26
		Import of treated articles	0,054	10	0,54	10	0,54	10	0,54
Human Health	0,20	Hormone related diseases and disorders	0,067	30	2,00	20	1,33	10	0,67
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,067	10	0,67	10	0,67	10	0,67
		Food safety	0,067	10	0,67	20	1,33	30	2,00
Environment	0,20	Chemical quality of water	0,067	30	2,00	20	1,33	10	0,67
		Wildlife vertebrate populations	0,067	30	2,00	20	1,33	10	0,67
		Animal welfare	0,067	10	0,67	10	0,67	10	0,67

[7] This sub scenario corresponds to Scenario 3 (Priority to health and environment) but considers hazard, which translates into a different relative performance of Option A with respect to the following MCA criteria, linked directly to ED effects: hormone related diseases and disorders, chemical quality of water, and wildlife vertebrate populations (highlighted in grey).

Table 19. Sub scenario 5/B[8]

Dimension	Dimension weight	SCENARIO 5/B - AIM: EXPOSURE ZERO Criteria	Criteria weight	Options Option A		Option B		Option C	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,11	Legal certainty and proportionality	0,022	10	0,22	20	0,44	30	0,66
		Operability for regulatory decision making	0,022	10	0,22	20	0,44	30	0,66
		Coherence between BP and PPP legislation	0,033	10	0,33	20	0,66	30	0,99
		Compliance with international obligations of the EU	0,033	10	0,33	20	0,66	20	0,66
Sectorial competitiveness: EU agriculture	0,12	Number of PPP affected	0,060	10	0,60	20	1,20	30	1,80
		Crops affected	0,036	10	0,36	20	0,72	30	1,08
		Existence of alternatives / risk of resistance of pests	0,024	10	0,24	20	0,48	30	0,72
Sectorial competitiveness: PPP, BP and	0,04	Functioning of the single market	0,013	10	0,13	20	0,27	30	0,40
		Innovation and research	0,013	10	0,13	20	0,27	30	0,40
		SME's	0,013	10	0,13	20	0,27	30	0,40
International trade	0,13	Import of food	0,046	10	0,46	20	0,91	20	0,91
		Import of feed	0,046	10	0,46	20	0,91	20	0,91
		Import of treated articles	0,039	10	0,39	10	0,39	10	0,39
Human Health	0,40	Hormone related diseases and disorders	0,200	30	6,00	20	4,00	10	2,00
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,100	10	1,00	10	1,00	10	1,00
		Food safety	0,100	10	1,00	20	2,00	30	3,00
Environment	0,20	Chemical quality of water	0,067	30	2,00	20	1,33	10	0,67
		Wildlife vertebrate populations	0,067	30	2,00	20	1,33	10	0,67
		Animal welfare	0,067	10	0,67	10	0,67	10	0,67

[8] This sub scenario builds on 5A which considers hazard, and translates into a different relative performance of Option A with respect to the following MCA criteria, linked directly to ED effects: hormone related diseases and disorders, chemical quality of water, and wildlife vertebrate populations (highlighted in grey). In addition, it increases the weight for Human Health (from 0,20 to 0,40) at the expenses of the other dimensions excluding Environment.

Table 20. Sub scenario 5/C[9]

Dimension	Dimension weight	SCENARIO 5/C - AIM: EXPOSURE ZERO Criteria	Criteria weight	Options Option A		Option B		Option C	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,16	Legal certainty and proportionality	0,032	10	0,32	20	0,64	30	0,96
		Operability for regulatory decision making	0,032	10	0,32	20	0,64	30	0,96
		Coherence between BP and PPP legislation	0,048	10	0,48	20	0,96	30	1,44
		Compliance with international obligations of the EU	0,048	10	0,48	20	0,96	20	0,96
Sectorial competitiveness: EU agriculture	0,19	Number of PPP affected	0,095	10	0,95	20	1,90	30	2,85
		Crops affected	0,057	10	0,57	20	1,14	30	1,71
		Existence of alternatives / risk of resistance of pests	0,038	10	0,38	20	0,76	30	1,14
Sectorial competitiveness: PPP, BP and	0,08	Functioning of the single market	0,027	10	0,27	20	0,53	30	0,80
		Innovation and research	0,027	10	0,27	20	0,53	30	0,80
		SME's	0,027	10	0,27	20	0,53	30	0,80
International trade	0,20	Import of food	0,070	10	0,70	20	1,40	20	1,40
		Import of feed	0,070	10	0,70	20	1,40	20	1,40
		Import of treated articles	0,060	10	0,60	10	0,60	10	0,60
Human Health	0,25	Hormone related diseases and disorders	0,083	30	2,50	20	1,67	10	0,83
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,083	10	0,83	10	0,83	10	0,83
		Food safety	0,083	10	0,83	20	1,67	30	2,50
Environment	0,12	Chemical quality of water	0,040	30	1,20	20	0,80	10	0,40
		Wildlife vertebrate populations	0,040	30	1,20	20	0,80	10	0,40
		Animal welfare	0,040	10	0,40	10	0,40	10	0,40

[9] This sub scenario corresponds to Scenario 4 (Health first) but considers hazard, which translates into a different relative performance of Option A with respect to the following MCA criteria, linked directly to ED effects: hormone related diseases and disorders, chemical quality of water, and wildlife vertebrate populations (highlighted in grey).

Table 21. Sub scenario 5/D[10]

Dimension	Dimension weight	SCENARIO 5/D - AIM: EXPOSURE ZERO Criteria	Criteria weight	Options Option A		Option B		Option C	
				Performance	Weighted P	Performance	Weighted P	Performance	Weighted P
Effectiveness and coherence	0,13	Legal certainty and proportionality	0,026	10	0,26	20	0,52	30	0,78
		Operability for regulatory decision making	0,026	10	0,26	20	0,52	30	0,78
		Coherence between BP and PPP legislation	0,039	10	0,39	20	0,78	30	1,17
		Compliance with international obligations of the EU	0,039	10	0,39	20	0,78	20	0,78
Sectorial competitiveness: EU agriculture	0,16	Number of PPP affected	0,080	10	0,80	20	1,60	30	2,40
		Crops affected	0,048	10	0,48	20	0,96	30	1,44
		Existence of alternatives / risk of resistance of pests	0,032	10	0,32	20	0,64	30	0,96
Sectorial competitiveness: PPP, BP and	0,05	Functioning of the single market	0,017	10	0,17	20	0,33	30	0,50
		Innovation and research	0,017	10	0,17	20	0,33	30	0,50
		SME's	0,017	10	0,17	20	0,33	30	0,50
International trade	0,17	Import of food	0,060	10	0,60	20	1,19	20	1,19
		Import of feed	0,060	10	0,60	20	1,19	20	1,19
		Import of treated articles	0,051	10	0,51	10	0,51	10	0,51
Human Health	0,40	Hormone related diseases and disorders	0,133	30	4,00	20	2,67	10	1,33
		Transmissible diseases caused by lack of appropriate disinfectants or insecticides	0,133	10	1,33	10	1,33	10	1,33
		Food safety	0,133	10	1,33	20	2,67	30	4,00
Environment	0,09	Chemical quality of water	0,030	30	0,90	20	0,60	10	0,30
		Wildlife vertebrate populations	0,030	30	0,90	20	0,60	10	0,30
		Animal welfare	0,030	10	0,30	10	0,30	10	0,30

[10] This sub scenario builds on 5C which considers hazard, and translates into a different relative performance of Option A with respect to the following MCA criteria, linked directly to ED effects: hormone related diseases and disorders, chemical quality of water, and wildlife vertebrate populations (highlighted in grey). In addition, it increases the weight for Human Health (from 0,25 to 0,40) while decreasing the weights for all other dimensions.

4. OUTRANKING MATRICES AND POLICY RANKING PERMUTATIONS: ASPECT I - SETTING SCIENTIFIC CRITERIA TO IDENTIFY EDS

1.11. Table 22 and 23. Scenario 1 - Homogeneity

Table 22. Sub scenario 1/A

	Outranking matrix			
	Option 1	Option 2	Option 3	Option 4
Option 1	-	0,24	0,35	0,08
Option 2	0,76	-	0,57	0,14
Option 3	0,65	0,43	-	0,11
Option 4	0,92	0,86	0,89	-

Policy ranking permutations (24)			
Permutations	Pairings		Scores
1234	12+13+14+23+24+34		1,50
1243	12+14+13+24+23+43		2,28
1324	13+12+14+32+34+24		1,36
1342	13+14+12+34+32+42		2,08
1423	14+12+13+42+43+23		3,00
1432	14+13+12+43+42+32		2,86
2134	21+23+24+13+14+34		2,01
2143	21+24+23+14+13+43		2,79
2314	23+21+24+31+34+14		2,31
2341	23+24+21+34+31+41		3,14
2413	24+21+23+41+43+13		3,63
2431	24+23+21+43+41+31		3,92
3124	31+32+34+12+14+24		1,65
3142	31+34+32+14+12+42		2,38
3214	32+31+34+21+24+14		2,17
3241	32+34+31+24+21+41		3,00
3412	34+31+32+41+42+12		3,21
3421	34+32+31+42+41+21		3,72
4123	41+42+43+12+13+23		3,83
4132	41+43+42+13+12+32		3,69
4213	42+41+43+21+23+13		4,35
4231	**42+43+41+23+21+31**		**4,64**
4312	43+41+42+31+32+12		3,99
4321	43+42+41+32+31+21		4,50

Table 23. Sub scenario 1/B

	Outranking matrix			
	Option 1	Option 2	Option 3	Option 4
Option 1	-	0,27	0,37	0,08
Option 2	0,73	-	0,56	0,14
Option 3	0,63	0,44	-	0,11
Option 4	0,92	0,86	0,89	-

Policy ranking permutations (24)			
Permutations	Pairings		Scores
1234	12+13+14+23+24+34		1,53
1243	12+14+13+24+23+43		2,31
1324	13+12+14+32+34+24		1,41
1342	13+14+12+34+32+42		2,13
1423	14+12+13+42+43+23		3,03
1432	14+13+12+43+42+32		2,91
2134	21+23+24+13+14+34		1,99
2143	21+24+23+14+13+43		2,77
2314	23+21+24+31+34+14		2,26
2341	23+24+21+34+31+41		3,09
2413	24+21+23+41+43+13		3,60
2431	24+23+21+43+41+31		3,87
3124	31+32+34+12+14+24		1,68
3142	31+34+32+14+12+42		2,40
3214	32+31+34+21+24+14		2,14
3241	32+34+31+24+21+41		2,97
3412	34+31+32+41+42+12		3,23
3421	34+32+31+42+41+21		3,69
4123	41+42+43+12+13+23		3,86
4132	41+43+42+13+12+32		3,74
4213	42+41+43+21+23+13		4,32
4231	**42+43+41+23+21+31**		**4,59**
4312	43+41+42+31+32+12		4,01
4321	43+42+41+32+31+21		4,47

1.12. Table 24. Scenario 2 - Priority to evidence

	Outranking matrix			
	Option 1	Option 2	Option 3	Option 4
Option 1	-	0,30	0,40	0,07
Option 2	0,70	-	0,56	0,12
Option 3	0,60	0,44	-	0,09
Option 4	0,93	0,89	0,91	-

Policy ranking permutations (24)			
Permutations	Pairings		Scores
1234	12+13+14+23+24+34		1,54
1243	12+14+13+24+23+43		2,36
1324	13+12+14+32+34+24		1,42
1342	13+14+12+34+32+42		2,19
1423	14+12+13+42+43+23		3,13
1432	14+13+12+43+42+32		3,01
2134	21+23+24+13+14+34		1,93
2143	21+24+23+14+13+43		2,75
2314	23+21+24+31+34+14		2,13
2341	23+24+21+34+31+41		2,99
2413	24+21+23+41+43+13		3,61
2431	24+23+21+43+41+31		3,81
3124	31+32+34+12+14+24		1,62
3142	31+34+32+14+12+42		2,39
3214	32+31+34+21+24+14		2,02
3241	32+34+31+24+21+41		2,88
3412	34+31+32+41+42+12		3,25
3421	34+32+31+42+41+21		3,65
4123	41+42+43+12+13+23		3,99
4132	41+43+42+13+12+32		3,87
4213	42+41+43+21+23+13		4,38
4231	**42+43+41+23+21+31**		**4,58**
4312	43+41+42+31+32+12		4,07
4321	43+42+41+32+31+21		4,46

1.13. Table 25. Scenario 3 - Priority to health and environment

	Outranking matrix			
	Option 1	Option 2	Option 3	Option 4
Option 1	-	0,29	0,39	0,10
Option 2	0,71	-	0,57	0,17
Option 3	0,61	0,43	-	0,13
Option 4	0,90	0,83	0,87	-

Policy ranking permutations (24)			
Permutations	Pairings		Scores
1234	12+13+14+23+24+34		1,65
1243	12+14+13+24+23+43		2,38
1324	13+12+14+32+34+24		1,52
1342	13+14+12+34+32+42		2,18
1423	14+12+13+42+43+23		3,05
1432	14+13+12+43+42+32		2,92
2134	21+23+24+13+14+34		2,06
2143	21+24+23+14+13+43		2,80
2314	23+21+24+31+34+14		2,29
2341	23+24+21+34+31+41		3,09
2413	24+21+23+41+43+13		3,60
2431	24+23+21+43+41+31		3,82
3124	31+32+34+12+14+24		1,74
3142	31+34+32+14+12+42		2,40
3214	32+31+34+21+24+14		2,15
3241	32+34+31+24+21+41		2,95
3412	34+31+32+41+42+12		3,20
3421	34+32+31+42+41+21		3,62
4123	41+42+43+12+13+23		3,85
4132	41+43+42+13+12+32		3,72
4213	42+41+43+21+23+13		4,26
4231	**42+43+41+23+21+31**		**4,49**
4312	43+41+42+31+32+12		3,94
4321	43+42+41+32+31+21		4,35

1.14. Table 26. Scenario 4 - Health first

	Outranking matrix			
	Option 1	Option 2	Option 3	Option 4
Option 1	-	0,27	0,36	0,06
Option 2	0,73	-	0,55	0,12
Option 3	0,65	0,45	-	0,10
Option 4	0,94	0,88	0,90	-

Policy ranking permutations (24)			
Permutations	Pairings		Scores
1234	12+13+14+23+24+34		1,46
1243	12+14+13+24+23+43		2,26
1324	13+12+14+32+34+24		1,36
1342	13+14+12+34+32+42		2,11
1423	14+12+13+42+43+23		3,01
1432	14+13+12+43+42+32		2,91
2134	21+23+24+13+14+34		1,92
2143	21+24+23+14+13+43		2,72
2314	23+21+24+31+34+14		2,21
2341	23+24+21+34+31+41		3,09
2413	24+21+23+41+43+13		3,60
2431	24+23+21+43+41+31		3,89
3124	31+32+34+12+14+24		1,65
3142	31+34+32+14+12+42		2,40
3214	32+31+34+21+24+14		2,11
3241	32+34+31+24+21+41		2,99
3412	34+31+32+41+42+12		3,28
3421	34+32+31+42+41+21		3,74
4123	41+42+43+12+13+23		3,89
4132	41+43+42+13+12+32		3,79
4213	42+41+43+21+23+13		4,35
4231	**42+43+41+23+21+31**		**4,64**
4312	43+41+42+31+32+12		4,08
4321	43+42+41+32+31+21		4,54

1.15. Table 27 to 30. Scenario 5 - Aim: exposure zero

Table 27. Sub scenario 5/A

	Outranking matrix			
	Option 1	Option 2	Option 3	Option 4
Option 1	-	0,29	0,39	0,10
Option 2	0,71	-	0,57	0,23
Option 3	0,61	0,43	-	0,20
Option 4	0,90	0,77	0,80	-

Policy ranking permutations (24)			
Permutations	Pairings		Scores
1234	12+13+14+23+24+34		1,78
1243	12+14+13+24+23+43		2,38
1324	13+12+14+32+34+24		1,65
1342	13+14+12+34+32+42		2,18
1423	14+12+13+42+43+23		2,91
1432	14+13+12+43+42+32		2,78
2134	21+23+24+13+14+34		2,20
2143	21+24+23+14+13+43		2,80
2314	23+21+24+31+34+14		2,42
2341	23+24+21+34+31+41		3,22
2413	24+21+23+41+43+13		3,60
2431	24+23+21+43+41+31		3,82
3124	31+32+34+12+14+24		1,87
3142	31+34+32+14+12+42		2,40
3214	32+31+34+21+24+14		2,29
3241	32+34+31+24+21+41		3,09
3412	34+31+32+41+42+12		3,20
3421	34+32+31+42+41+21		3,62
4123	41+42+43+12+13+23		3,71
4132	41+43+42+13+12+32		3,58
4213	42+41+43+21+23+13		4,13
4231	**42+43+41+23+21+31**		**4,35**
4312	43+41+42+31+32+12		3,80
4321	43+42+41+32+31+21		4,22

Table 28. Sub scenario 5/B

	Outranking matrix			
	Option 1	Option 2	Option 3	Option 4
Option 1	-	0,24	0,31	0,10
Option 2	0,76	-	0,56	0,37
Option 3	0,69	0,44	-	0,33
Option 4	0,90	0,63	0,67	-

Policy ranking permutations (24)			
Permutations	Pairings		Scores
1234	12+13+14+23+24+34		1,90
1243	12+14+13+24+23+43		2,24
1324	13+12+14+32+34+24		1,79
1342	13+14+12+34+32+42		2,06
1423	14+12+13+42+43+23		2,50
1432	14+13+12+43+42+32		2,39
2134	21+23+24+13+14+34		2,43
2143	21+24+23+14+13+43		2,77
2314	23+21+24+31+34+14		2,81
2341	23+24+21+34+31+41		3,61
2413	24+21+23+41+43+13		3,57
2431	24+23+21+43+41+31		3,94
3124	31+32+34+12+14+24		2,17
3142	31+34+32+14+12+42		2,43
3214	32+31+34+21+24+14		2,70
3241	32+34+31+24+21+41		3,50
3412	34+31+32+41+42+12		3,23
3421	34+32+31+42+41+21		3,76
4123	41+42+43+12+13+23		3,30
4132	41+43+42+13+12+32		3,19
4213	42+41+43+21+23+13		3,83
4231	**42+43+41+23+21+31**		**4,21**
4312	43+41+42+31+32+12		3,57
4321	43+42+41+32+31+21		4,10

Table 29. Sub scenario 5/C

	Outranking matrix			
	Option 1	Option 2	Option 3	Option 4
Option 1	-	0,27	0,36	0,06
Option 2	0,73	-	0,55	0,18
Option 3	0,65	0,45	-	0,16
Option 4	0,94	0,82	0,84	-

Policy ranking permutations (24)			
Permutations	Pairings		Scores
1234	12+13+14+23+24+34		1,58
1243	12+14+13+24+23+43		2,26
1324	13+12+14+32+34+24		1,48
1342	13+14+12+34+32+42		2,11
1423	14+12+13+42+43+23		2,89
1432	14+13+12+43+42+32		2,79
2134	21+23+24+13+14+34		2,04
2143	21+24+23+14+13+43		2,72
2314	23+21+24+31+34+14		2,33
2341	23+24+21+34+31+41		3,21
2413	24+21+23+41+43+13		3,60
2431	24+23+21+43+41+31		3,89
3124	31+32+34+12+14+24		1,77
3142	31+34+32+14+12+42		2,40
3214	32+31+34+21+24+14		2,23
3241	32+34+31+24+21+41		3,11
3412	34+31+32+41+42+12		3,28
3421	34+32+31+42+41+21		3,74
4123	41+42+43+12+13+23		3,77
4132	41+43+42+13+12+32		3,67
4213	42+41+43+21+23+13		4,23
4231	**42+43+41+23+21+31**		**4,52**
4312	43+41+42+31+32+12		3,96
4321	43+42+41+32+31+21		4,42

Table 30. Sub scenario 5/D

	Outranking matrix			
	Option 1	Option 2	Option 3	Option 4
Option 1	-	0,22	0,29	0,05
Option 2	0,78	-	0,54	0,21
Option 3	0,71	0,46	-	0,19
Option 4	0,96	0,79	0,81	-

Policy ranking permutations (24)			
Permutations	Pairings		Scores
1234	12+13+14+23+24+34		1,50
1243	12+14+13+24+23+43		2,11
1324	13+12+14+32+34+24		1,42
1342	13+14+12+34+32+42		2,00
1423	14+12+13+42+43+23		2,70
1432	14+13+12+43+42+32		2,61
2134	21+23+24+13+14+34		2,05
2143	21+24+23+14+13+43		2,67
2314	23+21+24+31+34+14		2,48
2341	23+24+21+34+31+41		3,39
2413	24+21+23+41+43+13		3,58
2431	24+23+21+43+41+31		4,00
3124	31+32+34+12+14+24		1,84
3142	31+34+32+14+12+42		2,42
3214	32+31+34+21+24+14		2,39
3241	32+34+31+24+21+41		3,30
3412	34+31+32+41+42+12		3,33
3421	34+32+31+42+41+21		3,89
4123	41+42+43+12+13+23		3,61
4132	41+43+42+13+12+32		3,52
4213	42+41+43+21+23+13		4,16
4231	**42+43+41+23+21+31**		**4,58**
4312	43+41+42+31+32+12		3,95
4321	43+42+41+32+31+21		4,50

5. OUTRANKING MATRICES AND POLICY RANKING PERMUTATIONS: ASPECT II - IMPLEMENTATION OF THE ED CRITERIA / APPROACH TO REGULATORY DECISION MAKING

1.16. Table 31 to 32. Scenario 1 - Homogeneity

Table 31. Sub scenario 1/A

	Outranking matrix		
	Option A	Option B	Option C
Option A	-	0,17	0,25
Option B	0,83	-	0,33
Option C	0,75	0,67	-

Policy ranking permutations (6)		
Permutations	Pairings	Scores
ABC	AB + AC + BC	0,74
ACB	AC + CB + AB	1,09
BAC	BA + AC + BC	1,41
BCA	BC + CA + CB	1,75
CAB	CA + AB + CB	1,59
CBA	**CB + CA + BA**	**2,26**

Table 32. Sub scenario 1/B

	Outranking matrix		
	Option A	Option B	Option C
Option A	-	0,16	0,25
Option B	0,84	-	0,33
Option C	0,75	0,67	-

Policy ranking permutations (6)		
Permutations	Pairings	Scores
ABC	AB + AC + BC	0,74
ACB	AC + CB + AB	1,08
BAC	BA + AC + BC	1,41
BCA	BC + CA + CB	1,75
CAB	CA + AB + CB	1,59
CBA	**CB + CA + BA**	**2,26**

1.17. Table 33. Scenario 2 - Priority to evidence

	Outranking matrix		
	Option A	Option B	Option C
Option A	-	0,15	0,21
Option B	0,85	-	0,32
Option C	0,79	0,68	-

Policy ranking permutations (6)		
Permutations	Pairings	Scores
ABC	AB + AC + BC	0,68
ACB	AC + CB + AB	1,04
BAC	BA + AC + BC	1,39
BCA	BC + CA + CB	1,79
CAB	CA + AB + CB	1,61
CBA	**CB + CA + BA**	**2,32**

1.18. Table 34. Scenario 3 - Priority to health and environment

	Outranking matrix		
	Option A	Option B	Option C
Option A	-	0,19	0,29
Option B	0,81	-	0,38
Option C	0,71	0,62	-

Policy ranking permutations (6)		
Permutations	Pairings	Scores
ABC	AB + AC + BC	0,87
ACB	AC + CB + AB	1,11
BAC	BA + AC + BC	1,48
BCA	BC + CA + CB	1,71
CAB	CA + AB + CB	1,52
CBA	**CB + CA + BA**	**2,13**

1.19. Table 35. Scenario 4 - Health first

	Outranking matrix		
	Option A	Option B	Option C
Option A	-	0,17	0,26
Option B	0,83	-	0,35
Option C	0,75	0,65	-

Policy ranking permutations (6)		
Permutations	Pairings	Scores
ABC	AB + AC + BC	0,78
ACB	AC + CB + AB	1,08
BAC	BA + AC + BC	1,43
BCA	BC + CA + CB	1,75
CAB	CA + AB + CB	1,57
CBA	**CB + CA + BA**	**2,22**

1.20. Table 36 to 39. Scenario 5 - Aim: exposure zero

Table 36. Sub scenario 5/A

	Outranking matrix		
	Option A	Option B	Option C
Option A	-	0,29	0,29
Option B	0,71	-	0,38
Option C	0,71	0,62	-

Policy ranking permutations (6)		
Permutations	Pairings	Scores
ABC	AB + AC + BC	0,97
ACB	AC + CB + AB	1,21
BAC	BA + AC + BC	1,38
BCA	BC + CA + CB	1,71
CAB	CA + AB + CB	1,62
CBA	**CB + CA + BA**	**2,03**

Table 37. Sub scenario 5/B

	Outranking matrix		
	Option A	Option B	Option C
Option A	-	0,44	0,44
Option B	0,56	-	0,50
Option C	0,56	0,50	-

Policy ranking permutations (6)		
Permutations	Pairings	Scores
ABC	AB + AC + BC	1,37
ACB	AC + CB + AB	1,37
BAC	BA + AC + BC	1,50
BCA	BC + CA + CB	1,56
CAB	CA + AB + CB	1,50
CBA	**CB + CA + BA**	**1,63**

Table 38. Sub scenario 5/C

	Outranking matrix		
	Option A	Option B	Option C
Option A	-	0,26	0,26
Option B	0,75	-	0,35
Option C	0,75	0,65	-

Policy ranking permutations (6)		
Permutations	Pairings	Scores
ABC	AB + AC + BC	0,86
ACB	AC + CB + AB	1,16
BAC	BA + AC + BC	1,35
BCA	BC + CA + CB	1,75
CAB	CA + AB + CB	1,65
CBA	**CB + CA + BA**	**2,14**

Table 39. Sub scenario 5/D

	Outranking matrix		
	Option A	Option B	Option C
Option A	-	0,30	0,30
Option B	0,70	-	0,38
Option C	0,70	0,62	-

Policy ranking permutations (6)		
Permutations	Pairings	Scores
ABC	AB + AC + BC	0,98
ACB	AC + CB + AB	1,22
BAC	BA + AC + BC	1,38
BCA	BC + CA + CB	1,70
CAB	CA + AB + CB	1,62
CBA	**CB + CA + BA**	**2,02**

6. SUMMARY OVERVIEW OF RESULTS

The MCA was carried out by using a step-wise approach, because there were two sets of options to consider (see Annex 6, section 3.2).

The MCA methodology was first applied to Options 1 to 4 (Aspect I: setting scientific criteria to identify EDs) in order to get the policy rankings for these options under all scenarios. The same MCA methodology (including the same criteria, weights, and performance assessment method) was then applied to Options A to C (Aspect II: implementation of the ED criteria / approach to regulatory decision making), in order to get the corresponding policy rankings.

The results obtained for the two sets of options are summarised in the following Tables 38 and 39, where for each scenario considered, the corresponding best policy ranking of the options is given (e.g., for scenario 1/A, the corresponding policy ranking means that Option 4 is better than Option 2, which is in turn better than Option 3, being Option 1 the worst among the four considered).

Table 40. Overview of results in terms of policy ranking of Options 1-4 (Aspect I: setting scientific criteria to identify EDs)

SENSITIVITY SCENARIO	POLICY RANKING OF OPTIONS
Scenario 1A – Homogeneity	4 > 2 > 3 > 1
Scenario 1B – Homogeneity	4 > 2 > 3 > 1
Scenario 2 – Priority to evidence	4 > 2 > 3 > 1
Scenario 3 – Health and Environment	4 > 2 > 3 > 1
Scenario 4 – Health first	4 > 2 > 3 > 1
Scenario 5A – Aim: exposure zero	4 > 2 > 3 > 1
*Scenario 5B – Aim: exposure zero **	*4 > 2 > 3 > 1*
Scenario 5C – Aim: exposure zero	4 > 2 > 3 > 1
Scenario 5D – Aim: exposure zero	4 > 2 > 3 > 1
Overall ranking	WHO + potency (Option 4) > > WHO (Option 2) > > WHO + categories (Option 3) > > Interim criteria (Option 1)

** The policy ranking remains unchanged when the weight assigned to the human health criteria "hormone related diseases and disorders" is increased to 25% with the weight for "food safety" and "transmissible diseases caused by lack of appropriate disinfectants or insecticides" set at 7,5% each*

Table 41. Overview of results in terms of policy ranking of Options A-C (Aspect II: implementation of the ED criteria / approach to regulatory decision making)

SENSITIVITY SCENARIO	POLICY RANKING OF OPTIONS
Scenario 1A – Homogeneity	C > B > A
Scenario 1B – Homogeneity	C > B > A
Scenario 2 – Priority to evidence	C > B > A
Scenario 3 – Health and Environment	C > B > A
Scenario 4 – Health first	C > B > A
Scenario 5A – Aim: exposure zero	C > B > A
*Scenario 5B – Aim: exposure zero **	*C > B > A*
Scenario 5C – Aim: exposure zero	C > B > A
Scenario 5D – Aim: exposure zero	C > B > A
Overall ranking	Alignment socio-economic considerations (Option C) > > Alignment risk assessment (Option B) > > no change to regulatory decision making (Option A)

** The policy ranking changes to B > A > C when the weight assigned to the human health criteria "hormone related diseases and disorders" in scenario (5B) is further increased to 25% with the weight for "food safety" and "transmissible diseases caused by lack of appropriate disinfectants or insecticides" set at 7,5% each.*

The results illustrated in tables 40 and 41 show that for both sets of options, the policy ranking remains the same whatever scenario is being considered, which indicates consistent results in terms of policy ranking.

Regarding the EU criteria to identify EDs, and considering the current legislative framework, Option 4 (WHO definition + potency) ranks consistently as the best in the MCA, followed by Option 2 (WHO definition).

Regarding the approaches to regulatory decision making, the policy ranking obtained through the MCA clearly identifies Option C (alignment of PPP with BP by introducing socio-economic considerations) as the best option, followed by Option B (alignment of PPP with BP by introducing further elements of risk assessment).

It is worth mentioning that the consistency of the policy rankings with respect to a change in the weights assigned to the different dimensions/criteria (whose values depend on the scenarios considered), was evaluated via a sensitivity analysis carried out by considering alternative scenarios (see Table 1). Consistent results have been obtained regardless the different weights (i.e. "importance") assigned to the dimensions in these different scenarios. Total weights on human health and environment have been set at up to 60% (Scenario "Aim: exposure zero" 5B), including up to a total of 20% priority to hormone related diseases and a total of 13.4% priority on environment-ED related issues (chemical quality of water and wildlife). In addition, scenario 5 (aim: exposure zero) is also ranking the options in a more conservative way (performance of the options), since this is based only on exposure and does not considers risk assessment based decision making as in scenarios 1 to 4. In summary, also with 33.4% total weight on ED issues related to protection of human health and the environment, and a regulatory decision making based on hazard (no consideration of risk decision making), the best performing policy ranking identifies Option 4 and Option A as the best, followed by Option 2 and Option B, respectively.

Additional simulations were run under Scenario 5/B (Aim: exposure zero) assuming a different distribution of the weights assigned to the Human Health criteria (hormone related diseases and disorders 0,25; food safety 0,075; transmissible diseases caused by lack of appropriate disinfectants or insecticides 0,75). In total, this scenario assumes a protective hazard based regulatory decision making and puts a total weight of 38,4 % on MCA-criteria directly related to ED effects (25% on hormone related diseases and disorders, 6,7 % on chemical quality of water and 6,7% on wildlife vertebrate populations). The MCA-analysis resulted in a different policy ranking for Options A to C: Option C was performing the worst as the ranking was B > A> C. However, the policy ranking of Options 1 to 4 remained unchanged, and Option 4 remained the best, followed by Option 2.

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PART 9/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annex 8 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

{COM(2016) 350 final}
{SWD(2016) 212 final}

ANNEX 8

ACHIEVEMENT OF EFFECTIVENESS AND COHERENCE

Contents

This Annex focuses on the assessment of potential impacts, which build on the results of the screening study explained in Annexes 3 to 5. The results of the screening do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation. The methods and results presented in this Annex are to be interpreted as an estimation of the potential impacts.

Annexes 8 to 15 describe the impacts expected when implementing the criteria to identify EDs (Options 1 to 4) under the current regulatory framework (Option A). In addition, it was assessed whether these expected impacts would remain the same or not under consideration of different regulatory implementations (Options B and C, only applicable to the PPP Regulation). The analyses of the impacts described in these Annexes translate into the "performance" of the options, which is one of the input parameters to the MCAs (Annex 6 and 7).

The MCAs results are not concluding on any preferred option for setting scientific criteria to identify endocrine disruptors, but aim at providing additional information to decision makers with regards to the potential impacts expected when implementing the criteria, after those would have been selected on the basis of science (two MCAs were performed: Options 1 to 4 under the current regulatory context, and Options A compared to Options B and C).

At a preliminary stage of the impact assessment it was anticipated that Option C should be discarded, nevertheless it was maintained for the analysis of the impacts for methodological reasons (see Section 4.2.3 of the main report and Annexes 6 and 7). Option C only applies to the PPP Regulation.

1. INTRODUCTION

The current regulatory consequences for substances considered to be endocrine disruptors (EDs) differ between Regulation (EC) No 1107/2009 and Regulation (EU) No 528/2012 (see for details Annex II, Section 3.6.5 and Article 4.7 of the PPP Regulation and Article 5 of the BP Regulation). Considering no change to the current decision making (Option A), the following regulatory consequences are foreseen for substances identified as ED:

- non-approval of active substances (BP for general public, most cases for PPP);
- approvals limited to situations where negligible exposure is demonstrated on a case by case basis (some PPP cases);
- approvals limited to situations where negligible risk is demonstrated on a case by case basis (BP professional uses);
- approvals limited to situations where certain socio/economic considerations are considered (PPP to fight a serious danger to plant health; BP professional uses, when the substances is needed to prevent or control serious dangers to human health, animal health or the environment or measures would lead to disproportionate negative effects on society).

In detail, substances having ED properties shall not be approved, unless any of the following derogations is applicable:

- For a Plant Protection Product:
  - *the exposure is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with point (b) of Article 18(1) of Regulation (EC) No 396/2005. […], or*
  - *the substance is necessary to control a serious danger to plant health which cannot be contained by other available means including non-chemical method (this provision can only be applied for a maximum period of 5 years);*
- For a Biocidal Product (professional use):
  - *the risk to humans, animals or the environment from exposure to the active substance […] is negligible […], or*
  - *[…]the substance is essential to prevent or control serious dangers to human health, animal health or the environment, or*
  - *not approving the substance would have disproportionate negative impacts on society when compared with the risk […].*

Article 19(4) of the BP Regulation stipulates that a biocidal product having ED properties (i.e. not specifying 'which may cause adverse effects') shall not be authorised for use by the general public.

This regulatory context needs to be considered in each of the sections below.

2. LEGAL CERTAINTY AND PROPORTIONALITY

Legal certainty would – in principle - be ensured by any of the options 1 to 4, since criteria to identify EDs would be in all cases defined in the context of Regulation (EC) No 1107/2009 and Regulation (EU) No 528/2012. This also applies to any of the options A to C, once they are defined in the respective legislation. However, it can be expected that some options may be inconsistent with the World Trade Organization (WTO) agreement, which was ratified by the EU, thus triggering consequence at international level or in front of the EU courts (see sections below).

Both the PPP and the BP Regulations entered into force recently and provide for transition periods in order to facilitate the transition from the previous legal rules. As a consequence, experience applying the derogations mentioned above is still scarce thus leaving uncertainty on the practical implementation of the regulatory consequences for EDs active substances.

For instance, technical guidance on how to interpret the wording "negligible exposure" in section 3.6.5 to the PPP Regulation is currently under discussion within the Standing Committee for Plants, Animals, Feed and Food (PAFF) after having consulted Member States (MS) and EFSA experts as well as stakeholders. Further, the European Food Safety Authority (EFSA) has been mandated for particular active substances to assess negligible exposure and to consider whether is it possible to grant derogations on the basis of Article 4.7 of the PPP Regulation regarding the need to control a serious danger to plant health. However, the experience gained during the progress on these mandates has shown that further discussion between EFSA and MS is needed in order to assess the concrete impact of these provisions. In fact, as demonstrated by the recent discussions at the Standing Committee PAFF concerning PPP, the implementation of these derogations is complex and still needs considerable discussions among MS and the European Food Safety Authority (EFSA) in order to draw a way forward. All this creates a situation of uncertainty to applicants, stakeholders, and MS when it comes to concrete cases of decision making (approval/non approval) regarding a particular active substance. Regarding the implementation of the derogations for BP active substances, it is so far not clear how MS would decide in case they would be applicable.

Based on the rationale explained in the previous paragraph, some options are linked to legal uncertainties (in particular Option A). Consequently the more derogations may be applied for, the higher the potential uncertainties. As a consequence, it can be concluded that the more substances identified as EDs, the more uncertainty to applicants and stakeholders could be expected due to the application of the case-by-case derogations. This implies that the options would be ranked like 4 > 2/3 > 1 based on the results of the screening, and C > B > A based on the fact that Option C (consideration of socio/economic elements) would lead to less non-approvals than Option B (consideration of risk elements) and Option A (decision making mainly based on hazard).

In addition, **Option 3** introduces the concept of **additional categories**, i.e. Category II and III. These additional categories would have no regulatory consequences but would identify substances so called "suspected EDs" (Category II) and "potential EDs or endocrine active substances" (Category III). In particular, substances would fall under Cat II when there is some evidence that they may be EDs, but the evidence is not convincing for instance because

of poor data quality. Substances would fall under Category III when there is some evidence of an endocrine mode of action but no evidence of an adverse effect.

However, using categories similarly to those used for classification under Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP Regulation) may lead to confusion. It may be misinterpreted that substances categorised under the criteria to identify ED as Category II or Category III are classified as such under the CLP, while this is not the case. The criteria to identify EDs were mandated by the legislators only for PPP and BP. It is assumed that if the legislators would have intended to classify and label all chemicals, they would have initiated such process under the CLP Regulation, which was not the case so far. Thus, using categories could be considered as expanding the scope of the mandates given under the PPP and BP Regulations. Further, it may be confusing with respect to other overarching pieces of EU legislation (CLP), and thus negatively affect legal certainty and operability.

Furthermore, the categories foreseen under Option 3 (Cat I, II and III) do not follow the same rationale as those used in the Regulation CLP. For instance, under the CLP Regulation, carcinogen substances are classified as Cat IA (confirmed carcinogen, evidence based on human data), Cat IB (carcinogen, evidence based on animal data) and Cat II (suspected carcinogen). Under Option 3, no distinction between categories Cat IA and Cat IB would be realised because human data on EDs are missing. Instead, Cat III is created additionally (potential EDs or endocrine active substances). From the different kind of categories used, it appears that EDs are not yet ready to be classified under the CLP Regulation, as it was done for mutagens, carcinogens and substances toxic for reproduction, and may be thus not proportionate at this point in time.

It may be considered that "flagging" through the criteria for identification of EDs all substances that are “suspected EDs” or “potential EDs” would be a benefit. For instance, it has been claimed that “potential concerns” would be identified through the legislation and that assessors would not be forced to choose between ED and non-ED, but they would be provided with intermediate categories for classification, in analogy with the system under classification and labelling of Regulation 1272/2008. However, in the context of the PPP and BP Regulation, no system for categories is in place. If the legislator's intention was to align EDs classification with the system under Regulation 1272/2008, this would have been specified. Thus, defining additional measures which are not regulatory and, so far, not provided in the legislation would imply a considerable degree of legal complexity, with no regulatory added value. In addition, such approach might go beyond what is necessary to reach the objective of protection of human and animal health that the EU co-legislator put into effect in the PPP and BP Regulations. As a consequence, a measure that would "flag" not only “EDs” but also “suspected EDs” or “potential EDs” might breach the proportionality principle. Such regulatory actions do not seem necessary and would likely determine fear in consumers′ minds towards substances that are safe, but labelled as “suspected or potential EDs” thus altering consumers behaviour and market share, while not introducing any added value for health and environmental protection. In fact, such additional categories could be used easily by media to generate mistrust of consumers towards certain products.

In addition, the creation of additional categories may lead to different interpretation among the MS during the assessment of active substances, or the authorisation of PPP and BP, decreasing as a consequence harmonisation in the EU with respect to the decision making regarding PPP and BP. In fact, it is reasonable to wonder which would be the regulatory consequences of these "suspected EDs" or "potential EDs" in the procedure for granting products authorisations at national level. In the absence of any reference in the legislation, it is likely to foresee that MS would take different approach in the evaluation of products containing such substances. This would hinder principles of the legislation in place, such as the mutual recognition of products under the PPP Regulation, and therefore will be in contradiction with the objectives of "strengthening the functioning of the internal market", without introducing any benefit for the objective "ensuring a high level of protection to human health and the environment" as no regulatory consequences are set in the legislation for Cat II and Cat III.

Under consideration of this additional factor, the options are ranked as 4 > 2 > 1 > 3 based on the results of the screening, and C > B > A based on the fact that Option C (consideration of socio/economic elements) would lead to less non-approvals than Option B (consideration of risk elements) and Option A (decision making mainly based on hazard).

3. OPERABILITY FOR REGULATORY DECISION MAKING

As mentioned above, the PPP and the BP Regulations entered recently into force and, as a consequence, experience in applying the derogations present in both regulations is scarce. Recent discussions at the Standing Committee for Plants, Animals, Feed and Food (PAFF) concerning PPP showed that the implementation of these derogations is far from reaching an operable stage because it still needs considerable discussions among MS and the European Food Safety Authority (EFSA).

It is also clear that the implementations of the derogations provided in Annex II, point 3.6.5 and Article 4.7 of Regulation (EC) No 1107/2009, are increasing the burden to national and EU administrations with respect to the standard risk assessment procedures, which were in place before the approval criteria ("cut-off" criteria) defined in the same Regulation were implemented. This is because the derogations mentioned above are applicable if a substance is falling under point 3.6.5 (the substance is identified as ED). However, even when a substance is identified as an ED and derogations are applicable, a full risk assessment will always be needed to verify whether a decision on approval can be taken. As a consequence, the cut-off criteria for EDs are not necessarily simplifying the decision making, but adding additional assessments. Thus, it can be expected that the more substances are identified as EDs, the more administrative burden is created to verify the applicability of the derogations. As foreseen in Article 82 of the same Regulation, the Commission is intending to present a report on the functioning of these and other provisions introduced by Regulation (EC) No 1107/2009.

In summary, it can be concluded that the more substances are identified as EDs, the higher operability difficulties and additional burden may be expected because of the application of the case-by-case derogations. This implies that the options would be ranked as 4 > 2/3 > 1, and C > B > A.

Option 3 introduces the concept of **additional categories**, i.e. Category II and III with no regulatory consequences, as detailed above in Section 1 in this annex. It is uncertain in the context of the PPP and BP legislation how these categories would be made operable. The legislation does not provide for a framework of categories with no regulatory consequences in addition to the substances identified as EDs but approved under the foreseen derogations (see above), which would be listed as "candidates of substitution"[1]. In addition, using categories similarly to those used for classification under Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP Regulation) may lead to confusion and thus negatively affect operability, as explained in the previous section. Further, the creation of additional categories may increase the burden to administrations and applicants, which would add to the implementation of derogations for the options which have regulatory consequences.

Under consideration of this additional factor, the options are ranked as 4>2>1>3 and C>B>A.

4. COHERENCE BETWEEN BP AND PPP LEGISLATION

As detailed above, the regulatory consequences for substances identified as EDs under the BP Regulation and the PPP Regulation are different. This seems in contradiction with the aim to present harmonised criteria for PPP Regulation and BP Regulation, as they would only be harmonised if they would be implemented following similar scientific principles.

The BP Regulation was adopted three years after the PPP Regulation. In the PPP Regulation, the derogation on negligible *exposure* is provided for in a long and complex sentence which is also giving examples. This sentence is raising controversial discussions among MS and stakeholders, so that a common interpretation has not yet been agreed because of differences in the technical interpretations. The corresponding derogation on negligible *risk* in the BP Regulation is provided for in a much shorter and clearer sentence, which seems easier to interpret from a technical point of view.

In addition, as regards EDs, European scientific committees have recently concluded that risk assessment makes best use of available information on EDs and that these substances *can therefore be subject to risk assessment and not only to hazard assessment* (EFSA Opinion 2013 on EDs, SCCS Memorandum on EDs, 2014).

As a consequence, coherence between provisions for EDs under the BP and the PPP Regulations would be given if the same criteria would be applied to scientifically similar derogations (e.g. aligning negligible exposure and negligible risk) or socio/economic derogations. This alignment would also have the benefit of a simpler and clearer text for the PPP Regulation, if aligned with the BP Regulation.

Based on this rationale, the options are ranked based on the number of substances identified under each option (for Options 1 to 4), and based on the regulatory decision making (Options A to C), as follows: 4 > 2/3 > 1; and C > B > A.

[1] "Candidates of substitution" are approved for a shorter period of time and it is required to carry out a comparative assessment before authorising a PPP or BP, in order to verify if a better alternative PPP or BP is available. See Article 24 in Regulation (EC) 1107/2009.

5. INTERNATIONAL OBLIGATIONS (WTO AND CODEX ALIMENTARIUS)

Several respondents to the public consultation (mostly public authorities from third countries) highlighted the potentially significant trade implications of setting criteria to identify EDs and asked for a risk-based approach to be taken. They indicated that any decision on the criteria to identify EDs must respect the principles of international law, including certain Agreements of the WTO.

The EU must respect its international obligations while exercising its powers.[2] Therefore, any measures taken by the EU institutions shall be consistent with provisions of international law that are binding the EU, such as customary international law and treaties ratified by the EU[3].

The European Union (EU) and its 28 EU MS are members of the WTO and hence need to comply with its agreements: in this matter with the Agreement on Technical Barriers to Trade (TBT Agreement) and the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement).

The TBT Agreement aims at ensuring non-discrimination in the adoption and implementation of technical regulations and standards.

The SPS Agreement sets constraints on WTO Members' policies restricting the use of unjustified sanitary and phytosanitary measures for the purpose of trade protection. Article 2.1 of the SPS Agreement states that "*Members have the right to take sanitary and phytosanitary measures necessary for the protection of human, animal or plant life or health, provided that such measures are not inconsistent with the provisions of this Agreement*". Further, Article 2.2. states that "*Members shall ensure that any sanitary or phytosanitary measure is applied only to the extent necessary to protect human, animal or plant life or health, is based on scientific principles and is not maintained without sufficient scientific evidence, except as provided for in paragraph 7 of Article 5".*

The TBT and SPS Committees meet regularly, three times per year. In the TBT and SPS Committees the issue of EDs was raised by the US for the first time in October 2013 and in March 2014 respectively. Since then it has been discussed, in one form or another, at every TBT and SPS Committee meeting.[4]

Overall, the pressure on the EU is mounting as demonstrated by the growing number of WTO Members taking the floor to express concerns or to question the EU's work on defining the criteria to identify EDs.

At the SPS Committee meeting in October 2015 a Specific Trade Concern was raised against the EU jointly by the US and Argentina, supported by 21 other countries (Brazil, Burkina Faso, Canada, Chile, China, Colombia, the Dominican Republic, Egypt, India, Jamaica, Kenya, Madagascar, Malaysia, Mexico, Nigeria, Paraguay, Peru, Senegal, Sierra Leone, and Vietnam).

[2] See e.g., ECJ, case C-286/90, Poulsen, [1992] ECR I-06019, para. 9; and ECJ, case C-162/96, Racke, ECR [1998] I-3655, para 46.
[3] See e.g., Joined Cases C-21/72 & C-24/74, International Fruit Company, [1972] ECR I-1219.
[4] The summary reports of these meetings can be found on the WTO website:
TBT Committee: https://www.wto.org/english/tratop_e/tbt_e/tbt_e.htm;
SPS Committee: https://www.wto.org/english/tratop_e/sps_e/sps_e.htm

This situation is unprecedented in the SPS Committee and is expected to continue in the future, which makes the EU position very difficult.

In the SPS Committee the main concerns and requests of WTO Members to the EU are the following:

- questioning the scientific evidence underlying the options, and the consideration of any hazard-based "cut off" option instead of risk from actual exposure;
- claiming that none of the options outlined by the EU in its roadmap appeared to take risk into consideration, as required under WTO obligations. The proposal, as drafted, could thus impact billions of dollars of trade worldwide and potentially result in the withdrawal a large number of substances, as well as the products that contain them, from the EU;
- stating that the EU's hazard-based approach could disrupt trade and unnecessarily create a level of uncertainty among exporting countries, while increasing costs for agricultural and agri-food stakeholders in both the EU and exporting countries;
- requesting the EU to recognise risk-based endocrine programmes developed by other countries;
- asking that special attention should be given to minimising adverse impacts on international trade and especially on trade in agricultural products, but also to minimising socioeconomic losses in commodity-producing countries, in particular developing countries;
- encouraging the EU to publish the draft legislation, once developed, including any risk and impact assessments carried out;
- asking that future actions should be taken on a case-by-case basis and based on solid scientific evidence after appropriate risk assessment;
- calling for continued transparency and for evidence-based and risk-based decision-making;
- encouraging the EU to adhere to relevant international standards and to keep informing the Committees of any relevant developments;
- asking that the measure should be compatible with the TBT and SPS Agreements and non-discriminatory.

Article 5.1 of the SPS Agreement states that "*Members shall ensure that their sanitary or phytosanitary measures are based on an assessment, as appropriate to the circumstances, of the risks to human, animal or plant life or health, taking into account risk assessment techniques developed by the relevant international organizations*."

Relevant EU legislative drafts need to be notified to the WTO[5] to allow Members to become familiar with the measures and to provide opportunity to present their observations. The comments from the EU's trading partners need to be taken into account, whenever justified, before the final legislation is eventually adopted. The WTO also provides for a procedure for resolving trade quarrels under the Dispute Settlement Understanding. A dispute arises when a member government believes another member government is violating an agreement or a

[5] See Article 7 and Annex B of the SPS Agreement, available on: https://www.wto.org/english/tratop_e/sps_e/spsagr_e.htm, and Article 10 of the TBT Agreement, available on: https://www.wto.org/english/docs_e/legal_e/17-tbt_e.htm

commitment that it has made in the WTO. When a case is decided, the ultimate goal for the country is to comply with the ruling.

The unprecedented broad coalition of WTO Members challenging the EU policy when setting criteria to identify EDs strongly suggests that, depending on the final decision, formal WTO dispute could be expected.

Further, the Commission contributes to the development of international standards which underpin food law, for instance the harmonised international food standards in the context of the Codex Alimentarius. International standards are a key element in ensuring the safety and quality of food in international trade. Codex is the pre-eminent body setting standards to ensure consumer health protection and fair practices in food trade. The status of Codex as an international standard-setting body in the field of food safety is recognised in two key WTO agreements: the Agreements on the Application of Sanitary and Phytosanitary Measures and on Technical Barriers to Trade.

The **Codex Alimentarius** or "Food Code" was established by FAO and the World Health Organization in 1963 to develop harmonised international food standards, which protect consumer health and promote fair practices in food trade. It recommends, inter alia, Maximum Residue Limits (MRLs) of pesticides in food and feed. These MRLs are based on risk analysis principles, which are evaluated and reviewed as appropriate in the light of new generated scientific data. The risk analysis should follow the structured approach comprising risk assessment, risk management, and risk communication. Each of these steps should be fully and transparently communicated.

Where international standards exist or their completion is imminent, they shall be taken into consideration in the development or adaptation of food law in accordance with Article 5 of Regulation (EC) No 178/2002. Further, Article 13 of the same regulation says that without prejudice to their rights and obligations, the Community and the MS shall, inter alia:

- contribute to the development of agreements on recognition of the equivalence of specific food and feed-related measures;
- give particular attention to the special development, financial and trade needs of developing countries, with a view to ensuring that international standards do not create unnecessary obstacles to exports from developing countries;
- promote consistency between international technical standards and food law while ensuring that the high level of protection adopted in the Community is not reduced.

As provided for in Regulation (EC) No 396/2005, the Community's trading partners should be consulted via the WTO about the MRLs proposed. MRLs set at the international level by the Codex Alimentarius Commission should also be considered when Community MRLs are being set, taking into account the corresponding good agricultural practices.

Against this background, it can be concluded that the more an option is hazard-based, the less it will be compliant with WTO and the worse performing it will be in the MCA analysis.

For assessing options 1 to 4, this argumentation considers only Option A of the roadmap (the current decision making applicable to the PPP and BP sectors remains unchanged). It is

mainly valid for the PPP sector as in the BP sector, the current decision making already considers risk/socio economic assessments, except for BP destined to consumers.

In this context, options 1, 2 and 3 are all based on the identification of hazard. However, Option 4, by including potency, which is one of the elements of hazard characterisation, goes one step further in the direction of risk assessment. Therefore, it can be considered that among the four options, Option 4 will perform comparatively better than the others in terms of compliance with WTO rules, i.e. option 4 > 2/3/1.

For assessing options A to C, the focus is on the PPP sector, because in the BP sector the decision making considers derogations with risk/socio economic elements, except for BP destined to consumers.

In Option A, the decision making is mainly based on hazard, while Option B considers the inclusion of further elements of risk assessment in the PPP sector (e.g. aligning PPP Regulation derogations on negligible exposure to BP Regulation derogation on negligible risk). Option C introduces elements of socio economy in the PPP sector, which would go beyond risk assessment. Therefore, the options regarding decision making would perform B/C > A.

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PART 10/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annex 9 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

{COM(2016) 350 final}
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ANNEX 9

HUMAN HEALTH - HORMONE RELATED DISEASES

Contents

This Annex focuses on the assessment of potential impacts, which build on the results of the screening study explained in Annexes 3 to 5. The results of the screening do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation. The methods and results presented in this Annex are to be interpreted as an estimation of the potential impacts.

Annexes 8 to 15 describe the impacts expected when implementing the criteria to identify EDs (Options 1 to 4) under the current regulatory framework (Option A). In addition, it was assessed whether these expected impacts would remain the same or not under consideration of different regulatory implementations (Options B and C, only applicable to the PPP Regulation). The analyses of the impacts described in these Annexes translate into the "performance" of the options, which is one of the input parameters to the MCAs (Annex 6 and 7).

The MCAs results are not concluding on any preferred option for setting scientific criteria to identify endocrine disruptors, but aim at providing additional information to decision makers with regards to the potential impacts expected when implementing the criteria, after those would have been selected on the basis of science (two MCAs were performed: Options 1 to 4 under the current regulatory context, and Options A compared to Options B and C).

At a preliminary stage of the impact assessment it was anticipated that Option C should be discarded, nevertheless it was maintained for the analysis of the impacts for methodological reasons (see Section 4.2.3 of the main report and Annexes 6 and 7). Option C only applies to the PPP Regulation.

1. ENDOCRINE DISRUPTORS AND HORMONE RELATED DISEASES - EVIDENCE

The evidence on potential impacts on human health associated to different policy options for setting criteria to identify EDs is analysed in the following subsections with the aim to rank them.

Endocrine disruption is a relatively recent way of looking at the toxicity of chemicals, which aims at understanding the mode of action (MoA), i.e. how chemicals lead to the adverse effects observed. In 1991, a group of scientists concluded that a large number of man-made chemicals have the potential to disrupt the endocrine system of animals, including humans (Wingspread Statement[1]), in particular because of the crucial role that hormones play in controlling the development of animals.

However, also natural substances are known to have endocrine disrupting properties. For instance, the soybean phytoestrogens (isoflavones) genistein and daidzein were reported to affect adversely thyroid function;[2,3,4] bisphenol F formed during mustard production from a natural ingredient of mustard grains[5,6] was reported to increase thyroxin levels of female rats[7]; caffeine was reported to exert embryo- and foeto-toxicity in rat and affect sperm quality in mice.[8,9]

The possible association between incidence of certain human diseases and exposure to endocrine disruptors (EDs) has been raised in some international reports on the state of science on EDs which are mentioned below. However, evidence is scattered and its interpretation controversial, so that a causal link or even a possible association between ED exposure at environmental levels and the diseases mentioned in connection is not agreed among experts. A recent study carried out for the European Commission[10] stresses that health outcomes are often the results of the synergies of multiple factors. For long latency diseases a

[1] Bern, H et al. 1992. Statement from the work session on chemically-induced alterations in sexual development: the wildlife/human connection. pp 1-8 in Chemically-Induced Alterations in Sexual and Functional Development: The Wildlife/Human Connection. Eds. Colborn T. and Clement C., Princeton Scientific Publishing Co., NJ, U.S. Retrieved from: http://www.ourstolenfuture.org/consensus/wingspread1.htm

[2] Patisaul, H. B., and Jefferson, W. 2010. The pros and cons of phytoestrogens. Frontiers in Neuroendocrinology, 31(4), 400–419. http://doi.org/10.1016/j.yfrne.2010.03.003

[3] Loutchanwoot, P., Srivilai, P., Jarry, H. 2013. Effects of the natural endocrine disruptor equol on the pituitary function in adult male rats. Toxicology Feb 8;304:69-75. doi: 10.1016/j.tox.2012.11.017.

[4] Sosić-Jurjević B, et al. 2010. Suppressive effects of genistein and daidzein on pituitary-thyroid axis in orchidectomized middle-aged rats. Exp Biol Med (Maywood). May;235(5):590-8. doi: 10.1258/ebm.2009.009279.

[5] Federal Department of Home Affairs FDHA. Federal Food Safety and Veterinary Office FSVO. Risk Assessment. Bisphenol F in mustard. Retrieved from: http://www.efsa.europa.eu/sites/default/files/assets/af150611a-ax11.6.pdf

[6] Zoller, O. et al. 2016. Natural occurrence of bisphenol F in mustard, Food Additives & Contaminants: Part A, 33:1, 137-146, DOI: 10.1080/19440049.2015.1110623

[7] Higashihara N, et al. 2007. Subacute oral toxicity study of bisphenol F based on the draft protocol for the "Enhanced OECD Test Guideline no. 407". Arch Toxicol. Dec;81(12):825-32. Epub 2007 Jul 13. Retrieved from: http://www.ncbi.nlm.nih.gov/pubmed/17628788

[8] Bars, R. et al. 2012. Risk assessment of endocrine active chemicals: Identifying chemicals of regulatory concern. Regulatory Toxicology and Pharmacology 64 (1): 143-154. doi:10.1016/j.yrtph.2012.06.013

[9] Tinwell, H,. S. Colombel, O. Blanck, R. Bars. 2013. The screening of everyday life chemicals in validated assays targeting the pituitary–gonadal axis. Regulatory Toxicology and Pharmacology 66 (2): 184-196 doi:10.1016/j.yrtph.2013.04.002

[10] Risk and Policy Analysts (RPA) et al. 2015. Study on the Calculation of the Benefits of Chemical Legislation on Human Health and the Environment, Final report for DG Environment, March 2016, Loddon, Norfolk, UK

number of assumptions are required which seriously limits the value of any indicator trying to measure the marginal contribution of chemicals legislation in lowering exposures.

The WHO-UNEP 2012 report "State of the science of Endocrine Disrupting Chemicals"[11] mentioned the following diseases in connection with ED exposure: prostate cancer and breast cancer, female and male reproductive health disorders, thyroid and metabolic disorders, neurodevelopment and immune disorders. The report highlighted the difficulties to prove an effective role of EDs exposure in the increasing incidence of these "*endocrine diseases and disorders"*. Scientific criticism to the general methodology used in the WHO-UNEP 2012 report was raised in 2014[12]. This initiated a response[13] by the authors of the WHO-UNEP 2012 report, triggering a further reply[14] by the authors of the scientific comments on the methodology in 2015. These recent publications show that the controversy about the methodology used in the WHO-UNEP 2012 report seems not resolved.

Other scientists[15] criticise the WHO-UNEP report 2012 (some of them ex-chair of European Commission Scientific Committees). They support the critics of Lamb et al. and further state: "the 2002 WHO/ICPS report demanded that a review of all data on endocrine disruption had to be appropriately performed according to the well-established principles of data evaluation. This was not adequately performed in the WHO/UNEP 2012 report and is also missing in the Zoeller et al.[16] article".

Finally, other critics[17,18] to the WHO-UNEP 2012 report regarded more general scientific issues of debate, such as the existence and relevance of low-dose effects and non-monotonic dose-response curves for EDs (among these authors, some were members of European Agencies Scientific Committees).

[11] World Health Organization (WHO) 2012. State of the science of Endocrine Disrupting Chemicals 2012. Summary for Decision-Makers. Ed. Bergman Å., Heindel, J.J., Jobling S., Kidd, K.A., and Zoeller R.T. Retrieved from: http://www.unep.org/pdf/WHO_HSE_PHE_IHE_2013.1_eng.pdf

[12] Lamb J.C. et al. 2014. Critical comments on the WHO-UNEP State of the Science of Endocrine Disrupting Chemicals – 2012. Regulatory Toxicology and Pharmacology 69 (1) 22-40. doi:10.1016/j.yrtph.2014.02.002

[13] Bergman, Å., et al. 2015. Manufacturing doubt about endocrine disrupter science – A rebuttal of industry-sponsored critical comments on the UNEP/WHO report "State of the Science of Endocrine Disrupting Chemicals 2012", Regulatory Toxicology and Pharmacology 73 (3) 1007-1017, ISSN 0273-2300. Doi: 10.1016/j.yrtph.2015.07.026.

[14] Lamb, et al. 2015. Comments on the opinions published by Bergman et al. (2015) on Critical Comments on the WHO-UNEP State of the Science of Endocrine Disrupting Chemicals, Regulatory Toxicology and Pharmacology. 73 (3) 754-757. ISSN 0273-2300, doi.org/10.1016/j.yrtph.2015.10.029

[15] Autrup, H., Barileb, F. A., Blaauboerc, B. J., Degend, G. H., Dekant, W., Dietrich, D., Domingog, J. L., Gorih G. B., Greim, H., Hengstlerd, J. G., Kacewj, S., Marquardtk, H., Pelkonenl, O., Savolainenm, K., and Vermeulenn, N. P. 2015. Principles of Pharmacology and Toxicology also Govern Effects of Chemicals on the Endocrine System. Toxicol Sci. 2015 Jul;146(1):11-5. Retrieved from: http://www.ncbi.nlm.nih.gov/pubmed/26026993

[16] Zoeller, R. T., Bergman, A., Becher, G., Bjerregaard, P., Bornman, R., Brandt, I., Iguchi, T., Jobling, S., Kidd, K. A., Kortenkamp, A., et al. 2014. A path forward in the debate over health impacts of endocrine disrupting chemicals. Environ. Health, 14, 118

[17] Testai, E., Galli, C.L., Dekant, W., Marinovich, M., Piersma, A.H., Sharpe, R.M., 2013. A plea for risk assessment of endocrine disrupting chemicals. Toxicology, http://dx.doi.org/10.1016/j.tox.2013.07.018

[18] Borgert, C. J., Baker, S. P., and Matthews, J. C. 2013. Potency matters: thresholds govern endocrine activity. Regul. Toxicol. Pharmacol., 67, 83–88.

In a recent external scientific report of EFSA [19] (2016) the evidence for the non-monotonic dose-response (NMDR) hypothesis was evaluated for substances in the area of food safety. The plausibility of NMDRs was assessed based on a systematic review methodology, which identified over 10'000 potentially relevant scientific studies. From these studies, 142 studies could be selected for the evaluation (49 in-vivo, 91 in-vitro, and 2 epidemiological studies). The report indicates that the empirical evidence for NMDR was limited or weak for most in vivo datasets that were selected for substances in the area of food safety. The report also indicates that *evaluation regarding the biological meaning (e.g. dose range studies, adversity of the effects, and toxicity at high doses leading to NMDR) and relevance for risk assessment were not part of this data analysis*, thus questioning the relevance of the evidence for the adverse effects.

In 2009 the Endocrine Society concluded that "*the evidence for adverse reproductive outcomes (infertility, cancers, malformations) from exposure to endocrine disrupting chemicals is strong, and there is mounting evidence for effects on other endocrine systems, including thyroid, neuroendocrine, obesity and metabolism, and insulin and glucose homeostasis*"[20]. In 2015, in a second statement, this is confirmed with further evidence from the past five years.[21;22] Based on the current information it can be concluded that: certain reviews suggest a significant association between exposure to low doses of chemicals and diseases (WHO-UNEP 2012 report[11], Endocrine Society 2nd statement 2015[21]); other reviews suggest that this association is not supported by evidence;[23;24] other publications criticise the methodology used by the reviews supporting the existence of such an association.[13,14,25,26] In addition, it needs to be mentioned that the WHO and Endocrine Society reviews do not consider the regulatory context for PPP and BP in Europe, but base their reports on general available information without consideration of the different regulatory systems in place worldwide.

[19] Beausoleil et al, 2016. Review of non-monotonic dose-responses of substances for human risk assessment. EFSA supporting publication 2016:EN-1027. 290pp.

[20] Diamanti-Kandarakis E. et al. 2009. Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement. Endocrine Reviews 30(4):293-342, doi:10.1210/er.2009-0002. Retrieved from: https://www.endocrine.org/endocrine-press/scientific-statements

[21] Gore, A.C., et al. 2015. EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals. Endocrine Reviews 36 (6) doi.org/10.1210/er.2015-1010

[22] Gore, A.C., et al. 2015. Executive Summary to EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals. Endocrine Reviews, 36(6):593–602. doi: 10.1210/er.2015-1093

[23] Ntzani EE, Chondrogiorgi M, Ntritsos G, Evangelou E, Tzoulaki I, 2013. Literature review on epidemiological studies linking exposure to pesticides and health effects. EFSA supporting publication 2013:EN-497, 159 pp. http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/497e.pdf

[24] Levêque-Morlais, N., et al. 2015. The AGRIculture and CANcer (AGRICAN) cohort study: enrollment and causes of death for the 2005–2009 period. International Archives of Occupational and Environmental Health. 88 (1): 61-73. DOI 10.1007/s00420-014-0933-x

[25] Gerhard J. Nohynek, Christopher J. Borgert, Daniel Dietrich, Karl K. Rozman. 2013. Endocrine disruption: Fact or urban legend? Toxicology Letters. 23 (6): 295-305, ISSN 0378-4274. DOI: http://dx.doi.org/10.1016/j.toxlet.2013.10.022

[26] Autrup, H., et al. 2015. Principles of Pharmacology and Toxicology Also Govern Effects of Chemicals on the Endocrine System. Toxicol. Sci. 146 (1): 11-15. doi: 10.1093/toxsci/kfv082

Since, the evidence regarding the causal link between ED exposure and some of the diseases seems to be still controversial among some experts, the following sections in this annex explore:

1) the evidence available at EU level on incidence of potentially hormone related diseases based on EUROSTAT and OECD data (section 1.1);
2) the epidemiological and laboratory evidence of a causal link between exposure to EDs and hormone related diseases (section 1.2);
3) the EU Regulation of active substances used in PPP and BP which are identified as EDs (section 1.3);
4) new methodological developments in addressing these issues (section 1.4).

1.1. Incidence of potentially hormone related diseases based on EUROSTAT and OECD data

Health statistic data available at EU28 or international level were analysed for the diseases mentioned in connection with EDs. A reference of the extent of a causal link with ED exposure mentioned in the source of the respective health statistic data was also given. In particular, data available via Eurostat and OECD were used for this analysis.

In general, it is difficult to conclude from health data available at EU and OECD level about the extent of a potential causal link between development of certain diseases and environmental exposure to endocrine disruptors. In fact, these health data are likely to be influenced by a better tracking of the diseases (e.g. cancer) resulting in higher scores of these diseases. Furthermore, many factors contribute to the development of these multifactorial diseases (e.g. obesity and diabetes are associated with various socio-economic factors). Below detailed information for cancer, obesity and diabetes is presented.

1.1.1. Causes of death - Annual standardised death rate (SDR) per 100 000 inhabitants (Eurostat, EU 28)

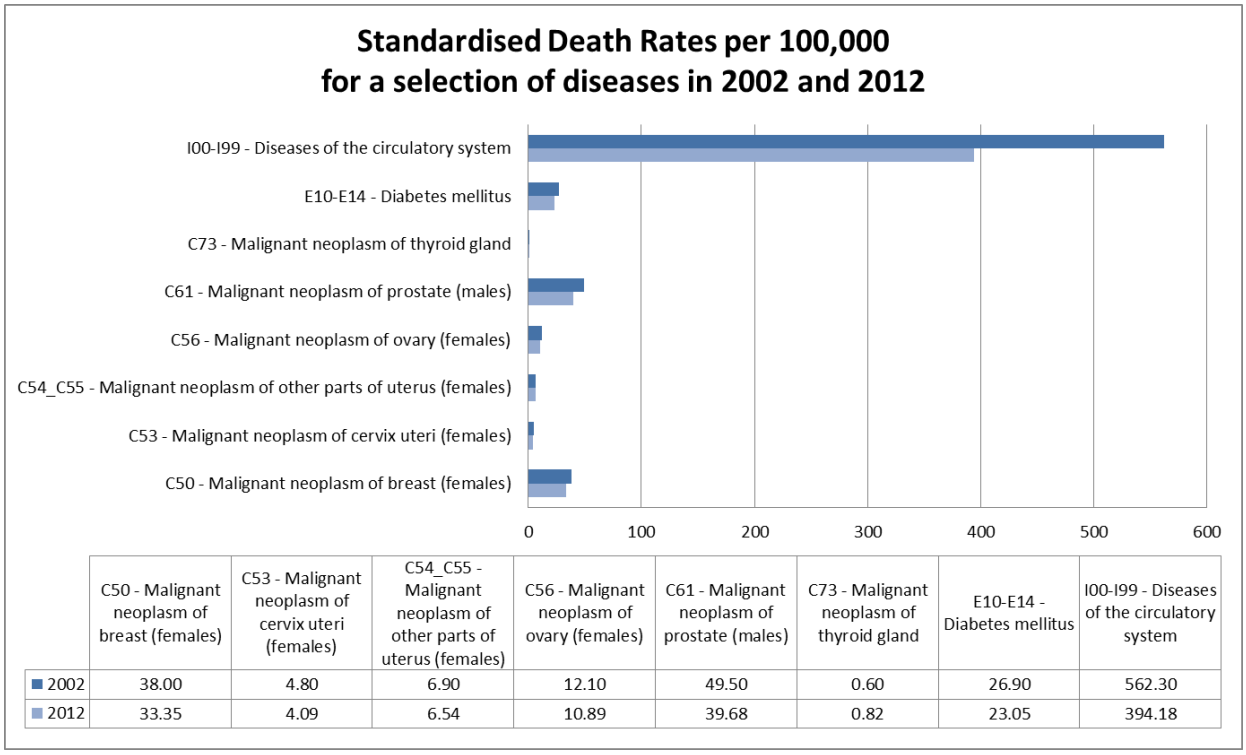
The following Eurostat data were selected for the analysis of diseases on the basis of the concerns raised by the international reports mentioned in Section 1.2 of this annex (Table 1).

Table 1. Eurostat data selected for the analysis

Malignant neoplasm of breast, total population
Malignant neoplasm of thyroid gland, total population
Diabetes mellitus, total population
Diseases of the circulatory system (I00-I99), total population
Malignant neoplasm of cervix uteri, female population
Malignant neoplasm of other parts of uterus, female population
Malignant neoplasm of ovary, female population
Malignant neoplasm of prostate, male population
Malignant neoplasm of testis, male population
Malignant neoplasms of cervix

Life expectancy has constantly increased at EU level over recent years (Figure 1). This is translated into decreasing standardised death rates[27] (SDR) for most causes of death.

This pattern applies to all diseases presented in Table 1 and Figure 1, making it difficult to assess the impact of EDs on these diseases, due to the generally decreasing - mortality rates. It is to note among these diseases that the SDR for thyroid cancer has very slightly increased at EU28 level from 0.6 in 2004 to 0.8 in 2012.



	C50 - Malignant neoplasm of breast (females)	C53 - Malignant neoplasm of cervix uteri (females)	C54_C55 - Malignant neoplasm of other parts of uterus (females)	C56 - Malignant neoplasm of ovary (females)	C61 - Malignant neoplasm of prostate (males)	C73 - Malignant neoplasm of thyroid gland	E10-E14 - Diabetes mellitus	I00-I99 - Diseases of the circulatory system
2002	38.00	4.80	6.90	12.10	49.50	0.60	26.90	562.30
2012	33.35	4.09	6.54	10.89	39.68	0.82	23.05	394.18

Figure 1. Standardised death Rates per 100,000 for a selection of diseases in 2002 and 2012.

1.1.2. Cancer morbidity, incidence per 100 000 females/males in some Member States (OECD data)

The following OECD data were selected for the analysis of diseases selected on the basis of the concerns raised by the international reports mentioned in Section 1.2 of this annex: malignant neoplasms of female breast, malignant neoplasms of cervix, and malignant neoplasms of prostate.

From 1998 to 2012, the incidence rate of female breast cancer has increased in most Member States (MS) except for Greece and Sweden (Figure 2). Over the same period, the incidence rate of prostate cancer has increased in most MS except for Greece (Figure 3). Decreasing or stable incidence rates of cervical cancer were observed during this period for most MS except for Ireland and Spain (Figure 4). However, as shown in Figure 1, the standardised death rate

[27] According to Eurostat; the standardised death rate, abbreviated as SDR, is the death rate of a population adjusted to a standard age distribution. It is calculated as a weighted average of the age-specific death rates of a given population; the weights are the age distribution of that population. Retrieved from: http://ec.europa.eu/eurostat/statistics-explained/index.php/Glossary:Standardised_death_rate_(SDR)

for female breast cancer and prostate cancer decreased. The increase of the incidence of female breast cancer and prostate cancer may be due to better diagnosis tools and/or systems for these diseases over the recent years (which would be also confirmed by the decreased death rate) and not necessarily to exposure to EDs. Further, established known risk factors for breast cancer include: increasing age, family history, exposure to estrogen, genetic predisposition, some breast conditions and lifestyle related factors[28]. This shows the challenge for establishing any causal link between exposure to EDs and this type of diseases.

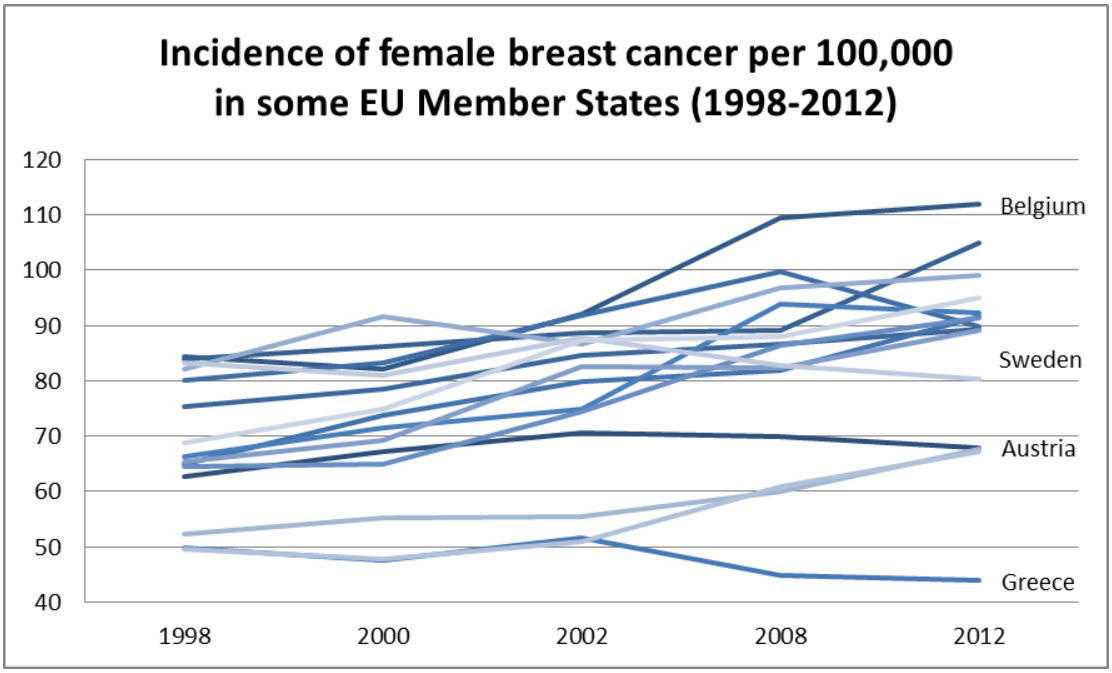


Figure 2. Incidence of female breast cancer per 100,000 in some EU MS (1998-2012)

[28] European Commission, JRC. European Network of Cancer Registries Factsheet 2014. Retrieved from: http://www.encr.eu/index.php/publications/factsheets

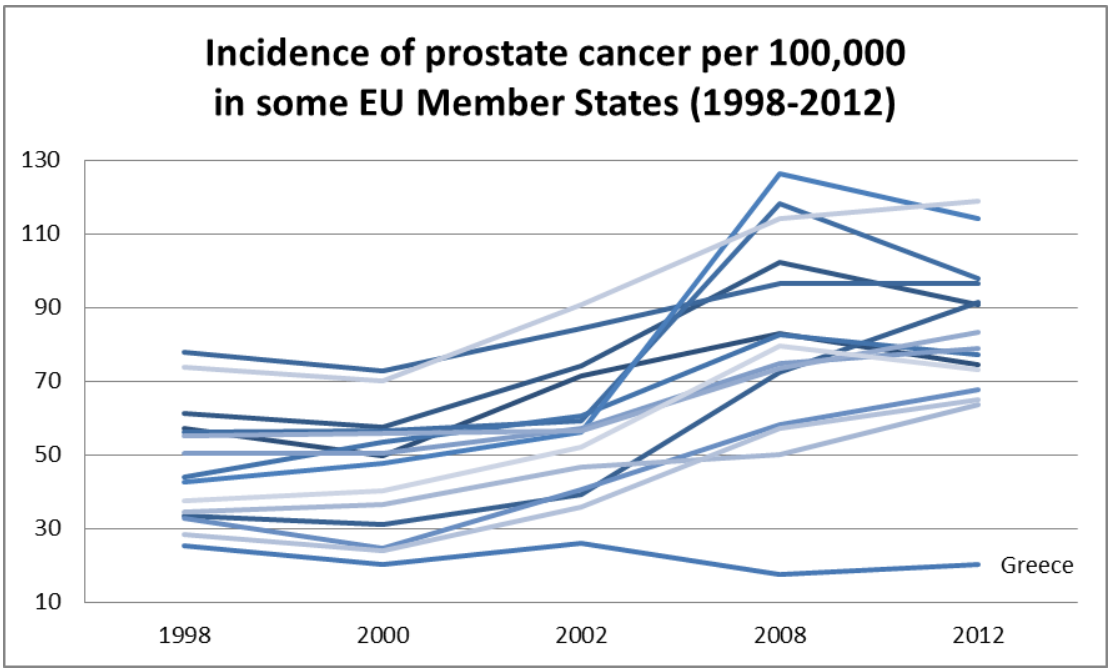


Figure 3. Incidence of prostate cancer per 100,000 in some EU MS (1998-2012)

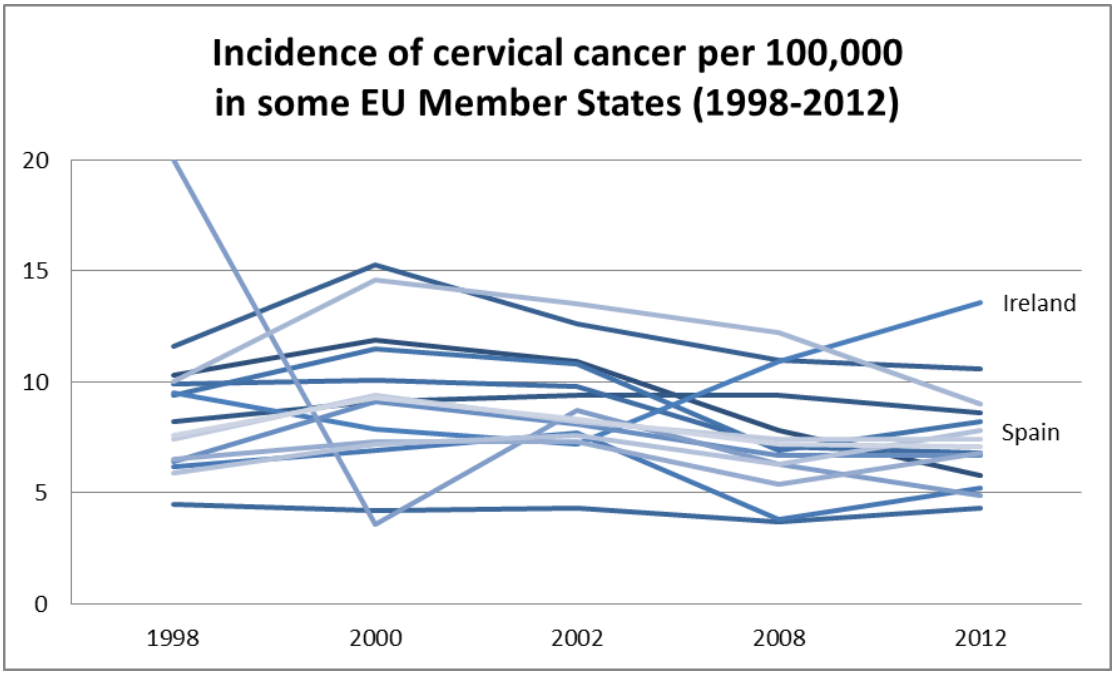


Figure 4. Incidence of cervical cancer per 100,000 in some EU Member States (1998-2012)

1.1.3. Obesity and Body Mass Index (BMI) (OECD data)

As a reference for obesity and BMI, section 2.5 of the OECD-report "Health at a Glance Europe 2014"[29] was analysed. It appears that the prevalence of obesity and overweight in

[29] OECD. 2014. Health at a Glance: Europe 2014, OECD Publishing. doi 10.1787/23056088

adults and children has increased in the EU over the last decade. The OECD[30], the WHO[31] and MS[32] have mainly pointed out socio-economic factors to explain the increase in obesity. For instance, the "Tackling Obesities: Future Choices – Project report",[32] produced by the UK Government's Foresight Programme in 2007, analyses a multitude of causes of obesity and does not even mention once chemical exposure as a possible driver for obesity. In this report, the Section "Causes of obesity" starts with the chapter "biology" where the following is reported: *Numerous studies involving thousands of people worldwide have failed to find evidence to support the widely held belief that obese people must have slower metabolic rates, either burning energy more slowly than thin people, or being metabolically more efficient. In fact, the converse appears true. Energy expenditure while resting actually increases with body weight, reflecting the metabolic costs of maintaining a larger body size. After adjustment for differences in body size and composition, there is a remarkable similarity in energy expenditure between individuals.*

There is therefore no evidence in these general reports on obesity about a possible impact of exposure to EDs on the observed increased incidence of obesity.

1.1.4. Diabetes (WHO EURO-HFA data)

The prevalence of diabetes mellitus has increased in the EU over the last decade. However, it is not possible to conclude on the link with exposure to EDs as no epidemiological data are available linking exposure to EDs and the incidence of diabetes. Moreover, impact on this increase may be linked to several other factors including increased obesity prevalence and better diagnosis of diabetes

[30] OECD. 2014. Obesity Update June 2014. Retrieved from http://www.oecd.org/health/obesity-update.htm

[31] World Health Organization (WHO). 2013. Country profiles on nutrition, physical activity and obesity in the 28 European Union Member States of the WHO European Region. Methodology and summary. Retrieved from http://www.euro.who.int/en/health-topics/disease-prevention/nutrition/country-work/country-profiles-on-nutrition,-physical-activity-and-obesity-in-the-28-european-union-member-states-of-the-who-european-region.-methodology-and-summary.

[32] Butland B., Jebb S., Kopelman P., et al. 2007. Foresight. Tackling obesities: future choices—project report, Government Office for Science, London. Retrieved from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/287937/07-1184x-tackling-obesities-future-choices-report.pdf.

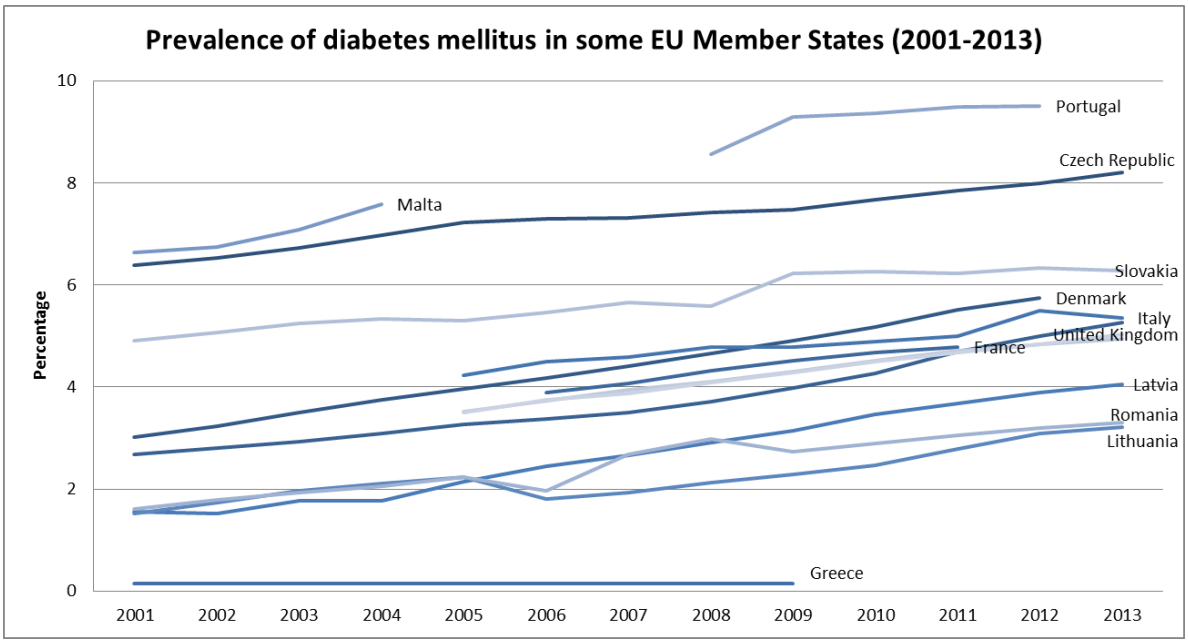


Figure 5. Prevalence of diabetes mellitus in some EU MS (2001-2013)

1.2. Epidemiological and laboratory data on a link between exposure to EDs and "hormone related diseases"

A group of scientists (mainly endocrinologists, most of them affiliated to the Endocrine Society) consider that the increased incidence of certain diseases in humans is at least partially linked to the exposure of environmental levels of EDs to which humans are daily exposed to.

Another group of scientists, mainly toxicologists/pharmacologists, including European Food Safety Authority (EFSA) and EU Scientific Committees, believe that reliable evidence of such possible associations is only available in case of high (occupational, accidental) exposure to certain chemicals.

This controversy is due to disagreement on:

- interpretation of epidemiological data;
- interpretation of laboratory data
- applicability of toxicological principles (e.g. potency of chemicals, shapes of dose-response curves, existence of safety thresholds);

These three topics are briefly explored below.

1.2.1. Interpretation of epidemiological data

The WHO-UNEP 2012 report report suggests association between chemicals with endocrine disrupting properties and several diseases (e.g. some cancers, female and male reproductive health disorders, thyroid and metabolic disorders, neurodevelopment and immune disorders).

One of the rationales provided in the report for this association is that the increasing incidence of many of these diseases cannot be explained by genetic factors and therefore must be related to environmental factors because the observed increase in diseases incidence occurs in a relatively short timeframe. The report points out that humans and wildlife are daily exposed to some levels of chemicals and that *only a small fraction of these chemicals have been investigated in tests capable of identifying overt endocrine effects in intact organisms*.

The report also acknowledges the difficulties to prove the effective role of EDs exposure in the increasing incidence of what the report describes as "*endocrine diseases and disorders"*. It concludes that adopting primary preventive measures would certainly bring large benefits to human health. The underlying suggestion is that primary preventive measures for the several diseases with high prevalence mentioned in the report (cancers, reproductive disorders, diabetes, obesity, neurological disorders, etc.) means reducing exposure to EDs.

However, primary preventive measures and evidence on associations needs to be considered in a more general context. For instance the likelihood of several other potential environmental factors should be discussed on the basis of evidence.

In this regard, it should be noted that - despite the general difficulties of epidemiological studies in finding causal associations with chronic diseases - epidemiological evidence exists pointing at other factors as causal associations. For instance, the excess of calories in the diet[33], lack of exercise[34], or unhealthy diet (e.g. high saturated fat intake or low fruit and vegetable intake[35]) are associated with chronic diseases including most of the cited *endocrine diseases and disorder.*[36,37] As regards obesity, for instance, the "Tackling Obesities: Future Choices – Project report"[32] analyses a multitude of causes of obesity and does not mention chemical exposure as a possible driver for obesity[38]. It is worth mentioning that "*only 3.6 percent of Japanese have a body mass index (BMI) over 30, which is the international standard for obesity, whereas 32.0 percent of Americans do*".[39,40,41] Considering that low

[33] Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. 2008. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet. 371:569–578

[34] Bull FC, Armstrong TP, Dixon TD, Ham S, Neiman A, Pratt M. 2004. Physical inactivity. In: Ezzati M, Lopez A, Rodgers A, Murray CJL, eds. Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Geneva, World Health Organization.

[35] Boeing H, Dietrich T, Hoffmann K, Pischon T, Ferrari P, Lahmann PH et al. 2006. Intake of fruits and vegetables and risk of cancer of the upper aero-digestive tract: the prospective EPIC-study. Cancer Causes and Control. 17:957– 969.

[36] World Health Organization (WHO). 2009. Global Health Risks: mortality and burden of disease attributable to selected major risks. Retrieved from: http://www.who.int/healthinfo/global_burden_disease/GlobalHealthRisks_report_full.pdf

[37] Lock K, Pomerleau J, Causer L, McKee M. 2004. Low fruit and vegetable consumption. In: Ezzati M, Lopez AD, Rodgers A, Murray CJL, eds. Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Geneva, World Health Organization, 597–728.

[38] Prentice, A. 2007. Are Defects in Energy Expenditure Involved in the Causation of Obesity? Short Science Review. Foresight Tackling Obesities: Future Choices. Obesity Reviews, 8(s1):89–91. Retrieved from: http://onlinelibrary.wiley.com/doi/10.1111/j.1467-789X.2007.00325.x/epdf

[39] Senauer B., Gemma M. 2006. Paper presented at the meetings of the International Association of Agricultural Economists. Why Is the Obesity Rate So Low in Japan and High in the US?: Some Possible Economic Explanations. Gold Coast, Australia, 12–18 August. Retrieved from: https://ideas.repec.org/p/ags/umrfwp/14321.html

[40] Senauer B., Gemma M. 2006. Reducing Obesity: What Americans Can Learn from the Japanese. Choices Magazine. Retrieved from: http://www.choicesmagazine.org/2006-4/grabbag/2006-4-12.htm

levels of chemicals are found in consumer products, food and environment of any developed country, it seems unlikely that this factor has a significant influence on obesity trends, while other factors (e.g. excessive energy intake, decreased energy expenditure, differences in food prices, car ownership, television viewing, and other social factors[42]) are recognised as main drivers for obesity in most reviews on the subject.[31]

Some epidemiological studies cited in the WHO-UNEP 2012 report refer to diseases associated with relatively high exposure to pesticides. These findings appear in contradiction with the systematic review "Literature review on epidemiological studies linking exposure to pesticides and health effects" published in 2013[23] and with the recent "Agrican cohort study"[24], both presented in more detail below.

The EFSA report **"Literature review on epidemiological studies linking exposure to pesticides and health effects"** was carried out applying a systematic review[43], which is a highly structured approach to reviewing and synthesising the scientific literature while limiting bias (see also section 1.4 below). A total of 603 epidemiological studies were considered to examine the association between pesticide exposure and a wide spectrum of health outcomes. Most studies pertained to cancer outcomes (N-164) and child health outcomes (N=84), but a large number also to neurological conditions and reproductive diseases. More than half of them examined occupational exposure to pesticides (N=329), i.e. exposure of farmers.

Despite the large volume of available data and the large number (more than 6000) of analyses available, firm conclusions could not be made for the majority of the health outcomes. The review acknowledges important methodological limitations in epidemiological studies, which in some cases are likely to overestimate associations. For instance, the review indicated that the overwhelming majority of evidence came from retrospective case-control analyses or cross-sectional analyses, rather than prospective cohort studies. Case-control and cross-sectional evidence are generally based on self-reported exposure and therefore prone to bias ("recall bias") in exposure measurement. In retrospective studies misclassification is differential with higher exposures reported in participants with disease (recall bias). Moreover, self-reported exposure to pesticides was defined as "ever" versus "never" use, or as "regular" versus "non-regular" use, adding considerable uncertainty to any outcome. Acknowledging all these limitations and the potential of overestimating exposure to pesticides in participants with diseases ("recall bias"), the review found significant associations with pesticides exposure only for childhood leukaemia and Parkinson's disease. In addition, the review concludes that results should be regarded as *suggestive* of associations *only* and limitations especially regarding the heterogeneity of exposure should always been taken into consideration.

[41] Food and agriculture organization of the United Nations (FAO). 2013. The State of Food and Agriculture 2013. ISSN 0081-4539 Retrieved from: http://www.fao.org/docrep/018/i3300e/i3300e.pdf

[42] Nguyen, D. M., & El-Serag, H. B. 2010. The Epidemiology of Obesity. Gastroenterology Clinics of North America, 39(1), 1–7. doi.org/10.1016/j.gtc.2009.12.014

[43] European Food Safety Authority. 2010. Application of systematic review methodology to food and feed safety assessments to support decision making. EFSA Journal 8(6):1637. [90 pp.] doi:10.2903/j.efsa.2010.1637.

The "Agrican" cohort study[24] is a recent epidemiological study carried out in France, which follows since 2005 a cohort of 180.000 participants (88% farmers, 12% working in forestry, landscape gardeners, etc.). In November 2014, the first report was published.

France is the country in the EU with highest overall pesticide use. Cohort studies are the most informative (and most expensive) studies in epidemiology. Differently from other epidemiological studies (e.g. retrospective case-control studies), they allow studying different diseases at the same time. In the Agrican study 40 types of cancers and several other diseases were followed.

Cohort studies allow following groups of people particularly exposed to the risk factors under study (e.g. farmers exposed to certain pesticides). In addition, in cohort studies exposure levels can be measured much more precisely, since participants can be questioned several times on the evolution of their exposure to different substances, so that they have less sources of uncertainty (like e.g. recall bias).

The Scientific Council for this study was composed by members belonging to the International Centre of Research on Cancer (IARC), the French Institute INSERM, the League Against Cancer, the US National Cancer Institute, Paris University, Metz University and the Coordination for the study cohort Agricultural Health Study (AHS). Funding of this study was from French Public Institutes, Farmer Social Security, League Against Cancer, Centre for Fight Against Cancer and Universities.

The results of this study show that farmers have a higher life expectancy than the general population. The report mentions it is now widely accepted that agricultural populations present lower rates of mortality globally and for the main causes of death (cardiovascular diseases, cancer overall).[44,45,46] This can be largely explained by specificities in farmers' life habits: their lower prevalence of smoking decreases the risk of contracting cardiovascular diseases and some cancers (lung, bladder, pancreas), as their level of physical activity reduces the risk of some other cancers (colon and rectum). Several causes of mortality were followed during the Agrican study, namely tumours, endocrine related diseases (e.g. diabetes), digestive diseases (e.g. cirrhosis), neurological diseases (e.g. Alzheimer, Parkinson), cardiovascular diseases, respiratory diseases, renal and genital diseases, dermatological diseases, bone diseases, infective diseases, accidents, suicides and others.

Considering all together the several causes of mortality followed during this study, mortality was lower compared to the general population of 29% for men and 28% for women, respectively. More in particular, as regards the diseases often referred to as possibly associated to exposure to EDs, mortality was lower among farmers than in the general population for tumours (M: - 30% and F: - 24%), for diabetes and other endocrine related diseases (M: - 33% and F: - 30%), for genital/urinary diseases (M: - 36% and F: - 43%), for neurological diseases (M: - 38% and F: - 39%).

[44] Blair A, Dosemeci M, Heineman EF . 1993. Cancer and other causes of death among male and female farmers from twenty-three states. Am J Ind Med 23:729–742

[45] Acquavella J, Olsen G, Cole P, Ireland B, Kaneene J, Schuman S et al. 1998. Cancer among farmers: a meta-analysis. Ann Epidemiol 8:64–74

[46] Blair A, Beane Freeman L. 2009. Epidemiologic studies of cancer in agricultural populations: observations and future directions. J Agromed 14:125–131

Since mortality depend on incidence and several other factors (e.g. appropriate treatment, early diagnosis, additional risk factors and protective factors), the "Agrican" study also analysed the incidence rates of several type of cancer (other diseases could not be analysed because of the absence of appropriate registers in France).

The review shows that incidence of cancer is higher in farmers than in the general population for following type of cancers: skin melanoma (+26%), myeloma multiple (+26%), lymphoma Hodgkin (F: +19%; M: +38%), lymphoma non-Hodgkin (F: +18%; M: +14%), lips cancer (M: +49%). On the other hand, incidence of cancer is lower in farmers than in the general population for following type of cancers: breast (F: -18%), pancreas (M: -17%), lungs (F: -36%; M: -46%), oral cavity/pharynx (F: -59%; M: -44%), oesophagus (M: -28%), larynx (M: -50%), liver (M: -24%), mesothelioma (M: -62%), colon (M: -13%), rectum (M: -20%), bladder (M: -38%).

Considering that farmers are generally exposed to higher levels of pesticides than the general population – including pesticides which may be identified as EDs - the results of the Agrican study suggest no link between exposure to EDs in the EU and onset of hormone related cancers (e.g. breast, prostate, testis cancer).

A large prospective cohort study, the Agricultural Health Study (AHS)[47] has been conducted in the USA since the beginning of the 1990s. It has enrolled around 90 000 individuals including more than 50 000 active farm owners using pesticides in two states where agriculture is mainly devoted to open field and livestock. This large prospective North American cohort is part of a newly established International Consortium for Agricultural Cohorts (AGRICOH) coordinated by the National Cancer Institute and the International Agency for Research on Cancer. The consortium now includes 26 prospective cohorts from 12 countries. The AGRICAN study is included in AGRICOH.

1.2.2. Interpretation of laboratory data

As regards interpretation of laboratory data, there is some disagreement among scientists on which evidence would be sufficient to identify a substance as an ED. The authors of the 2nd Endocrine Society Scientific Statement[48] endorse a definition of an ED which is not widely agreed, as it does not explicitly refer to an adverse effect (an ED is "*an exogenous chemical, or mixture of chemicals, that interferes with any aspect of hormone action*").

Differently, the WHO/IPCS 2002 definition of an ED is widely agreed among toxicologists, pharmacologists and it was endorsed for instance by the EFSA Scientific Opinion 2013[49], the

[47] Alavanja MC, Sandler DP, McMaster SB, Zahm SH, McDonnell CJ, Lynch CF et al. 1996. Characteristics of pesticide use in a pesticide applicator cohort: the Agricultural Health Study. Environ Health Perspect 104: 362–369

[48] Gore A.C., Chappell V.A., Fenton S.E., Flaws J.A., Nadal A., Prins G.S., Toppari J., Zoeller R.T. 2015. EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals, Endocr Rev. 36(6):E1-E150. DOI: 10.1210/er.2015-1010

[49] EFSA Scientific Committee; Scientific Opinion on the hazard assessment of endocrine disruptors: scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing effects mediated by these substances on human health and the environment. EFSA Journal 2013; 11(3):3132. [84 pp.] doi: 10.2903/j.efsa.2013.3132.

JRC report 2013[50], Kortenkamp report 2011[51] (an ED is "*an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations"*).

The results of laboratory data are interpreted differently depending on whether or not an observed adverse effect is considered necessary to identify an ED. Even when agreeing on the WHO/IPCS 2002 definition of an ED, the interpretation of laboratory data can vary depending on what is considered an adverse effect, considering that the definition does not better specify it. In the EFSA Scientific opinion 2013 it is indicated that scientific criteria for assessment of adversity have not been generally defined. In this opinion it is concluded that it is difficult to propose ED-specific criteria for adversity and expert judgement in a weight-of-evidence approach is needed to assess substances for possible endocrine disrupting properties. Finally, an additional source for different views is the extrapolation from high doses, as typically used in laboratory animals, to the lower levels of exposure of humans in practice. As mentioned above, endocrinologists often refer to non-monotonic dose-response curves for EDs and therefore do not support the generally accepted principle of risk assessment where extrapolations are done to estimate exposures and effects from high to low doses.

1.2.3. Toxicological principles (e.g. existence of safety thresholds, potency of chemicals, shapes of dose-response curve, low dose effects)

The scientific debate on safety thresholds, non-monotonic dose-response curves, "window of vulnerability" and the impact of exposure to relatively low levels of EDs is on-going. As mentioned before, some scientists believe that the increased incidence of certain diseases in humans is at least partially linked to the low doses (low environmental levels) of EDs, while others believe that evidence of such possible associations is only available in case of high (occupational, accidental) exposure to certain chemicals.

This controversy is also reflected in ongoing discussions on some other issues: e.g. EDs to be treated differently from other chemicals, threshold/no threshold, windows of susceptibility, non-monotonic response curves. This issue was also addressed in the "meeting with the former Chief Scientific Advisor of the European Commission Ms Ann Glover[52]", but has not yet been settled as shown in the conference "Endocrine disruptors: criteria for identification and related impacts" (1st June 2015, Brussels)[53] organised by the European Commission, where different scientific views were presented. Further, on the occasion of an expert conference organised by the German Federal Institute for Risk Assessment (BfR), held in

[50] Munn S., Goumenou M-P., 2013. Key scientific issues relevant to the identification and characterisation of endocrine disrupting substances - Report of the Endocrine Disrupters Expert Advisory Group. JRC-IHCP [29pp.] DOI: 10.2788/8659 (online). Retrieved from: http://publications.jrc.ec.europa.eu/repository/bitstream/JRC79981/lbna25919enn.pdf

[51] Kortenkamp, A., Martin, O., Faust, M., Evans, R., McKinlay, R., Orton, F., Rosivatz, E., 2011. State of the art assessment of endocrine disrupters. Final Report. Retrieved from: http://ec.europa.eu/environment/chemicals/endocrine/pdf/sota_edc_final_report.pdf

[52] European Commission. 2013. Minutes of the expert meeting on endocrine disruptors. Retrieved from http://sciences.blogs.liberation.fr/files/glover-u-s-perturbateurs-endocriniens.pdf

[53] European Commission. 2015. Conference "Endocrine disruptors: criteria for identification and related impacts". Retrieved from: http://ec.europa.eu/health/endocrine_disruptors/events/ev_20150416_en.htm

Berlin in April 2016, a consensus statement on "Scientific principles for the identification of endocrine disrupting chemicals" was signed by the 23 internationally renowned scientists present at the conference. Among other things, the document produces lists the criteria for identifying the hazard potential of harmful endocrine substances. It also indicates that the assessment of the corresponding risks from endocrine disruptors on human health and wildlife would further require consideration of dose-response relationships, including potency, exposure assessment, and risk characterization, including susceptible sub-populations, severity and reversibility of effects.

Some key toxicological principles where there seems to be disagreement between toxicologists and endocrinologist are explained below. They are relevant to the assessment and regulation of EDs.

Are EDs different from other chemicals? Can safety thresholds be set?

Endocrinologists believe EDs should be treated differently from most other chemicals because of their MoA, and that in particular no safety threshold can be identified for them.

Toxicologists argue that EDs represent chemicals with different kind of effects (some of which already regulated by the legislation) and various endocrine-mediated modes of action, so that the entire class cannot be assimilated to a single one. They add further that when assessing and managing the risk posed by a chemical, it is the effective possibility that an adverse effect is produced that is ultimately important, and not the MoA through which an effect may eventually, possibly occur. Toxicologists generally contest that no safety threshold can be set. If this would be assumed, even the lowest/negligible exposure would imply a regulatory action, although no risk to human health and the environment could be identified.

Are windows of susceptibility, non-monotonic dose-response curves, mixture effects aspects specific to endocrine disruption?

The concept of windows of susceptibility (e.g. foetal exposure) is central to the "no threshold concept" for EDs. The "no threshold concept" is also related to the claimed presence of "non-monotonic dose-response curves" for EDs, meaning that effects may be higher at low doses than at higher doses of the chemical. Endocrinologists also often refer to the fact that mixtures of chemicals are not yet considered in the regulatory assessment and that this may underestimate risks, particularly for what concern EDs.

The "State of the Art Assessment of Endocrine Disrupters" report[54] commissioned through public procurement by the European Commission, considers critical windows of susceptibility a key issue for EDs. However, the European Food Safety Authority[55] and the Scientific

[54] Kortenkamp, A., Martin, O., Faust, M., Evans, R., McKinlay, R., Orton, F., Rosivatz, E., 2011. State of the art assessment of endocrine disrupters. Final Report. Retrieved from: http://ec.europa.eu/environment/chemicals/endocrine/pdf/sota_edc_final_report.pdf

[55] EFSA Scientific Committee; Scientific Opinion on the hazard assessment of endocrine disruptors: scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing

Committee for Consumer Safety[56] stated that mixtures, windows of susceptibility and non-monotonic dose-response curves are general issues applicable to all chemicals (and not specific to EDs) and that "*EDs can therefore be treated like most other substances of concern for human health and the environment, i.e. be subject to risk assessment and not only to hazard assessment*".

Potential mixture effects are indeed not yet addressed in any legislation in the EU or elsewhere, although extensive research is growing on this topic, including also research projects funded by the European Commission, such as the four-year projects EDC-MixRisk[57] and EuroMix[58] financed through the Programme Horizon 2020. As regards regulatory action, the PPP sector is pioneering on this work, as EFSA is developing a methodology to consider cumulative risk of pesticide residues in food products.[59]

It is however worth mentioning that in vivo evidence continues to accumulate that additional effects are absent at low doses/concentrations, which is consistent with pharmacological theory.[60,61,62]

Low doses effects or thresholds of adversity for EDs like for other chemicals?

Toxicologists and pharmacologists generally agree that the statement from Paracelsus is still valid ('*All compounds are poisons, it is the dose that makes the compound not a poison*'), implying that up to a threshold of adversity, the body can effectively neutralise hazards through homeostatic mechanisms.[63] This is reflected in the fact that it is generally agreed that no adversity in humans can be expected up to a certain threshold of exposure. It is also common practice for all chemicals to consider that threshold levels are different depending on the chemical and on the susceptibility of the individual or group of population exposed (depending on age, sex, physical status, medical treatment, etc.). A wealth of experience with thousands of chemicals evaluated in animal studies for reproductive hazard and risk

effects mediated by these substances on human health and the environment. EFSA Journal 2013;11(3):3132. doi: 10.2903/j.efsa.2013.3132.

[56] European Commission 2014. Scientific Committee on Consumer Safety. Memorandum on Endocrine Disruptors. Retrieved from: http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_009.pdf

[57] EDC-MixRisk: safe chemicals for future generations. Information available on: http://edcmixrisk.ki.se/aboutedcmixrisk/

[58] EuroMix: a tiered strategy for risk assessment of mixtures of multiple chemicals. Information available on: http://www.euromixproject.eu/

[59] EFSA. 2016. Pesticides: breakthrough on cumulative risk assessment. Retrieved from: http://www.efsa.europa.eu/en/press/news/160127

[60] Gerhard J. Nohynek, Christopher J. Borgert, Daniel Dietrich, Karl K. Rozman, 2013. Endocrine disruption: Fact or urban legend?, Toxicology Letters. 223 (3): 295-305, ISSN 0378-4274. doi.org/10.1016/j.toxlet.2013.10.022.

[61] C.J. Borgert, E.V. Sargent, G. Casella, D.R. Dietrich, L.S. McCarty, R.J. Golden. 2011. The human relevant potency threshold: Reducing uncertainty by human calibration of cumulative risk assessments, Regulatory Toxicology and Pharmacology. 62 (2): 313-328, doi.org/10.1016/j.yrtph.2011.10.012.

[62] Lorenz R. Rhomberg, Julie E. Goodman. 2012. Low-dose effects and nonmonotonic dose–responses of endocrine disrupting chemicals: Has the case been made?, Regulatory Toxicology and Pharmacology. 64(1): 130-133. doi.org/10.1016/j.yrtph.2012.06.015

[63] This is applicable for most substances. For few substances (mutagen and/or genotoxic sustances) this is assumed not to be the case.

identification corroborates that threshold of adversity exists also for foetuses exposed to chemicals in utero. The threshold dose approach used so far in the risk assessment of reproductive toxicants[64] can be therefore considered as justified.

Most toxicologists consider that when low-dose adverse effects were observed in laboratory animals exposed to certain endocrine active agents, the findings could not be replicated. The validity and toxicological significance of many of these observations has therefore not yet been determined.[65]

The Kortenkamp report discusses the fact that the existence of thresholds for EDs is highly debated and not yet solved, mainly due to issues relating to reproducibility. Confounding issues are also discussed as important, since *thresholds are obscured at population level by inter-individual variations in sensitivity and by background exposures*. The report concludes that as regards endocrine disruption, because of pre-existing internal exposures to hormones, even low doses of an ED would add to the effect of the internal background, with no threshold. This concept was however contested by one group of experts in the meeting with the European Commission Chief Scientific Advisor Anne Glover in October 2013 (see published minutes, p.2[66]).

The EFSA Opinion 2013 indicated that safe doses/concentrations of EDs can be established if:

1. follow up of exposure at critical windows of susceptibility to later life stages is addressed; and
2. all available information is used in a weight of evidence approach.

Potency of chemicals and other elements of hazard characterisation (severity, specificity and irreversibility of effect, lead toxicity).

Endocrinologists generally refuse considering potency for identification of EDs. They believe that no prioritisation of EDs of higher concern can be set, since even low doses of a low potent ED may pose a danger to specific groups of population.

Toxicologists believe that risk assessment should consider potency together with exposure levels. Indeed, natural or synthetic (i.e. man-made) hormones (e.g. the oral contraceptive ethinyloestradiol) are 10,000 to 1,000,000 fold more potent than other man-made chemicals used for other purposes which have an estrogenic activity. This needs to be taken into account when assessing the risk posed by chemicals. For instance (see Table 2): if the potency of daidzein (a natural chemical in soy-beans) is similar to the one of bisphenol A, but the daily intake of the latter is 1000 times lower, the risk posed by bisphenol A to humans is likely to be orders of magnitude lower than the one posed by daidzein. Similarly, if the potency of

[64] Piersma, A.H., et al. 2011. Reproductive toxicants have a threshold of adversity. Critical reviews in Toxicology 41(6) 545-554. doi: 10.3109/10408444.2011.554794

[65] Kroes, R., et al. 2004. Structure-based thresholds of toxicological concern (TTC): guidance for application to substances present at low levels in the diet. Food and Chemical Toxicology 42: 65–83. doi:10.1016/j.fct.2003.08.006

[66] European Commission. 2013. Minutes of the expert meeting on endocrine disruptors. Retrieved from: http://sciences.blogs.liberation.fr/files/glover-u-s-perturbateurs-endocriniens.pdf

ethinyloestradiol is 100000 higher than the one of butylparaben, this needs to be considered when comparing the risks posed by the two chemicals.

Table 2. Calculations of Hygiene-Based Margins of Safety (HBMOS) for environmental oestrogens[67]

SUBSTANCE	DAILY INTAKE	RELATIVE POTENCY	HBMOS[68]
Daidzein	1 mg/kg bw	1	1
Nonylphenol	2 µg/kg bw	2	250
Bisphenol A	1 µg/kg bw	1	1000
Ethinyloestradiol	0.5 µg/kg bw	40.000	0.05
Butylparaben	0.1 mg/kg bw	0.4	24

The Kortenkamp report considers that EDs should be identified according to the 2002 WHO-IPCS definition and using a weight of evidence approach which considers all the elements of hazard characterisation together, i.e. potency together with other factors such as severity, lead toxicity, specificity of effect and irreversibility. Rigid potency-based cut-off values as decisive decision criteria are not recommended. The EFSA Opinion on EDs 2013 indicated that to inform on a level of concern for EDs, severity, irreversibility and potency should be evaluated in relation to degree, timing and duration of exposure, i.e. using risk assessment.

In summary, the available relevant reports indicate that:

- There is consensus on the WHO/IPCS definition (2002) for identifying ED
- There are different endocrine modes of actions. Four modalities (pathways) are relatively well known and internationally agreed tests exist (the estrogen, androgen, thyroid and steroidogen modalities). There are other modalities which are not yet well known and for which no internationally agreed tests exist. For these modalities, still under discussion, science is under development and there is no consensus on the extent of evidence (e.g. diabetes) available.
- There is no consensus on the relevance of some scientific aspects for regulatory decision making (e.g. non-monotonic dose response curve, low dose effects and existence of safety thresholds for EDs), but a recent EU review on the empirical evidence and the BfR consensus statement mentioned above indicate that the evidence for this kind of curves is weak for most in vivo data.
- There is consensus that the assessment of potential risks from ED on human health and the environment would require consideration of dose-response relationships, exposure assessment, and risk characterisation (risk assessment).

[67] Bolt HM, Janning P, Michna H, Degen GH. 2001. Comparative assessment of endocrine modulators with oestrogenic activity: I. Definition of a hygiene-based margin of safety (HBMOS) for xeno-oestrogens against the background of European developments. Archives of Toxicology. 74: 649-662. Retrieved from: http://www.ncbi.nlm.nih.gov/pubmed/11218041

[68] HBMOS are defined as hygiene-based margin of safety in Bolt et al. 2001.

1.3. Regulation of active substances used in PPP and BP which are identified as EDs

The suggestion in the WHO-UNEP 2012 report that introducing primary preventive measures to reduce exposure to EDs contributes to a health effect is true in general terms. However, the statement is not considering the particular situation for the chemical active substances used in plant protection products (PPP) or biocidal products (BP) in the EU.

The PPP Regulation and BP Regulation are among the strictest chemicals regulations worldwide and they are underpinned by the precautionary principle as stated in recitals of these regulations.[69;70] The EU authorisation system for PPP and BP is based on prior approval ("positive list") shifting responsibility for producing scientific evidence (burden of proof) to the business community. In other words, it is up to applicants asking for approval of a substance to produce studies and information demonstrating the substance can be safely used. The dossier will be then evaluated by Competent Authorities first at EU level and then also at national level. Only substances present on the positive list agreed at EU level can be used in PPP or BP placed on the EU market, provided they also pass the second step of national authorisation of the formulated products. The EU legislation in place implies that both PPP and BP are among the most "data rich" regulated product groups in the EU. Under both regulations, a detailed list of exhaustive data[71;72] has to be submitted by the applicant before any approval of active substance or authorisation of a product containing the approved substances can be considered. These core data requirements include in vivo animal studies able to detect most adverse effects even in the second generation (offspring of treated animals).

It should be noted that in most cases where convincing evidence is presented in the WHO-UNEP 2012 for pesticides with endocrine disrupting properties, this is related to substances that are not anymore approved in the EU for use in PPP since years (e.g. DDT, vinclozolin, methoxychlor) (see Table 3). In particular, the report refers in total to 44 non-approved PPP and 14 approved PPP (among the 14 approved PPP, some are close to the renewal decision). The report also refers in total to three non-approved biocidal products (triphenyltin, tributyltin and triclosan), five approved (fenoxycarb, fipronil, permethrin, iodine, pyriproxyfen) and two under review (formaldehyde and linuron).

The WHO-UNEP 2012 report also refers to some epidemiological studies showing possible association between exposure to pesticides and rise in chronic diseases. Those studies in most cases refer to pesticides already banned in the EU: e.g. atrazine cited as associated to ovarian

[69] Article 1.4 of Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309.

[70] Article 1.1 of Regulation (EU) No 528/2012 of the European Parliament and of the Council concerning the making available on the market and use of biocidal products. OJ L 167/1.

[71] Regulations EU 283/2013 and EU 284/2013, setting data requirements for active substances and for PPP, respectively; Communications 2013/C 95/01 and 2013/C 95/02, detailing the list of test methods and guidance documents for active substances and for PPP, respectively.

[72] Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products. Official Journal of the European Union, L 167, 27 June 2012. doi:10.3000/19770677.L_2012.167.eng

cancer; dicofol cited as associated to higher incidence of early childhood leukaemia; phorate cited as associated to prostate cancer.

Table 3. Pesticides mentioned as EDs in the WHO-UNEP 2012 report but already removed from the EU market based on Directive 91/414/EC and Directive 79/117/EC[73]

ACTIVE SUBSTANCE	BANNED SINCE	CLASS OR USE
methyl bromide	2011	fumigant pesticide
chlozolinate	2000	fungicide
hexachlorobenzene	2004/1979*	fungicide
procymidone	2006	fungicide
tributylin (3AS)	2002	fungicide
trichlorophenate (derivative of 2,4,5-T)	1993**	fungicide
triphenyltin (fentin)	2002	fungicide
vinclozolin	2005	fungicide
2,4,5 T	2002	herbicide
acetochlor	2008	herbicide
alachlor	2006	herbicide
atrazine	2004	herbicide
bromacil	2002	herbicide
butylate	2002	herbicide
ethylene thiourea	1993**	herbicide
pentachloronitrobenzene (quintozene)	2000	herbicide
prodiamine (dithiopyr)	1993	herbicide
simazine	2004	herbicide
thiazopyr	2002	herbicide
pentachlorphenol	2002	herbicide, fungicide
carbaryl	2007	insecticide
coumpahos	1993	insecticide
permethrin	2000	insecticide
desethylatrazine	2004	metabolite atrazine ***
oxychlordane	2004	metabolite chlordane ***
heptachlor epoxide	2004/1979*	metabolite heptachlor***
2,4'-DDD	1993**	organochlorine insecticide
2,4'-DDT	1993**	organochlorine insecticide

[73] Council Directive 79/117/EEC of 21 December 1978 prohibiting the placing on the market and use of plant protection products containing certain active substances. OJ L 33, 8.2.1979, p. 36–40 (DA, DE, EN, FR, IT, NL). http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:31979L0117

ACTIVE SUBSTANCE	BANNED SINCE	CLASS OR USE
4,4'-DDD	1993**	organochlorine insecticide
4,4'-DDE	1993**	organochlorine insecticide
4,4'-DDT	1993**	organochlorine insecticide
chlordane	2004/1979*	organochlorine insecticide
chlordecone (kepone)	2004	organochlorine insecticide
DDT	2004/1979*	organochlorine insecticide
dicofol	1979	organochlorine insecticide
dieldrin	2004/1979*	organochlorine insecticide
endosulfan	2005	organochlorine insecticide
endrin	2004/1979*	organochlorine insecticide
heptachlor	2004/1979*	organochlorine insecticide
lindane	2000	organochlorine insecticide
methoxychlor	2002	organochlorine insecticide
mirex	2004	organochlorine insecticide
nonachlor (trans and cis chlordane)	2004	organochlorine insecticide
toxaphene (campechlor)	1979	organochlorine insecticide
fenitrothion	2007	organophosphate insecticide
fonofos	2002	organophosphate insecticide
parathion	2001	organophosphate insecticide
phorate	2002	organophosphate insecticide
dibromochloropropane (DBCP)	1993**	pesticide/soil fumigant
*= banned in principle in 1979, with few exceptional uses left on the market		
**= not on the EU market since at least 1993: were never notified for assessment under the EU review program		
***= date of ban equivalent of the one of the parent compound		

Also the 1st and 2nd Statements of the Endocrine Society (2009[20], 2015[74,75]), which conclude that "*the evidence for adverse reproductive outcomes (infertility, cancers, malformations) from exposure to endocrine disrupting chemicals is strong, and there is mounting evidence for effects on other endocrine systems, including thyroid, neuroendocrine, obesity and metabolism, and insulin and glucose homeostasis.*", refer to pesticides where evidence for

[74] Gore, A.C., et al. 2015. EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals. Endocrine Reviews 36 (6) doi.org/10.1210/er.2015-1010

[75] Gore, A.C., et al. 2015. Executive Summary to EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals. Endocrine Reviews, 36(6):593–602. doi: 10.1210/er.2015-1093

endocrine disrupting properties exists (e.g. atrazine, DDT) but which are already banned in the EU.

In addition, the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) published in 2014 an Opinion[76] analysing the French National Institute for Health and Medical Research (INSERM) collective expert appraisal report "Pesticides. Health effects" on the health effects of pesticides, biocides and PPP. This Opinion points out that *the vast majority of substances identified by the INSERM report as having a presumed moderate or strong association with the occurrence of health effects concern substances that are now prohibited* in the EU. The Opinion concludes that among substances authorised for use in the EU, only for seven substances a presumed association with one or more health outcomes was observed.

It can be concluded that many of the active substances used in pesticides referred to in international studies and reports as EDs are not anymore approved in the EU. This shows that the past and current EU regulatory framework has been able to identify hazardous chemicals and ban them based on the risk of the occurrence of unacceptable adverse effects to human health, even if they were not specifically identified as EDs.

1.4. New methodological developments

1.4.1. Validated test methods and test guidelines

The "State of the Art Assessment of Endocrine Disrupters" report[77] commissioned through public procurement by the European Commission, maps ways of addressing EDs in EU chemicals legislation (e.g. PPP Regulation, BP Regulation, REACH). It stated that the data required in EU chemicals regulation did not capture the range of endocrine disrupting effects that can be measured with internationally agreed and validated test methods.

Methods are currently under development at OECD[78], both for in-vivo and in-vitro tests. Adverse outcome pathways (AOP)[79] are also under development and may provide a useful tool for understanding the endocrine MoA. An AOP is a structured representation of biological events leading to adverse effects. It links existing knowledge along one or more series of causally connected key events, connecting a molecular initiating event with an adverse outcome that occur at a level of biological organisation relevant to risk assessment. The linkage between the events is described by key event relationships that describe the causal relationships between the key events. AOPs increase the use of mechanistic

[76] ANSES Opinion. 2014. OPINION of the French Agency for Food, Environmental and Occupational Health & Safety on the INSERM collective expert appraisal report "Pesticides. Health effects". Request No. 2013-SA-0116. Retrieved from https://www.anses.fr/en/system/files/PHYTO2013sa0116EN.pdf

[77] Kortenkamp, A., Martin, O., Faust, M., Evans, R., McKinlay, R., Orton, F., Rosivatz, E., 2011. State of the art assessment of endocrine disrupters. Final Report. Retrieved from: http://ec.europa.eu/environment/chemicals/endocrine/pdf/sota_edc_final_report.pdf

[78] OECD. 2016. OECD Work Related to Endocrine Disrupters. Retrieved from: http://www.oecd.org/env/ehs/testing/oecdworkrelatedtoendocrinedisrupters.htm

[79] OECD. 2016. Adverse Outcome Pathways, Molecular Screening and Toxicogenomics. Retrieved from: http://www.oecd.org/env/ehs/testing/adverse-outcome-pathways-molecular-screening-and-toxicogenomics.htm

toxicological data for risk assessment and regulatory applications. EFSA and ECHA recognised the importance of these tools for risk assessment.[80,81]

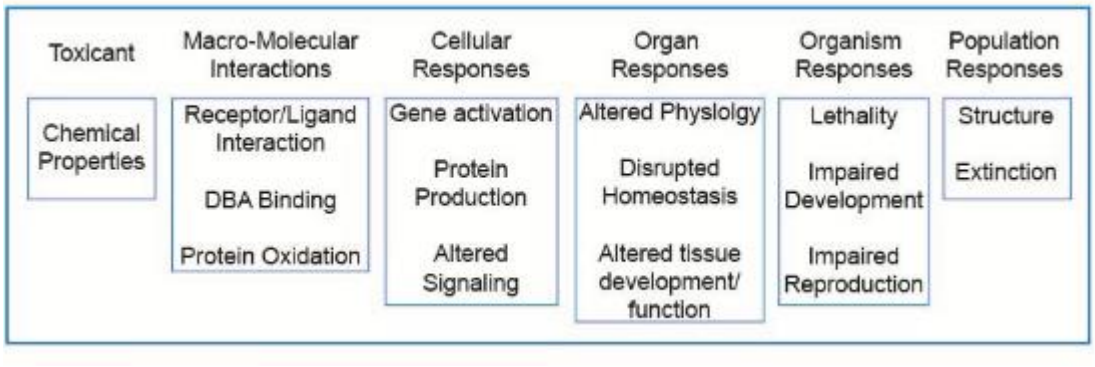


Figure 6. Schematic representation of the Adverse Outcome Pathway (AOP) illustrated with reference to a number of pathways.[82]

These developments are followed by the European Commission closely and current data requirements are updated where needed. For instance, the PPP data requirements have been updated in 2013, including updated test guidelines which also consider ED (Regulations 283/2013 and 284/2013 and the respective Communications 2013/C 95/01 and 2013/C 95/02 listing relevant test methods and guidance documents), as for example the extended one-generation reproduction study (Test Guideline 443). This Test Guideline is able to detect serum thyroid hormone and thyroid-stimulating hormone levels following exposure during critical stages of development, as well as developmental neurotoxicity and immunotoxicity endpoints.

However, regarding the different "axes" or “modalities” of endocrine MoA for which methods are available, the EFSA Opinion 2013 highlights that a reasonably complete suite of standardised assays for testing the effects of EDs is currently available only for the estrogenic, androgenic, thyroid and steroidogenic (EATS) “modalities” of the endocrine system.

This is also reflected in the Kortenkamp report, which illustrates that the level of information differs among the different endocrine modalities. For instance, it considers that, for male reproductive health, there is a good coherent mechanistic evidence for explaining how ED may interfere with male reproductive development. The same is not true for female reproductive health, where an adequate mode for most female reproductive diseases is lacking, due to critical differences between rodents and humans. Overall, the current state of

[80] European Food Safety Authority, 2014. Modern methodologies and tools for human hazard assessment of chemicals. EFSA Journal 2014;12(4):3638, 87 pp. doi:10.2903/j.efsa.2014.3638

[81] ECHA. New web platform available on adverse effects of chemicals. http://echa.europa.eu/view-article/-/journal_content/title/new-web-platform-available-on-adverse-effects-of-chemicals

[82] OECD. 2016. Adverse outcome pathways, molecular screening and toxicogenomics. "What is an adverse outcome pathway". Retrieved from: http://www.oecd.org/chemicalsafety/testing/adverse-outcome-pathways-molecular-screening-and-toxicogenomics.htm

knowledge prevents the establishment of a clear causal link between an endocrine MoA and an adverse effect for most endpoints in female reproductive health.

As regards "hormonal cancers", the Kortenkamp report refers that no suitable animal model is available for prostate, testis, or thyroid cancers. However, the Kortenkamp report supports the "plausibility" of a role for exposure to EDs in breast, prostate, testicular and to some extent thyroid cancers.

The Kortenkamp report also mentions that for metabolic disorders such as obesity, scientific interest is very novel and test methods are still unable to detect endpoints related to these disorders.

The EFSA Opinion on EDs points out that in principle, no single assay currently available or under development is likely to provide all the information needed to decide whether a substance is an ED (according to the WHO/IPCS definition endorsed by the EFSA Opinion). This is because of the need to provide both mechanistic information showing how the substance interacts with the endocrine system, and apical information[83] describing the adverse effects this interaction may cause.

1.4.2. Evidence-based toxicology (EBT) and systematic reviews

Further relevant methodological developments are **evidence-based toxicology (EBT)** and **systematic reviews** in general.

A systematic review is a highly structured approach to reviewing and synthesising the scientific literature while limiting bias. The method has been developed and is successfully applied since early '90s in evidence based medicine by associations like Cochrane[84]. The steps to carrying out a systematic review include – before starting the review itself - framing the question to be addressed; appraising and deciding how relevant studies will be identified and retrieved; determining if any studies need to be excluded from the analysis; and deciding how the included studies will be appraised in terms of their quality and risk of bias. Ultimately the data will be synthesised across studies, often by a meta-analysis. A protocol of how the review will be conducted is prepared as first step and is often peer reviewed before the review starts.

[83] Definition of apical endpoint: *Traditional, directly measured whole-organism outcomes of exposure in in vivo tests, generally death, reproductive failure, or developmental dysfunction. Observable effects of exposure to a toxic chemical in a test animal. The effects reflect relatively gross changes in animals after substantial durations of exposure. An observable outcome in a whole organism, such as a clinical sign or pathologic state, that is indicative of a disease state that can result from exposure to a toxicant*. Definition available in: Appendix I. OECD Collection of Working Definitions 2012. Retrieved from: http://www.oecd.org/chemicalsafety/testing/49963576.pdf

[84] Cochrane is a global independent network of researchers, professionals, patients, carers, and people interested in health, Cochrane exists so that healthcare decisions get better. During the past 20 years, Cochrane has helped to transform the way health decisions are made, by gathering and summarising the best evidence from research to help you make informed choices about treatment. See Cochrane website: http://www.cochrane.org

EFSA has recently issued guidance in order to apply this methodology also in a food safety context and for PPP.[85;86] Also the emerging discipline of evidence-based toxicology (EBT) is calling for this kind of reviews. Researchers using systematic reviews to address toxicological concerns include the non-profit Evidence-based Toxicology Collaboration (EBTC).[87]

These developments are particularly important considering the need of a weight of evidence approach, suggested also by Kortenkamp. The Kortenkamp report considers that EDs should be identified according to the 2002 WHO-IPCS definition[88] and using a weight of evidence approach which considers all the elements of hazard characterisation together, i.e. potency together with other factors such as severity, lead toxicity, specificity of effect and irreversibility. This view to apply a weight-of-evidence approach was also advised in the EFSA 2013 report on EDs. The Scientific Committee concluded that all the available information on adversity and endocrine activity should be considered together, by adopting a weight-of-evidence approach.

2. ESTIMATION OF DISEASE COSTS RELATED TO EXPOSURE TO ENDOCRINE-DISRUPTING CHEMICALS

The analysis of the economic impact of ill-health, which can be considered distinct but complementary to the clinical or epidemiological approaches to disease burden, has been mainly carried out by using some variant of the Cost-of-Illness (COI) methodology, first formalised in the mid-1960s[89], though macroeconomic growth models have increasingly been used to better understand the dynamic and multifaceted nature of losses at the societal level[90].

The aim of COI studies is to assess the economic burden that a specific health problem (or groups of health conditions) imposes on a society, usually with respect to the utilisation of health care resources and productivity losses. This is done by identifying and measuring all the costs of a particular disease, including the direct, indirect, and intangible dimensions, and expressing the output in monetary terms.

COI studies can be described according to the following three dimensions:[91]

a. the epidemiological data used: prevalence versus incidence approach;
b. the methods chosen to estimate the economic costs: top down versus bottom-up;

[85] European Food Safety Authority; Application of systematic review methodology to food and feed safety assessments to support decision making. EFSA Journal 2010; 8(6):1637. doi:10.2903/j.efsa.2010.1637.
[86] European Food Safety Authority; Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (OJ L 309, 24.11.2009, p. 1-50). EFSA Journal 2011;9(2):2092. [49 pp.]. doi:10.2903/j.efsa.2011.2092.
[87] See Evidence-based Toxicology Collaboration website http://www.ebtox.com/
[88] WHO/IPCS. 2002. Definition of an Endocrine Disruptor: *an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations.*
[89] Rice D.P. 1967. Estimating the Cost of Illness. Washington, DC: US Department of Health, Education, and Welfare, Public Health Services, 1966. Rice D.P. Estimating the cost of illness. Am J Public Health Nations Health 57(3):424–40. DOI http://dx.doi.org/10.2105/AJPH.57.3.424
[90] WHO. 2009. WHO guide to identifying the economic consequences of disease and injury, Geneva (App. C).
[91] Tarricone R. 2006. Cost-of-illness analysis. What room in health economics? Health Policy 77(1):51-63. DOI http://dx.doi.org/10.1016/j.healthpol.2005.07.016

c. the temporal relationship between the initiation of the study and the data collection: retrospective versus prospective studies.

Prevalence-based approaches estimate the direct and indirect economic burden to society incurred during a period of time (the base period, usually a year) as a result of the prevalence of the disease. This approach measures the value of resources used or lost during that specified period of time, irrespective of the time of disease onset. Prevalence-based studies estimate the number of cases of death and hospitalisations attributable to diseases in a given year, then, they estimate the costs that flow from those deaths or hospitalisations.

Incidence-based approaches represent the lifetime costs resulting from a disease or illness based on all cases with onset of diseases in a given base year; incidence-based studies estimate the number of new cases of death or hospitalisation in a given year and apply a lifetime cost estimate to these new cases[92].

The incidence approach requires that the analysis be performed "from the bottom-up", totalling the lifetime costs of illness. This, in turn, requires that input data be gathered at a level of detail much greater than that employed in the prevalence approach where, in general, the analysis is performed "from the top-down", allocating portions of a known total expenditure to each of several broad disease category.

The difference in results between these two approaches is determined by several aspects, but assuming no changes in treatment regimens and constant incidence and prevalence patterns, the cost figures resulting from the two methods may be different for the different time horizons; it can be shown that in case of a disease with a short duration, the prevalence method leads to lower results, while in case of diseases with a long duration, it's the incidence method which leads to lower figures.[93]

COI studies can also be performed prospectively or retrospectively, depending on the temporal relationship between the initiation of the study and the data collection. In retrospective COI studies, all the relevant events have already occurred when the study is initiated; this means that the process of data collection must refer to data already recorded. Conversely, in prospective COI studies, the relevant events have not already occurred when the study is initiated; this means that the process of data collection needs to be done by following-up the patients over time.

In COI studies, the cost of illness is estimated by identifying the cost-generating components and attributing a value to them. Costs are traditionally stratified into three categories: direct, indirect, and intangible costs, though COI studies have mainly focused on the first two cost categories, for the reasons explained in the following page.

Direct costs are those incurred by the health system, society, family and individual patient; they consist of healthcare and non-healthcare costs. The former include hospitalisation services, physician and nurse services, long-term care, prescription drugs, medical supplies and laboratory tests. The latter are related to the consumption of non-healthcare resources like

[92] Rice D.P. 1994. Cost-of-illness studies: fact or fiction? Lancet 344 (8936): 1519-20.
[93] Ament A., Evers S. 1993. Cost of illness studies in health care: a comparison of two cases. Health Policy 26: 29-42

transportation, household expenditures, relocating, property losses, and informal cares of any kinds[94]. Six steps are necessary to calculate them:[95]

1. identify a cohort who has received the standard treatment for the disease;
2. determine the costs of each phase or component of treatment and the timing of these costs;
3. combine the cost estimates with probability data regarding the likelihood of receiving specific treatments and their timing. Incorporate survival data[96] in probability estimates based on the age of onset of the disease and life expectancy;
4. if total medical costs are used (rather than disease-specific cost elements), determine the background medical costs that would be incurred in the absence of the disease. Modify the disease-related costs as needed to obtain incremental costs;
5. discount the stream of treatment costs over time to estimate present value treatment costs;
6. aggregate the discounted stream to obtain an estimate of the total medical costs of the disease.

Indirect costs, in COI studies, occasionally refer to productivity losses due to morbidity and mortality, borne by the individual, family, society, or the employer. They are estimated through either one of the three following methods[97], though until recently little effort has been devoted to assess the validity or reliability of instruments for measuring productivity losses[98]:

a. Human Capital Approach (HCA)[99], which estimates the value of human capital as the present value of future earnings (estimated by examining the earnings of comparable individuals in a cross section of the population, adjusted by the probability of survival at each age and discounted to adjust for the difference in the value of benefits received

[94] On the economic valuation of informal care see, for instance, Van Den Berg B., Brouwer W.B.F, Koopmanschap M.A. 2004. Economic valuation of informal care: an overview of methods and applications. Eur J Health Econ 5(1):36-45. DOI http://dx.doi.org/10.1007/s10198-003-0189-y

[95] For a systematic review of methodologies used to calculate direct costs see, for instance, Clabaugh G., Ward M.M. 2008. Cost-of-illness studies in the United States: a systematic review of methodologies used for direct cost. Value Health 11(1):13-21. DOI http://dx.doi.org/10.1111/j.1524-4733.2007.00210

[96] In reality, data rarely exist regarding the probability of survival and direct costs for a specific disease for each age of diagnosis and sex. If there were such data, however, the estimated average direct costs would be calculated by weighting the direct costs for each age and sex by the percentage of incidence in each sex/age grouping.

[97] Jo C. 2014. Cost-of-illness studies: concepts, scopes, and methods. Clin Mol Hepatol 20(4):327-37. DOI http://dx.doi.org/10.3350/cmh.2014.20.4.327

[98] A systematic review of such instruments has been performed by Mattke S, Balakrishnan A, Bergamo G, et al. 2007. A review of methods to measure health-related productivity loss. Am J Manag Care 13(4):211-7. The authors, furthermore, point out how presenteeism (being present at work but working at a reduced capacity) may account for a larger proportion of losses than absenteeism (being absent from work). Retrieved from http://www.ajmc.com/journals/issue/2007/2007-04-vol13-n4/apr07-2472p211-217/ On the issue of presenteeism, and the impact of health conditions to employers, a review of the literature has been carried out by Schultz A.B., Chen C.-Y., Edington D.W. 2009. The cost and impact of health conditions on presenteeism to employers: a review of the literature. Pharmacoeconomics 27(5):365-78. DOI http://dx.doi.org/10.2165/00019053-200927050-00002 After reviewing the literature, they conclude that many health conditions are significantly associated with on-the-job productivity losses ("presenteeism"); what cannot be stated yet is the dollar value of those losses.

[99] The Human Capital Approach represents the simplest version of the Salary Conversion Methods, which attempt to estimate productivity losses based on self-reported lost time or decreased productivity.

today and in the future), under the assumption that future earnings are used as a proxy for future productivity[100]. Depending on the available data sources, authors have used actual salaries of the respondents, mean salaries for the corporation, or national median wages;

b. Friction Cost method, which estimates the value of human capital when the sick or impaired worker is taken over by another person (either through a reallocation of employees over jobs or by someone drawn from the ranks of the unemployed), who replaces the present value of a worker's future earnings until the sick or impaired worker returns or is eventually replaced[101]. This method is very demanding in terms of data requirements, as four questions need to be answered and corresponding data obtained[102]: 1) When does a friction period occur? 2) How long does a friction period last? 3) What are the costs during the friction period? 4) How can the medium term economic consequences of illness that extends beyond the friction period be estimated?;

c. Willingness-to-pay method, which measures, through various methods (e.g. surveys, examining the extra wages for highly risky jobs, examining the demand for products that leads to greater level of health or safety), the amount that an individual is eager to pay in order to reduce the probability of illness or mortality[103]. In practice this method has been difficult to implement and its applications have been debated and have not produced generally accepted and validated figures, with empirical studies giving a broad range of results.[104] On the European Chemical Agency (ECHA) website willingness to pay values are available for health outcomes in relation to chemicals. Those values were specifically developed for socio-economic analysis in restriction proposals and applications for authorisation.[105]

Intangible costs capture the psychological dimensions of the illness to the individual (and their family), i.e. the pain, anxiety and suffering; these costs are not usually monetised, because objective valuations of these impacts are rarely available or easily validated, due to

[100] On the empirical strengths of this method, see for instance, Glied S. 1996. Estimating the indirect cost of illness: an assessment of the forgone earnings approach. Am J Public Health 86 (12):1723-8.

[101] Koopmanschap M.A., Rutten F.F.H, van Ineveld B.M., et al. 1995. The friction cost method for measuring indirect costs of disease. J Health Econ 14(2):171-89. DOI http://dx.doi.org/10.1016/0167-6296(94)00044-5 These authors argue that the HCA overestimates the true absence-related productivity losses because short-term absences might be partially compensated with greater effort or unpaid overtime, whereas longer-term absences would lead to replacement of workers with new hires. They show that application of the HCA to calculate the indirect costs of disease in The Netherlands in 1988 resulted in these costs being 8.5 times higher than the indirect costs resulting from using the friction method.

[102] Koopmanschap M.A., Rutten FFH. 1996. A practical guide for calculating indirect costs of disease. Pharmacoeconomics 10 (5): 460-6. Figure 2 on page 464 provides a schematic overview of the many estimations needed in order to calculate the indirect costs of diseases according to the friction method.

[103] Attempts to implement this approach using survey responses or revealed preferences estimates have produced values affected by statistical problems and measurement difficulties. On this issue see, for instance, Landefeld J.S., Seskin E.P. 1982. The economic value of life: linking theory to practice. Am J Public Health 72 (6): 555-66.

[104] Ament A., Evers S. 1993. Cost of illness studies in health care: a comparison of two cases. Health Policy 26: 29-42

[105] ECHA. 2016. Willingness to pay to avoid certain health impacts. Retrieved from: http://echa.europa.eu/support/socio-economic-analysis-in-reach/willingness-to-pay-to-avoid-certain-health-impacts

the measurement difficulties and related controversies.[106] These costs have therefore been expressed as non-monetary measures, such as DALYs (Disability Adjusted Life Years) or QALYs (Quality Adjusted Life Years); these are measures that combine and standardise health care costs and the 'lost economic or societal contribution' resulting from premature death or disability.

DALY measures the loss of one year of healthy life, therefore illustrating the negative impact of a condition, and they are commonly used to quantify the burden of disease at a population level;[107] QALYs are used to illustrate health benefits; they are life years adjusted by a quality weight, which is measured on a preference scale, where 'full health' equals a score of 1.0, being 'dead' a score of 0.0.[108]

1.5. Cost of Illness (COI) studies related to Endocrine Disruptors

During the last couple of years a certain number of COI studies related to EDs were published; the main findings, and the underlying assumptions and simplifications involved, are summarised below.

The **Nordic Council of Ministers** published a report[109] estimating the costs for society related to negative effects on human male reproductive health suspected to be linked to exposure to EDs in Denmark, Finland, Iceland, Norway and Sweden. The figure below summarises the estimates of the direct, indirect and intangible costs (loss of life years and loss of quality of life) of effects on human male reproduction in the Nordic countries[110].

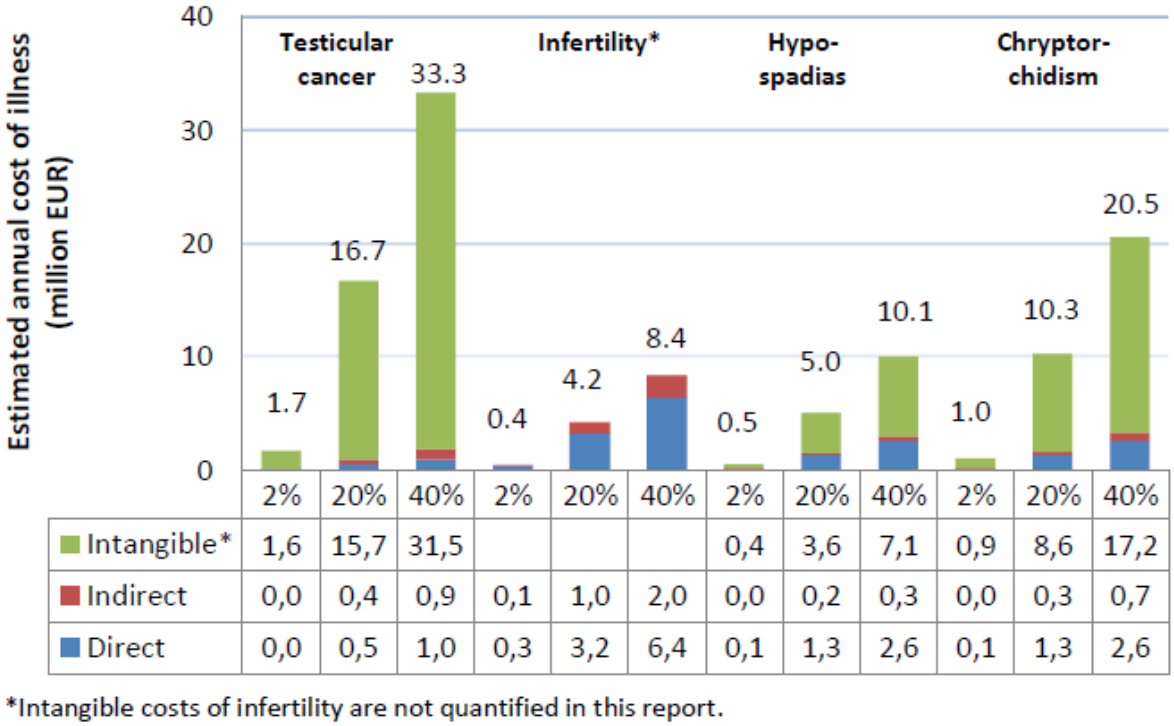
[106] Cooper BS, Rice DP. 1976. The economic cost of illness revisited. Soc Secur Bull 39(2):21-36, who conclude that estimates based on the human capital approach, reformulated using a willingness-to-pay criterion, produce the only clear, consistent, and objective values.

[107] A DALY comprises two other health gap indicators: YLL (Years of Life Lost), measuring the social burden of fatal health outcomes and YLD (Years Lost due to Disability), estimating non-fatal outcomes.

[108] The number of QALYs is calculated by weighting the time spent in health states with the preference-based scores associated with those states.

[109] Olsson, I-M, et al. 2014 The cost of inaction - A Socioeconomic analysis of costs linked to effects of endocrine disrupting substances on male reproductive health, Copenhagen: Nordisk Ministerråd, retrieved from: http://norden.diva-portal.org/smash/get/diva2:763442/FULLTEXT04.pdf

[110] Direct and indirect costs were discounted by a rate of 4% per year, while the intangible costs were discounted by a pure time preference rate of 1.5% per year.



	2%	20%	40%	2%	20%	40%	2%	20%	40%	2%	20%	40%
Intangible*	1,6	15,7	31,5				0,4	3,6	7,1	0,9	8,6	17,2
Indirect	0,0	0,4	0,9	0,1	1,0	2,0	0,0	0,2	0,3	0,0	0,3	0,7
Direct	0,0	0,5	1,0	0,3	3,2	6,4	0,1	1,3	2,6	0,1	1,3	2,6

*Intangible costs of infertility are not quantified in this report.

Figure 7. Cost of effects on human male reproduction in the Nordic countries due to EDs at different levels of assumed etiological fractions (millions of EUR per year of exposure)

Assuming an etiologic fraction[111] of 20%, the estimated cost of illness related to negative effects on male reproduction due to the present yearly exposure to EDs in the Nordic countries was estimated to be EUR 36 million per year of exposure.

Extrapolations to EU28 were made to estimate the equivalent costs in the EU assuming that the numbers of incidences of the different relevant health effects in the next 30 years would have been the same as today. Assuming etiological fractions of 2%, 20%, and 40%, the discounted socio-economic costs for the EU-28 due to yearly exposure to EDs were estimated to be respectively EUR 59, EUR 592, and EUR 1,200 million per year of exposure, while the undiscounted costs were estimated to be equal to EUR 1,267 million per year of exposure to EDs at an etiological fraction of 20%.

The following considerations need to be kept in mind, among others:

1. the basic assumption of the report was that exposure to EDs leads to the assessed negative health effects in human populations. However, the strength of the evidence for this causal link was not documented;

[111]The Etiologic Fraction, in multifactorial diseases, is the fraction of all cases with a specific outcome (disease) that can be attributed to certain causing (etiological) factor (e.g. exposure to EDs, or lack of exercise, or other causing factors). In this respect, the EF is interpreted as a partioning of causality; however, it could be interpreted also as proportion of preventable disease. These interpretations, although related, are not equivalent. See Levine B.J. 2007. What does population attributable fraction mean? Prev Chronic Dis 40(1): 1-5

2. to estimate the overall cost associated to an illness, etiologic fractions were estimated. However, an exact estimate of the etiological fraction is associated with large uncertainties, in particular for the health effects considered which are multifactorial. The report acknowledges that other factors which have been linked to the observed effects were dietary factors, obesity, smoking, degree of physical activity, and alcohol consumption. The chosen etiological fractions were based on expert advice and on current knowledge about the importance of genetic factors versus various environmental factors. However, establishing the etiological fraction attributed to exposure to EDs versus other environmental factors is always crucial, thus the selection of experts for this step played a key role in the final outcome of this study in particular considering that scientists still have different views on the evidence available on a causal link between exposure to EDs and health outcomes (Section 1.2 of this annex).
3. the incidence of the illnesses included in the report were different among the countries considered, and could depend on both genetic and environmental factors;
4. incidence rates for some of the conditions considered (e.g. hypospadias[112]) were not well covered, and no central source with information about incidence rates was available;
5. direct costs were derived from registry data from Swedish hospitals, but uncertainty was involved in extrapolating these estimates to the Nordic countries and to the EU;
6. intangible costs were evaluated by losses in Quality Adjusted Life Years (QALY). Bearing in mind that the validity of a QALY estimate might vary from country to country and greatly depends on how successful the treatment is, the extrapolation of QALY-measures from one country to another might give an uncertain measure.[113]

A series of articles were published in 2015 by authors affiliated to the **Endocrine Society**. The papers were all based on the same method and assessed different diseases associated with EDs.

Trasande et al.[114] estimated the "Burden and Disease Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union". This study focussed on those diseases for which evidence for causation by exposure to EDs was considered strongest, according to the experts consulted for this study. The ranges for etiological fractions of disease burden that could be attributed to EDs were then estimated.

[112] Hypospadias is a condition in which the opening of the urethra is any place along the underside of the penis, instead of at the tip of the penis. The meatus (hole) is most often found near the end of the penis ("distal" position), but it may also be found from the middle of the penile shaft to the base of the penis, or even within the scrotum ("proximal" positions). Sources: Urology care foundation, The official foundation of the American Urological association; Mayo Clinic.

[113] For testicular cancer, e.g., there is an alternative QALY-loss estimate; this alternative estimate implies that 1.98 (rather than 1.09) QALYs are lost per case, and if this estimate was used, then the total discounted costs per year in the Nordic countries at an etiological fraction of 20% would have increased from EUR 36 to EUR 49 million.

[114] Trasande, L., et al. 2015. Estimating Burden and Disease Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union, Journal of Clinical Endocrinology and Metabolism . 100(4):1245-1255. DOI http://dx.doi.org/10.1210/jc.2014-4324

Three general approaches on which to base attribution to EDs were used:

1. trends in incidence/prevalence over and above a baseline that would be difficult to attribute to genetics, accompanied by information on likely causal mechanisms by EDCs and/or increasing exposure;
2. data from genetic studies that allowed to quantify the remaining environmental contribution;
3. dose-response relationships between exposure to EDs and health outcomes, extrapolated by the epidemiological and toxicological literature and considered reliable by the experts consulted for this study.

For determining the probability of causation, the Intergovernmental Panel on Climate Change weight-of-evidence characterisation[115] was adapted by a Steering Committee of scientists.

Starting from the WHO State of the Science of ED Chemicals (2012)[116], which identified three distinct sets of health endpoints with the most substantial evidence for EDC attribution (obesity/diabetes, male reproductive health, and neurodevelopmental disability), the panel achieved consensus that "EDs causation was probable (> 20%)" for IQ loss and associated intellectual disability, autism, attention-deficit hyperactivity disorder, childhood obesity, adult obesity, adult diabetes, cryptorchidism, male infertility, and mortality associated with reduced testosterone.

The total costs of all conditions probably attributable to EDCs were EUR 191 billion, with sensitivity analyses suggesting costs ranging from EUR 81.3 to EUR 269 billion annually for the whole EU population.

Accounting for probability of causation, using the midpoint of each range for probability of causation produced costs ranging between EUR 2.5 and EUR 239 billion annually (median, EUR 157 billion); using the lowest end of the probability range produced a range of EUR 44 to EUR 235 billion (median, EUR 109 billion), while using the highest end of the probability ranges produced costs ranging from EUR 17.6 to EUR 246 billion (median, EUR 180 billion).

Even though the primary finding is that there is a substantial probability of very high disease costs across the life span associated with EDC exposure in the EU, the following elements should be considered:

1. an expert elicitation approach was used to estimate the probability that EDCs contribute to disease and disability. However, expert opinion is not a substitute for solid epidemiological evidence or for systematic toxicological documentation;
2. the assumption that a certain "attributable fraction" of health costs can be attributed to EDs is still very controversial among scientists.

[115] Intergovernmental Panel on Climate Change. Guidance notes for lead authors of the IPCC Fourth Assessment Report on addressing uncertainties. WMO-UNEP, 2005. Retrieved from: http://www.ipcc.ch/meetings/ar4-workshops-express-meetings/uncertainty-guidance-note.pdf

[116] Bergman Å, Heindel J, Jobling S, Kidd KA, Zoeller RT, 2012. eds. State of the science of endocrine disrupting chemicals, Geneva: United Nations Environment Programme and the World Health Organization, 2013, retrieved from: http://unep.org/pdf/9789241505031_eng.pdf

3. a recent scientific publication by Cartier et al. on organophosphorus pesticides (OPs) and neuro-development reported about the PELAGIE cohort (Brittany)[117]. The study from Cartier does not find any evidence for an association of pre-natal OP exposure and intelligence scores in the Brittany cohort. The authors speculate on what the reason(s) may be and discuss the US studies that underpin the study of Trasande et al.

4. The external report provided by the Ioannina School of Medicine to EFSA in 2013 may also provide additional information: they reviewed 32 publications in the area of pesticide exposure and mental and psychomotor development outcomes (including ADHD, autism, IQ loss)[23]

Bellanger et al.[118] applied the same approach for estimating "Neurobehavioral Deficits, Diseases, and Associated Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union". The expert panel focused on four exposure-outcome relationships that they considered having the greatest evidence for causation: PolyBrominated Diphenyl Ethers (PBDEs) exposure with reduced cognition, OrganoPhosphates (OP) exposure with reduced cognition, ED exposures (including phthalates) with Autism Spectrum Disorder (ASD), and ED exposures (including OP and PBDE) with Attention Deficit Hyperactivity Disorder (ADHD).

After evaluating the epidemiological and toxicological evidence, the experts consulted for this study concluded[119]:

1. assessment of a 70–100% probability that Organophosphates-associated IQ loss (and additional cases of intellectual disability) costs annually the EU EUR 146 billion (base-case scenario with a 5% estimate of AF (with 2% and 10% values as inputs for sensitivity analyses leading to EUR 46.8 billion and EUR 195 billion for a low and high case scenarios, respectively);

2. assessment of a 20-39% probability that EDC-associated Autism Spectrum Disorder costs annually the EU EUR 199 million (base-case scenario with a 5% estimate of AF, with 2%-10% as inputs for sensitivity analyses leading to EUR 79,7 million and EUR 399 million for a low and high case scenarios, respectively);

3. assessment of a 20-69% probability that EDC-associated Attention Deficit Hyperactivity Disorder costs annually the EU EUR 2,40 billion (base-case scenario with a 12,53% estimate of AF, with 10,76-17,28% as inputs for sensitivity analyses leading to EUR 1,21 billion and EUR 2,86 billion for a low and high case scenarios, respectively).

[117] Cartier C., Warembourg C., Le Maner-Idrissi G., Lacroix A., Rouget F., Monfort C., Limon G., Durand G., Saint-Amour D., Cordier S., Chevrier C. 2015. Organophosphate Insecticide Metabolites in Prenatal and Childhood Urine Samples and Intelligence Scores at 6 Years of Age: Results from the Mother-Child PELAGIE Cohort (France). Environ Health Perspect. DOI: http://dx.doi.org/10.1289/ehp.1409472

[118] Bellanger, M., Demeneix, B., Grandjean, P., Zoeller, R. T., and Trasande, L. 2015. Neurobehavioral Deficits, Diseases, and Associated Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union. The Journal of Clinical Endocrinology & Metabolism 100(4): 1256-1266. DOI http://dx.doi.org/10.1210/jc.2014-4324

[119] Findings regarding the exposure to PolyBrominated Diphenyl Ethers (PBDEs) are not reported as this group of substances is not falling into the scope of the PPP or BP legislation, and therefore they cannot be considered relevant for the purpose of this IA.

These findings need to be considered in the light of the following:

1. estimates were limited due to uncertainties in the evidence (scarcity of European data on exposure-outcome relationships);
2. attributable fractions for the base-case scenario and for the sensitivity analysis were based on the expert panel's judgements;
3. some of the extrapolations were from subpopulations (e.g., Mexican American), and therefore the results rely on the generalisability of exposure-outcome relationships to European populations;
4. biomarker data were not available for all EU countries, and therefore judgment was used in extrapolating to the EU as a whole;
5. finally, none of the studies referred to data on PPP/BP exposure, except for the study on organophosphates as a whole class of pesticides. This class includes substances with very different toxicity and the study does not allow distinction of different substances within the class. In addition, the most toxic organophosphates have been removed from the EU market several years ago (e.g. diazinon, parathion, paraquat, fenitrothion, fonofos, phorate). Therefore, besides the fundamental methodological limitations of this study (in particular on the calculation of the etiological fraction attributed to ED exposure), the results of this study cannot be considered as directly relevant for this Impact Assessment (IA) which focusses on PPP and BP.

Hauser et al.[120] applied the same approach to estimating "Male reproductive disorders, diseases, and costs of exposure to endocrine-disrupting chemicals in the European Union".

The expert panel focused on four exposure-outcome relationships: 1) phthalates and infertility; 2) polybrominated diphenyl ethers (PBDEs) and testicular cancer; 3) PBDEs and cryptorchidism; and 4) phthalates and reduced serum T, selected after assessing the availability of well-conducted human and animal studies to assess reproductive effects of these EDCs. None of these groups of substances is falling into the scope of the PPP or BP legislation, and therefore their findings cannot be considered directly relevant for the purpose of this IA.

Finally, **Legler et al.**[121] followed the approach to estimate "Obesity, diabetes, and associated costs of exposure to endocrine-disrupting chemicals in the European Union".

The expert panel focused on five exposure-outcome relationships: 1) prenatal DichloroDiphenyldichloroEthylene (DDE) exposure with obesity; 2) adult DDE exposure with diabetes; 3) adult phthalate exposure and obesity; 4) adult phthalate exposure and diabetes; 5) prenatal BPA exposure and obesity, selected after assessing the availability of well-conducted human and animal studies to assess reproductive effects of these EDCs.

[120] Hauser, R., et al. 2015. Male reproductive disorders, diseases, and costs of exposure to endocrine-disrupting chemicals in the European Union. The Journal of Clinical Endocrinology & Metabolism. 100(4):1267-1277.

[121] Legler, J., Fletcher, T., Govarts, E., Porta, M., Blumberg, B., Heindel, J. J., & Trasande, L. 2015. Obesity, diabetes, and associated costs of exposure to endocrine-disrupting chemicals in the European Union. The Journal of Clinical Endocrinology & Metabolism . 100(4):1278-1288. DOI http://dx.doi.org/10.1210/jc.2014-4325

Also in this case, BPA is not falling into the scope of the PPP or BP legislation. In addition, DDE is not on the market in Europe as PPP or BP since at least 1993 (Table 3).Because of this, also in the case the findings of the study cannot be considered as relevant for the purpose of this IA.

The Health and Environment Alliance (**HEAL**) published a study[122] estimating the health costs possibly associated to exposure to EDs in the EU, based on a paper by **L. Trasande**[123] (which estimated the contribution of exposure of a single EDC - Bisphenol A - to two different health conditions, childhood obesity and adult coronary heart disease, and this was equal to a 2-5% range).

The cost calculation, using the human capital approach, was performed for a list of diseases and conditions identified by HEAL as being associated with EDs exposure (on the basis of a review of the scientific literature): reproductive and fertility problems; abnormalities of the penis and testicles in baby boys; cancer of the breast, prostate, testes; children's behavioural disorders (such as autism and attention deficit hyperactivity disorder), obesity and diabetes[124].

Incidence rates and costs of treating the health effect considered were calculated, and for each health effect considered, total cost estimates for the EU28 countries were scaled up, on the basis of population size, from the estimates derived from the documented cost studies.

The estimates of total costs (direct and indirect) associated to EDs exposure, for those health conditions considered, amounted to EUR 636 billion per year in the EU; considering the assumption that EDs could contribute to 2-5% of the total health costs, HEAL concluded with a range comprised between EUR 13 and EUR 31 billion each year.

Even though the primary finding is that substantial costs for the EU health care systems could be attributable to EDs exposure, the following caveats should be carefully considered before any conclusion could be drawn:

1. the attributable fraction of 2-5% is based on just one study estimating the contribution of exposure of a single EDC, Bisphenol A, to two different health conditions; This chemical is not falling into the scope of the PPP or BP legislation, thus the findings cannot be considered as directly relevant for the purpose of this IA.
2. the country-disaggregated costs do not reflect differences in either prevalence or unit costs;
3. figures were not available for all the endocrine-related health problems selected for the analysis;

[122] HEAL 2014. Health costs in the European Union. How much is related EDCS? Edited by G. K. Jensen. Retrieved from: http://www.env-health.org/IMG/pdf/18062014_final_health_costs_in_the_european_union_how_much_is_realted_to_edcs.pdf

[123] Trasande. L. 2014. Further limiting Bisphenol A in food uses could provide health and economic benefits. Health Affairs. 33(2):316-323. DOI http://dx.doi.org/10.1377/hlthaff.2013.0686

[124] For each of these, the justification for the analysis was found in the Berlaymont declaration of 24 May 2013, when a group of the world's scientific experts on EDCs launched a plea calling on the European Commission "to implement regulatory measures that are in line with the best available science"

4. as acknowledged in the "Incidence and Costs" section of the report, even though many trends are upward, it is not always possible to distinguish between environmental factors, and specifically EDs, and improved diagnostics for the increases in incidence.

Further, **HEAL** published a technical briefing[125] on the economic evaluation of health impacts from EDCs, which builds on the previous report and on recent papers estimating costs attributable to EDC exposure, by broadening the previous approach, based on the human capital approach, and considering also the disutility costs of the health impacts (pain, suffering, discomfort and anxiety linked to the illness). HEAL's findings are summarised in Table 4.[126]

The main conclusions reached by HEAL were the following:

1. the cost data given were judged to be defensible mid-range estimates, but given that the review was not comprehensive, these findings should have been considered as indicative;
2. however, with the evidence available, it was tentatively concluded that the disutility component might have been considered to be a non-trivial multiplier to the aggregate cost estimates that have been published in recent years, given that the inclusion of the disutility component seemed to double the estimates based on the two COI components of resources and opportunity costs.

Table 4. HEAL findings on the cost of health impacts.

Health Impact	Resource & Opportunity Costs	Disutility (WTP) Costs	COI:WTP ratio
Human Fertility	10,000	20,000	1:2
Cancer	15,000	75,000	1:5
Neurodevelopmental conditions	15,000	14,000	1:1
ADHD	12,000	N/A	
ASDs	1,500,000	N/A	
Diabetes	3000	16,000	1:5
Obesity	15,000	18,000	1:1.2

N/A = Not available

1.6. Relevance of the available COI studies in the context of PPP and BP

COI studies are considered to be an important measurement technique in health sciences. By measuring and comparing the economic burden of disease to society allows to improve the information in socio-economic analysis for regulatory decisions can be taken.

[125] HEAL, Towards Comprehensive Economic Valuation of Health Impacts from Endocrine Disrupting Chemicals. Retrieved from: http://env-health.org/IMG/pdf/2015.09.08_edcs_willingness_to_pay_heal_technical_briefing_final.pdf

[126] HEAL, Box 4, page 11 - figures per case expressed in EUR, at 2014 prices

The studies illustrated in the previous pages have provided estimates of the burden of disease associated to exposure to some endocrine-disrupting chemicals, showing that in the EU, EDCs may contribute substantially to:

- male reproductive health disorders and diseases, with up to EUR 1,2 billion of associated annual costs;[127]
- male reproductive health disorders and diseases, with nearly EUR 15 billion of associated annual costs;[128]
- obesity and diabetes, with more than EUR 18 billion of associated annual costs;[129]
- neurobehavioral deficits and disease, with more than EUR 150 billion of associated annual costs;[130]
- IQ loss and associated intellectual disability, autism, attention-deficit hyperactivity disorder, childhood obesity, adult obesity, adult diabetes, cryptorchidism, male infertility, and mortality associated with reduced testosterone, with a median value comprised between EUR 109 and EUR 180 billion of associated annual costs, depending on the probability of causation;[131]
- reproductive and fertility problems, abnormalities of the penis and testicles in baby boys; cancer of the breast, prostate, testes; children's behavioural disorders, obesity and diabetes, with between EUR 13 and EUR 31 billion of associated annual costs.[132]

The indicated costs in the studies are substantial, and they could be underestimates as it is claimed that they are based on conservative assumptions and consider only those EDCs with the highest probability of causation.

These findings should be assessed in the light of the following considerations:

- the three distinct sets of health endpoints claimed to have the most substantial evidence for EDs attribution and considered in the analyses (obesity/diabetes, male reproductive health, and neurodevelopmental disability) have been based on the main

[127] Olsson, I-M., et al. 2014. The cost of inaction - A Socioeconomic analysis of costs linked to effects of endocrine disrupting substances on male reproductive health, Copenhagen: Nordisk Ministerråd. Retrieved from http://norden.diva-portal.org/smash/get/diva2:763442/FULLTEXT04.pdf

[128] Hauser, R., et al. 2015. Male reproductive disorders, diseases, and costs of exposure to endocrine-disrupting chemicals in the European Union. The Journal of Clinical Endocrinology & Metabolism.100(4):1267-1277. DOI http://dx.doi.org/10.1210/jc.2014-4325

[129] Legler, J., et al.2015. Obesity, diabetes, and associated costs of exposure to endocrine-disrupting chemicals in the European Union. The Journal of Clinical Endocrinology & Metabolism. 100(4):1278-1288. DOI http://dx.doi.org/10.1210/jc.2014-4326

[130] Bellanger, M., Demeneix, B., Grandjean, P., Zoeller, R. T., & Trasande, L. 2015. Neurobehavioral Deficits, Diseases, and Associated Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union. The Journal of Clinical Endocrinology & Metabolism. 100(4):1256-1266. DOI http://dx.doi.org/10.1210/jc.2014-4324

[131] Trasande, L., et al. 2015. Estimating Burden and Disease Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union, Journal of Clinical Endocrinology and Metabolism. 100(4):1245-1255. DOI http://dx.doi.org/10.1210/jc.2014-4324

[132] HEAL. 2014. Health costs in the European Union. How much is related EDCS? Edited by G. K. Jensen. Retrieved from: http://www.env-health.org/IMG/pdf/18062014_final_health_costs_in_the_european_union_how_much_is_realted_to_edcs.pdf

findings of the 2012 World Health Organization/United Nations Environment Programme State of the Science of Endocrine Disrupting Chemicals, whereas no consensus exists among scientists about the conclusions of this report;[12]

- assessment of the epidemiological and toxicological evidence available, as well as the probability that an ED contribute to disease and disability (etiological fractions) have been established via expert elicitation by a selected group of few experts. Available guidance on this approach was not considered (e.g. the EFSA guidance on expert knowledge elicitation in food and feed safety risk assessment[133]);
- no consideration has been given to available recent systematic reviews on pesticide exposure and associated health outcomes where results indicate that farmers have lower incidence of most cancers compared to the general population;[24]
- judgment regarding reference levels, impact of covariates, and steepness of the dose-dependence of the outcomes was based on consensus among the authors or steering committees selected by the authors;
- whereas control for confounding was performed in many of the studies used, some of the extrapolations were from subpopulations (e.g., Mexican American), and therefore the results rely on the generalisability of exposure-outcome relationships to European populations;
- calculations could not take into account potential differences between exposure levels in the EU MS (e.g. biomarker data were not available for all EU countries, and therefore judgment was used in extrapolating to the EU as a whole);
- most of the EDs considered for the cost quantifications in these studies are outside the scope of the current IA, as they are not PPP or BP (for example Bisphenol A, PolyBrominated Diphenyl Ethers, OrganoPhosphates, Phthalates), or the PPP or BP have been banned in the EU years ago (DichloroDiphenyldichloroEthylene). Further, other conclusions were drawn referring to a whole class of pesticides (e.g. organophosphates), while this class includes substances of different toxicity. The most toxic substances of this class of pesticides have been banned in the EU already several years ago (Table 3).

In addition to the points highlighted before, it should always be kept in mind that performing a COI analysis is very challenging;[134] the choice of cost methodology (and their accuracy) for assessing both direct costs and losses in productivity, is largely driven by data availability, which varies among countries. This applies also to epidemiological data (i.e., disease prevalence, incidence, and associated mortality). COI studies imply also the assessment of the epidemiological and toxicological evidence which are available, as well as assumptions regarding, for instance, the discount rate chosen for reflecting the present value of future costs and health effects and the proportion of a disease that may be attributable to a substance's

[133] EFSA (European Food Safety Authority). Guidance on Expert Knowledge Elicitation in Food and Feed Safety Risk Assessment. EFSA Journal 2014; 12(6):3734. DOI http://dx.doi.org/10.2903/j.efsa.2014.3734

[134] Greenberg, D. et al. 2014. What Are the Challenges in Conducting Cost-of-Illness Studies? Value in Health Regional Issues. 4C:115-116. DOI http://dx.doi.org/10.1016/j.vhri.2014.08.003

exposure. As far as the population attributable fractions are concerned, errors in computations and interpretation may exist and, in some settings, the value of the estimates may be questionable;[135] also, conceptual problems in the definition and interpretation of attributable fractions exist.[136]

One of the outcomes of these complexities is that reported estimates have been sometimes found inconsistent across studies, thereby raising concerns over the validity of these estimates and the methods used to calculate them.[137]

Considering these limitations, the conclusions reached by the recent COI studies analysed should be taken with great caution, and viewed as suggestive about the costs of diseases related to exposure to EDs.

3. ASSESSMENT OF THE PERFORMANCE OF THE OPTIONS PRESENTED IN THIS IMPACT ASSESSMENT UNDER CONSIDERATION OF THE REGULATORY DECISION MAKING AND PROTECTION OF HUMAN HEALTH

In the previous sections the evidence related to endocrine mediated diseases and associated costs was discussed. The evidence shows that robust conclusions cannot be drawn on the link between exposure to environmental levels of EDs and increased incidence of endocrine mediated diseases and disorders. Nevertheless, protection of human health remains the highest priority, as it is a mayor objective in the PPP and BP Regulations, and thus guides this IA.

Protection of human health is therefore analysed under consideration of the current regulatory decision making under the PPP and BP Regulations, in particular evaluating if this regulatory framework is adequately protecting human health, as requested by those pieces of EU legislation and by the EU Treaty.

The precautionary principle underpins the EU legislation on placing on the market of PPP and BP, as stated in the corresponding recitals of these regulations.[138,139] The EU authorisation system for PPP and BP is based on prior approval ("positive list") and shift the responsibility

[135] Rockhill B., Newman B., Weinberg C. Use and misuse of population attributable fractions. Am J Public Health 1998; 88(1):15-9; Greenland S., Robins J.M. Conceptual problems in the definition and interpretation of attributable fractions. Am J Epidemiol 1988; 128(6):1185-97.

[136] Greenland S., Robins J.M. 1988. Conceptual problems in the definition and interpretation of attributable fractions. Am J Epidemiol. 128(6):1185-97. The authors argue that there is the need to distinguish three concepts of attributable fractions: the excess fraction, the etiologic fraction, and the incidence density fraction. These quantities do not necessarily approximate one another, and the etiologic fraction is not generally estimable without strong biologic assumptions. For this reasons, they conclude, care is needed in deciding which of the concepts is a appropriate for a particular situation.

[137] Akobundu E, Jing J, Blatt L, et al. 2006. Cost-of-illness studies: a review of current methods. Pharmacoeconomics. 24(9):869-90.

[138] Article 1.4 of Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309.

[139] Article 1.1 of Regulation (EU) No 528/2012 of the European Parliament and of the Council concerning the making available on the market and use of biocidal products. OJ L 167/1.

for producing scientific evidence (burden of proof) to the industry.[140] In other words, the legislation requires that the substances be deemed hazardous until proven otherwise, and the burden of proof lies with the applicant requiring an authorisation to place the substance on the EU market to provide the scientific information needed to evaluate the possible risk. Also the preceding legislations put in place in the 90s (Directive 91/414/EC and Directive 98/8/EC, respectively) asked for a sound scientific risk assessment as a basis for regulatory decision making.

The Communication from the commission on the precautionary principle[141] states that this principle is particularly relevant to the management of risk. It should be considered within a structured approach to the analysis of risk which comprises risk assessment, risk management, and risk communication. Further, the implementation of an approach based on the precautionary principle should start with a scientific evaluation, as complete as possible. Where action is deemed necessary, measures based on the precautionary principle should be, inter alia:

- proportional to the chosen level of protection,
- non-discriminatory in their application,
- consistent with similar measures already taken,
- based on an examination of the potential benefits and costs of action or lack of action (including, where appropriate and feasible, an economic cost/benefit analysis),
- subject to review, in the light of new scientific data, and
- capable of assigning responsibility for producing the scientific evidence necessary for a more comprehensive risk assessment.

In the EU, Plant Protection Products (PPP) and Biocidal Products (BP) are regulated products that need to be approved before they can be placed on the market. This pre-market approval system is considered as one of the strictest worldwide: any PPP or BP must be authorised – based on a sound scientific risk assessment[142] - before it can be placed on the market and used. MS can only authorise PPP and BP which contain active substances placed on this "positive lists", and need to carry out additional evaluation of the specific product formulations and uses.

Both the PPP Regulation (EC) No 1107/2009 and the BP Regulation (EU) No 528/2012, as well as their corresponding preceding legislations, specify a detailed list of data requirements[143,144] which have to be submitted by the applicant before any approval of active

[140] These are elements of the precautionary principle, see Communication from the Commission on the precautionary principle, COM(2000) 1 final. Retrieved from: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52000DC0001

[141] European Commission, Communication from the Commission on the precautionary principle, COM(2000) 1 final. Retrieved from: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52000DC0001

[142] Risk assessment considers the hazard of a substance and the exposure levels to which humans and the environment are exposed to. Comparing safety thresholds based on hazard data (hazard assessment) with exposure levels (exposure assessment), risk is calculated (risk assessment).

[143] Regulations EU 283/2013 and EU 284/2013, setting data requirements for active substances and for PPP, respectively; Communications 2013/C 95/01 and 2013/C 95/02, detailing the list of test methods and guidance documents for active substances and for PPP, respectively.

substance or authorisation of a product containing approved substances can be considered. This implies that both PPP and BP are among the most "data rich" regulated product groups in the EU.

As mentioned before in Section 1.3, several substances have been banned in the EU, sometimes since years, thanks to the EU on legislation on PPP and BP (Directive 91/414 and Directive 98/8/EC) which was based on risk assessment,[145] demonstrating the regulatory system in the EU worked efficiently in protecting human health.[146] Actually, Directive 98/8/EC already contained some hazard-based provisions for substances classified as toxic, very toxic, mutagens, carcinogens or toxic for reproduction for use by the general population. The rational was that the general population may not be able to adequately control exposure and therefore hazard-based provisions would ensure highest safety.

The PPP Regulation introduced and additional step for all uses (no distinction of use by professionals or by the general population): for substance with particular hazard properties (e.g. endocrine disruption), the exposure is in principle not considered but the substance is banned, irrespectively of whether realistic levels of exposure to it would pose or not a real risk to human health (so called “cut-off criteria”). However, cut-off criteria may remove from the market substances which do not pose any risk to human health and the environment, due to the levels of exposure which are very far from the safety threshold established for those substances. In cases the foreseen derogations would be applied for, a "standard" risk assessment covering all areas would still be needed, as done also for any substance which is not identified as belonging to one of the particularly hazardous classes. As a consequence, even if a substance is not identified as an ED, it may still be non-approved if the adverse effects observed are considered to pose a risk to human health or the environment. The BP Regulation follows a similar rationale for the regulatory decision making, although differences in the derogations and their implementation exist with respect to the PPP Regulation. The regulatory decision process, including the approval of ED substances, for both PPP Regulation and BP Regulation is depicted in Figure 8.

[144] Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products. Official Journal of the European Union, L 167, 27 June 2012. doi:10.3000/19770677.L_2012.167.eng

[145] Risk assessment considers the hazard of a substance and the exposure levels to which humans and the environment are exposed to. Comparing safety thresholds based on hazard data (hazard assessment) with exposure levels (exposure assessment), risk is calculated (risk assessment).

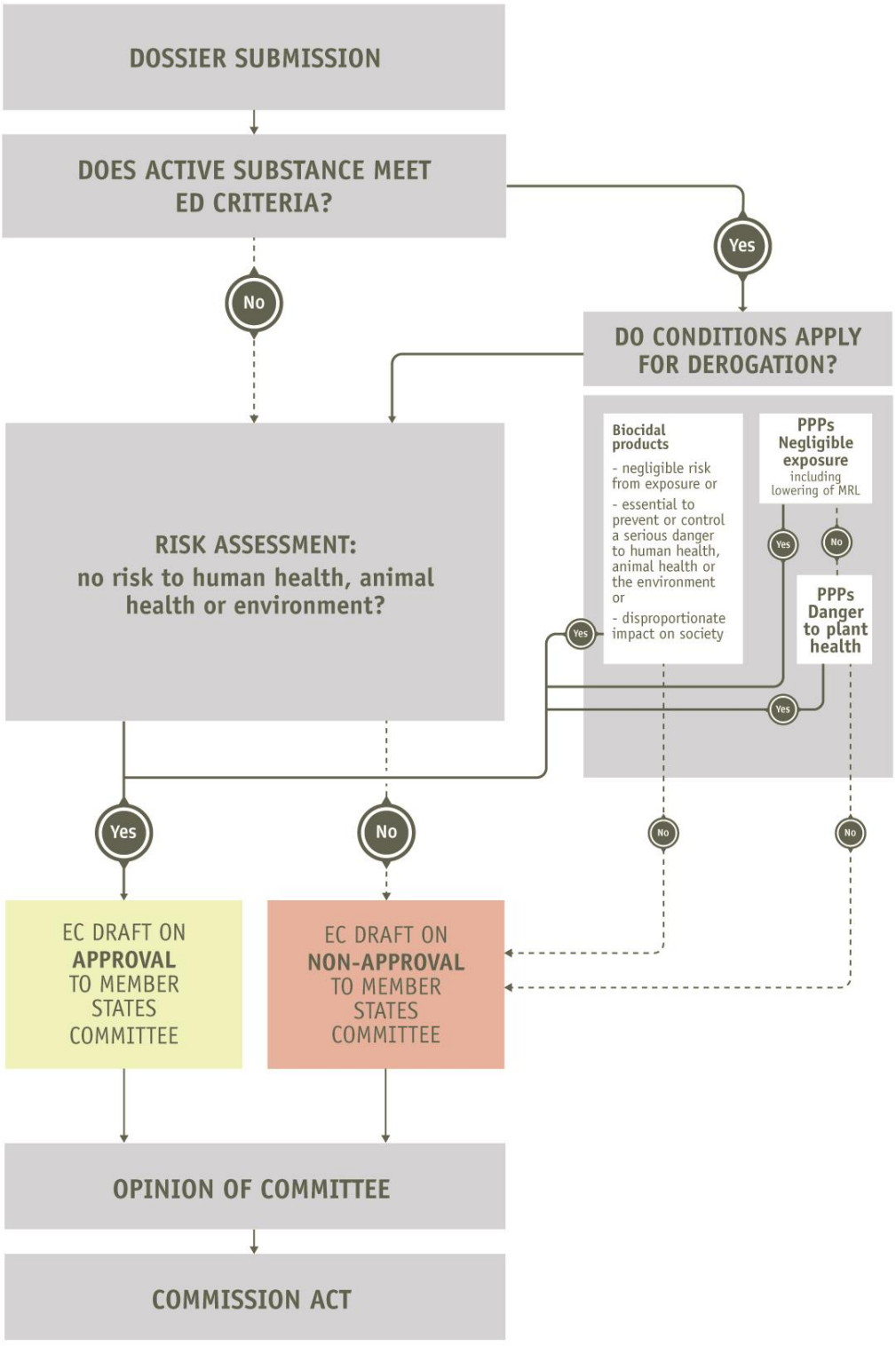


Figure 8. Regulatory decision making in the PPP and BP Regulations, under consideration of derogations for active substances identified as EDs

The EFSA opinion on EDs supports a case-by-case risk assessment approach to assess ED for decision making, which would be in line with the precautionary principle approach as defined in the Communication mentioned above. For instance, EFSA states that "*to inform on risk and level of concern for the purpose of risk management decisions risk assessment (taking into account hazard and exposure data/predictions) makes best use of available information. EDs can therefore be treated like most other substances of concern for human health and the environment, i.e. be subject to risk assessment and not only to hazard assessment*" (page 47).

Moreover, the EFSA opinion (page. 16) is "*in agreement with Kortenkamp et al. (2011) that, since points have not been defined where „threshold of adversity" is crossed, it is difficult to propose specific criteria to differentiate between effects that represent an endocrine modulation and adverse effects on the endocrine system. Expert judgement will therefore be required to assess on a case-by-case basis the toxicological relevance of such changes. In general, transient, inconsistent and minor fluctuations at the biochemical and molecular level may be considered adaptive (i.e. non-adverse), whilst sustained, consistent and permanent changes at the cell-, organ- or organism-level, resulting in pathology or functional impairment in vivo, as well as altered timing of development, may be considered adverse.*

The point at which endocrine modulation becomes an adverse effect cannot be determined on the basis of an absolute response value, but on the basis of a relative response (compared to the control/background response). The SC is therefore of the opinion that, as adversity is a prerequisite for identifying a substance as an ED, it is necessary to determine a biological threshold between endocrine modulation and adverse effect. For the time being, it is difficult to propose generic criteria to determine when this biological threshold is crossed. This is therefore likely to be done on a case-by-case basis through expert judgement."

Also the **Scientific Committee on Consumer Safety (SCCS)** supports the use of risk assessment to assess EDs for decision making.[147] In particular, the Memorandum *states that the SCCS supports the conclusions of EFSA that: "Critical effect, severity, (ir)reversibility and potency aspects are part of the hazard characterisation of EDs. To inform on risk and level of concern for the purpose of risk management decisions, risk assessment (taking into account hazard and exposure data/predictions) makes best use of available information. EDs can therefore be treated like most other substances of concern for human health and the environment, i.e. be subject to risk assessment and not only to hazard assessment." [EFSA 2013]*. The SCCS adds that "*due to the ban on animal testing for cosmetic ingredients effective since 2013, it will be extremely difficult in the future to differentiate between a potential ED and an ED, if the substance is registered solely for use in cosmetics products. The replacement of animal test methods by alternative methods in relation to complex toxicological endpoints (such as endocrine disruption) remains scientifically difficult, despite the additional efforts launched at various levels. With regard to substances with endocrine activity (potential endocrine disruptors), the assessment of their impact to human health without animal data remains a challenge*." (page 5)

[147] Scientific Committee on Consumer Safety (SCCS) Memorandum on Endocrine Disruptors. Retrieved from: http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_009.pdf

Options 2/3 and 4 will identify a different number of EDs (see Annex 5 on screening results). Considering that no robust evidence is available to support a causal link between exposure to environmental levels of substances identified as EDs and certain human diseases (see section 1 and 2 of this annex), the impact on human health cannot be related to the number of substances identified as EDs. On the other hand, the current rules (**i.e. the risk assessment step following identification or non-identification of a substance as an ED**) ensure that authorised products do not have unacceptable effects on the health of humans. Therefore, it can be assumed that no differences on impacts on human health are expected between Option 2, Option 3, and Option 4 as human health will be equally protected. Differently, Option 1 is known to identify "false positives", i.e. substances that appear to have no endocrine MoA. These substances may be removed from the market although they are not EDs according to the WHO/IPCS definition, as they do not act via an endocrine MoA. There is indeed a scientific consensus that interim criteria are not fit for correctly identifying EDs since they are unable to detect an ED mode of action. They detect many false positives because the interim criteria identify EDs even when no ED mode of action is present. They also detect many false negatives, as shown by the limited overlap between substances identified under option 1 (interim criteria) and option 2 (WHO definition). This overlap is visible in Fig 2 of the main report and in Table 1 of Annex A5. Therefore, the options rank 2/3/4 > 1 and this ranking of options has been considered for most of the MCA-scenarios, with exception of the MCA-scenarios "aim: exposure zero" for which the performance of the options is detailed further down.

It can be assumed that, based on recent scientific opinions from the EU Authority EFSA[55] and from the EU Scientific Committee SCCS[56], a risk assessment approach would protect human health from EDs in a similar way as a hazard approach followed by a risk assessment step. In fact, a product can be only placed on the market after a risk assessment has taken place (see Figure 7). Therefore it is ensured that no unacceptable effects will occur on the health of humans.[148]. Supporting this conclusion are the recent WHO reports[149,150] which recommend identifying risks from exposure to EDs. Furthermore, as a consequence of the PPP and BP EU legislation in place since the 90s, many active substances used in PPP and BP have been taken out from the EU market or restricted over the last decades based on regulatory decisions building on sound scientific risk assessments (see previous sections of this annex). This is due to the fact that some of the adverse effects which may be caused by EDs (e.g. carcinogenicity and reproductive effects) were studied and regulated before, without detailed knowledge of their potential endocrine MoA. In other words, as endocrine disruption is a new way of looking at the toxicity of chemicals (which considers[151] adverse effect, MoA, and a causal

[148] It may even be argued that a risk assessment approach would ultimately protect human heath better than a hazard approach followed by a risk assessment step. With an hazard preliminary step, we may ban substances posing no effective risk to human health and substitute them with less studies alternatives (which would pose more risk to human health because their assessment has more uncertainties)

[149] WHO 2014. Identification of risks from exposure to EDCs at the country level.

[150] WHO 2015 Identification of risks of EDCs: overview of existing practices and steps ahead. Report of a meeting in Bonn, Germany 7-8 July 2014

[151] WHO/IPCS defines an ED as "*an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations*"

link between the two), irrespectively from the MoA, many of the adverse effects often associated to endocrine disruption were already detected in the context of the evidence provided for approval of chemicals. Where a risk was identified, those substances were removed from the market.

Option B Option B only applies to the PPP Regulation. The derogations to the non-approval of active substances, currently mainly hazard-based, would be updated in light of new scientific evidence (e.g. recent scientific opinions of EFSA , Scientific Committee SCHER , expert meeting in Berlin) to risk based derogations. While the general hazard approach for EDs would be maintained, the derogations would be based on a stronger risk component compared to the current situation. Amendments to the Annexes, via Regulatory Procedure with Scrutiny (RPS) are foreseen in Regulation (EC) No 1107/2009 taking into account current scientific and technological knowledge (cf. Article 78 of the PPP Regulation). This option is therefore feasible within the remit of the mandate of the Commission as it does not imply changes by ordinary legislative procedure to the basic act.

The inclusion of socio-economic considerations (Option C) may consider a risk/benefit analysis and protect human health to a less extent. This option would request a modification via ordinary legislative procedure of the current PPP Regulation.

As a consequence, the performance of options with respect to ED-related diseases and disorders is as follows: A/B > C. Also this ranking of options has been considered for most of the MCA-scenarios, with exception of the MCA-scenario "aim: exposure zero" for which the performance of the options is detailed further down.

In order to carry out a sensitivity analysis on the performance of the options, the MCA-scenario "aim: exposure zero" was developed. It assessed the performance of the options based on a different assumption which only aims at minimizing exposure: the higher the number of active substances identified as EDs, the better the performance of the option for human health with respect to exposure (without consideration of any risk assessment) . As a consequence, within this scenario, the options perform as follows: 2/3 > 4 > 1 only based on exposure considerations. Regarding options A to C, the assessment was based on the number of correctly identified ED substances which will not be approved. As Option A would take from the market (non-approval) more substances identified as EDs than options B or C, it is assumed that it would perform the best with respect to exposure. Under this scenario, the options consequently perform as follows: A > B > C only based on exposure considerations.

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PART 11/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annex 10 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

{COM(2016) 350 final}
{SWD(2016) 212 final}

ANNEX 10

HUMAN HEALTH - TRANSMISSIBLE DISEASES AND FOOD SAFETY

Contents

This Annex focuses on the assessment of potential impacts, which build on the results of the screening study explained in Annexes 3 to 5. The results of the screening do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation. The methods and results presented in this Annex are to be interpreted as an estimation of the potential impacts.

Annexes 8 to 15 describe the impacts expected when implementing the criteria to identify EDs (Options 1 to 4) under the current regulatory framework (Option A). In addition, it was assessed whether these expected impacts would remain the same or not under consideration of different regulatory implementations (Options B and C, only applicable to the PPP Regulation). The analyses of the impacts described in these Annexes translate into the "performance" of the options, which is one of the input parameters to the MCAs (Annex 6 and 7).

The MCAs results are not concluding on any preferred option for setting scientific criteria to identify endocrine disruptors, but aim at providing additional information to decision makers with regards to the potential impacts expected when implementing the criteria, after those would have been selected on the basis of science (two MCAs were performed: Options 1 to 4 under the current regulatory context, and Options A compared to Options B and C).

At a preliminary stage of the impact assessment it was anticipated that Option C should be discarded, nevertheless it was maintained for the analysis of the impacts for methodological reasons (see Section 4.2.3 of the main report and Annexes 6 and 7). Option C only applies to the PPP Regulation.

1. INTRODUCTION

Diseases can be passed from person to person or transmitted from a host to a person. This can occur by direct contact or through a vector (for example mosquitos). The diseases are caused by pathogenic microorganisms, such as bacteria, viruses, parasites or fungi. Biocidal products (for example disinfectants and insecticides) are being used to prevent or control these transmissible diseases.

In the next section the incidence is indicated of infectious disease in health care settings and vector-borne diseases in the EU. In the third section will be discussed, the role of disinfectants and insecticides to control these diseases and the potential impacts of the different options for setting endocrine disrupting (ED) criteria.

There is no single universal disinfectant which will kill all pathogenic organisms. Therefore the availability of a range of effective biocidal products with different modes of action, and the selection of the most appropriate disinfectant for the required result, is extremely important

Disinfectants are extensively used in hospitals or other health care settings, and in the food industry to ensure the microbial safety of products, to destroy or inhibit the growth of harmful microorganisms. Some disinfectants may be used in cleaning processes (physical removal of material). Disinfectants have different modes of actions and biocidal activities. Insecticides are used, among others, to control insects which transmit human disease(s) (vectors).

The European Centre for Disease Prevention and Control (ECDC) was asked by DG SANTE[1] to provide an expert advice on this subject. The ECDC advice forms the basis for this section.

2. TRANSMISSIBLE DISEASES CAUSED BY LACK OF APPROPRIATE DISINFECTANTS OR INSECTICIDES

2.1. The incidence of transmissible diseases

2.1.1. Infectious diseases in health care facilities

Available data on the incidence or prevalence of infections in healthcare facilities (in particular hospitals) are limited to healthcare-associated infections (HAIs), i.e. infections with onset during stay of the patient in the healthcare facility and related to healthcare or associated with a previous exposure to healthcare.

From the ECDC Point Prevalence Survey of HAIs 2011-2012, the total annual number of patients with at least one HAI in the EU/EEA was estimated at 3.2 million patients with at least one HAI each year in acute care hospitals.[2] The hospital population-weighted EU/EEA HAI incidence was estimated at 3.5%. The hospital population-weighted estimated incidence

[1] Letter of 29 January 2016 to ECDC (Ares(2016)496069); ECDC provided its advice on 12th February 2016.

[2] European Centre for Disease Prevention and Control. Point prevalence survey of healthcare associated infections and antimicrobial use in European acute care hospitals. Stockholm: ECDC; 2013. Retrieved from: http://ecdc.europa.eu/en/publications/Publications/healthcare-associated-infections-antimicrobial-use-PPS.pdf

and total number of patients with HAIs, by infection type and per year for the EU/EEA, is shown in Table 1. The most common type of HAI type (in terms of number of HAIs per year) was urinary tract infections (888 106 each year), closely followed by pneumonia and other lower respiratory tract infections (860 938 each year).

The microorganisms most frequently isolated from HAIs were, in decreasing order, *Escherichia coli* (15.9%), *Staphylococcus aureus* (12.3%), *Enterococcus* spp. (9.6%), *Pseudomonas aeruginosa* (8.9%) *Klebsiella* spp. (8.7%), coagulase-negative staphylococci (7.5%), *Candida spp. (*6.1%), *Clostridium difficile* (5.4%), *Enterobacter spp*. (4.2%), *Proteus spp.* (3.8%) and *Acinetobacter spp*. (3.6%).

Table 1. Estimation of the annual number of HAIs in acute care hospitals, by type of HAI, EU/EEA.

Type of HAI	Estimated HAI incidence % (95% CI)	Number of HAIs (95% CI)	% of total HAIs (95% CI)
Pneumonia /Lower respiratory tract infection	0.95 (0.58-1.66)	860 938 (522 771-1 500 038)	24.4 (14.8-42.5)
Urinary tract infection	0.98 (0.58-1.72)	888 106 (527 129-1 554 275)	25.2 (14.9-44.0)
Surgical site infection	0.60 (0.33-1.17)	543 149 (298 167-1 062 673)	15.4 (8.4-30.1)
Bloodstream infection	0.35 (0.19-0.93)	312 822 (171 262-844 423)	8.9 (4.9-23.9)
Gastro-intestinal infection	0.29 (0.14-0.66)	258 327 (127 121-593 452)	7.3 (3.6-16.8)
Systemic infection	0.26 (0.11-1.82)	236 387 (100 646-1 647 657)	6.7 (2.9-46.7)
Skin/soft tissue infection	0.11 (0.05-0.31)	103 146 (43 564-277 627)	2.9 (1.2-7.9)
Other types of HAI	0.36 (0.17-0.85)	326 903 (151 302-770 238)	9.3 (4.3-21.8)
Total HAIs		**3 529 778 (1 941 962-8 250 382)**	

2.1.2. Infectious diseases in community settings

Norovirus infection, often called as a "winter-vomiting disease", is a highly contagious infection and once symptoms develop, it spreads easily and rapidly from person-to-person, particularly in crowded settings and mass gatherings. Due to the antigenic shift of noroviruses, similar to influenza viruses, immunity plays a minor role in preventing the infection leading to a high proportion of susceptible people for the various circulating genotypes[3]. Norovirus infections and norovirus outbreaks are not under mandatory

[3] Donaldson EF, Lindesmith LC, Lobue AD, Baric RS. 2010. Viral shape-shifting: norovirus evasion of the human immune system. Nat Rev Microbiol. 8(3):231-41. DOI: 10.1038/nrmicro2296.

surveillance in the EU. Therefore, the data on incidence is not available from the European Surveillance System.

With respect to risks of infection, the initial infection may be food- or waterborne, which has a potential to cause large gastrointestinal outbreaks particularly in school settings due to centralised school catering followed by person-to-person spread[4]. Norovirus outbreaks due to contaminated berries have been repeatedly recorded in the EU countries, and it is one of the most commonly reported causative agents for foodborne outbreaks in the EU[5,6]. Norovirus is also a well-described problem in semi-closed communities like cruise ships, causing gastrointestinal outbreaks with high attack rates among passengers and crew members.

ECDC influenza surveillance system is based primarily on two separate surveillance systems. Sentinel influenza surveillance is based on nationally organised networks of primary care physicians, mostly general practitioners, covering at least 1–5% of the population in their countries. Depending on the country, physicians report the weekly number of patients seen with influenza-like illness (ILI) or acute respiratory infection (ARI), or both, to the national focal point for influenza surveillance. In addition to the sentinel surveillance, national influenza centres receive respiratory specimens from a range of sources in their countries (so-called non-sentinel sources, such as hospital laboratories, schools, nursing homes and similar settings where influenza outbreaks may have occurred). However, ECDC does not receive surveillance data reported by setting (e.g. schools, nursing homes or day-care centres)[7].

Outbreaks of influenza and other respiratory viruses occur in the settings defined as being of interest, where close proximity in indoor settings favours direct airborne spread of infection. Transmission via contaminated surfaces may also occur.

2.1.3. Mosquito-borne diseases (West Nile Fever, Dengue, Chikunguya and Malaria)

Between 2010 and 2014, ten EU Member States (MS) (Austria, Bulgaria, Croatia, Czech Republic, Greece, Hungary, Italy, Romania, Slovenia and Spain) have reported more than 1 000 locally acquired human West Nile fever cases. Greece is the country that reported the majority of those cases. During this period, the yearly number of cases reported has been fluctuating. Over time, the geographic spread of cases has been expanding.

In the EU, dengue, chikungunya and malaria are primarily travel-related diseases. Table 2 shows an overview of the number of cases imported in the EU. Zika-virus, an emerging

[4] Bernard H, Faber M, Wilking H, Haller S, Hohle M, Schielke A, et al. 2014. Large multistate outbreak of norovirus gastroenteritis associated with frozen strawberries, Germany, 2012. Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin. 19(8):20719.

[5] Tavoschi L, Severi E, Niskanen T, Boelaert F, Rizzi V, Liebana E, et al. 2015. Food-borne diseases associated with frozen berries consumption: a historical perspective, European Union, 1983 to 2013. Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin. 20(29): 21193.

[6] European Food Safety Authority, European Centre for Disease Prevention and Control. The European Union, summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2014. EFSA Journal [Internet]. 2015; 13(12):[191 p.]. Retrieved from: http://ecdc.europa.eu/en/publications/Publications/zoonoses-trends-sources-EU-summary-report-2014.pdf

[7] The weekly influenza surveillance data is reported in: http://www.flunewseurope.org

health concern, is also transferred by mosquitos and it is considered an emerging infectious disease with the potential to spread to new areas where the *Aedes* mosquito vector is present[8].

In southern Europe, local transmission of the dengue virus was reported in Croatia in 2010 and in France in 2010, 2013, 2014 and 2015. Rapid detection and investigation of imported or suspected local cases, during the period of vector activity (mostly from May to October in southern Europe), allow taking preventive measures to control the spread of the virus in infested areas.

In 2007, an outbreak of chikungunya was reported for the first time in Europe in Italy. A total of 217 cases were reported in July–September 2007 in the Emilia-Romagna. Two autochthonous cases were reported in September 2010 in southern France and in September 2014 in total eleven autochthonous cases occurred in Montpellier, a town recently colonised by the vector mosquito species *Aedes albopictus* in France.

Autochthonous transmission of malaria has occasionally been reported over the last 10 years. In Greece local transmission was for the first time recorded in 2009 – 2013. In 2014 no local transmission was recorded in Greece, most likely due to the implemented control measures including active surveillance, early treatment and vector control. However, in 2015 six locally acquired cases were reported again in Greece.

Table 2. Overview of the imported dengue, chikungunya and malaria cases in the EU/EEA 2010-2014.[9]

Year	Dengue	Chikungunya	Malaria
2010	1622	179	6759
2011	610	55	5482
2012	1209	51	5184
2013	2515	72	5873
2014	1796	1461	6017

2.2. The role of biocides in the control of transmissible diseases

2.2.1. Biocidal products used for hand hygiene

The importance of hand hygiene as a cornerstone of standard precautions for infection prevention and control has been demonstrated for more than one century and biocides play a crucial role in it. This because an important proportion of HAIs are caused by microorganisms transmitted through the hand of healthcare workers, from patient to patient

[8] Zika virus infection information is available on the ECDC website: http://ecdc.europa.eu/en/healthtopics/zika_virus_infection/pages/index.aspx

[9] Data retrieved from The European Surveillance System (TESSy) at ECDC website. Data accessible at http://ecdc.europa.eu/en/activities/surveillance/Pages/data-access.aspx

or indirectly after contact with the hospital environment.[10;11;12] Hand hygiene is, therefore, the leading measure for preventing the spread of antimicrobial-resistant bacteria and for reducing the incidence of HAIs.[13;14;15] WHO recommends the use of alcohol-based hand rubs for hand hygiene.[16]

Consumption of alcohol-based hand rubs (in litres per 1 000 patient-days) is considered a good proxy indicator of hand hygiene compliance of healthcare workers. In a review of literature, Boyce found that in 77% of studies looking at both indicators, alcohol hand rub consumption and hand hygiene compliance were correlated[17]. Alcohol hand rub consumption was also found to be associated with reduction of meticillin-resistant *Staphylococcus aureus* (MRSA) and HAI rates in several studies.[18;19]

Since the beginning of the WHO hand hygiene campaign "SAVE LIVES: Clean Your Hands", alcohol-based hand rub solutions are increasingly used in hospitals and other healthcare facilities worldwide as first choice for hand hygiene. Data on the consumption of alcohol hand rub solutions in acute care hospitals in EU/EEA Member States were collected during the ECDC point prevalence survey of HAIs and antimicrobial use in 2011-2012 (data on alcohol hand rub consumption were from 2010 or 2011) and will be collected by ECDC during a similar point prevalence survey in 2016-2017.

The median hand rub consumption in acute care hospitals that participated in the ECDC point prevalence survey was 18.7 litres per 1000 patient-days and was significantly lower in primary hospitals than in tertiary hospitals ($p<0.001$).

The median hospital alcohol hand rub consumption varied greatly between EU/EEA Member States, from less than 10 litres per 1000 patient-days in Bulgaria, Hungary, Lithuania, Italy, Romania and Slovakia to more than 50 litres per 1000 patient-days in Denmark, Greece, Norway, Malta and Sweden (Figure 1). The WHO guidelines on hand hygiene in healthcare

[10] Dancer S.J. 2014. Controlling hospital-acquired infection: focus on the role of the environment and new technologies for decontamination. Clin Microbiol Rev. Oct;27(4):665-90.
[11] Grundmann H, Barwolff S, Tami A, Behnke M, Schwab F, Geffers C, et al. 2005. How many infections are caused by patient-to-patient transmission in intensive care units? Crit Care Med.May;33(5):946-51.
[12] Weber DJ, Anderson D, Rutala WA. 2013. The role of the surface environment in healthcare-associated infections. Curr Opin Infect Dis. 26(4):338-44.
[13] Allegranzi B, Pittet D. 2009. Role of hand hygiene in healthcare-associated infection prevention. J Hosp Infect. 73(4):305-15.
[14] Chen YC, Sheng WH, Wang JT, Chang SC, Lin HC, Tien KL, et al. 2011. Effectiveness and limitations of hand hygiene promotion on decreasing healthcare-associated infections. PloS One. 6(11):e27163.
[15] Pittet D, Hugonnet S, Harbarth S, Mourouga P, Sauvan V, Touveneau S, et al. 2000. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. Infection Control Programme. Lancet. 356 (9238): 1307-12.
[16] World Health Organization (WHO). 2009. WHO guidelines on hand hygiene in health care. Retrieved from: http://www.who.int/gpsc/5may/tools/9789241597906/en/
[17] Boyce JM. 2011. Measuring healthcare worker hand hygiene activity: current practices and emerging technologies. Infect Control Hosp Epidemiol. 32(10):1016-28.
[18] Marimuthu K, Pittet D, Harbarth S. 2014. The effect of improved hand hygiene on nosocomial MRSA control. Antimicrob Resist Infect Control. 3:34.
[19] Sroka S, Gastmeier P, Meyer E. 2010. Impact of alcohol hand-rub use on meticillin-resistant *Staphylococcus aureus*: an analysis of the literature. J Hosp Infect. 74(3):204-11.

provide a review of products other than alcohols that are used for hand hygiene and surgical disinfection[20] (summary in Table 4).

Table 3. Alcohol hand rub consumption in acute care hospitals that participated in the ECDC point prevalence survey of HAIs and antimicrobial use, by hospital type, EU/EEA (data for 2010 or 2011)[21]

Type of hospital	Number of hospitals	Alcohol hand rub consumptions (litres per 1000 patient-days)					
		Mean	10th percentile	25th percentile	Median	75th percentile	90th percentile
Primary	237	20.3	3.2	8.6	15.6	25.7	39.2
Secondary	247	23.5	4.0	8.2	16.8	28.8	52.0
Tertiary	177	27.2	6.8	13.1	21.0	35.3	55.1
Specialised	85	25.2	4.6	11.5	20.6	34.2	44.6
Unknown	59	28.0	11.9	18.4	25.2	32.6	48.7
All types of hospital	**805**	**23.9**	**4.7**	**10.3**	**18.7**	**30.6**	**49.9**

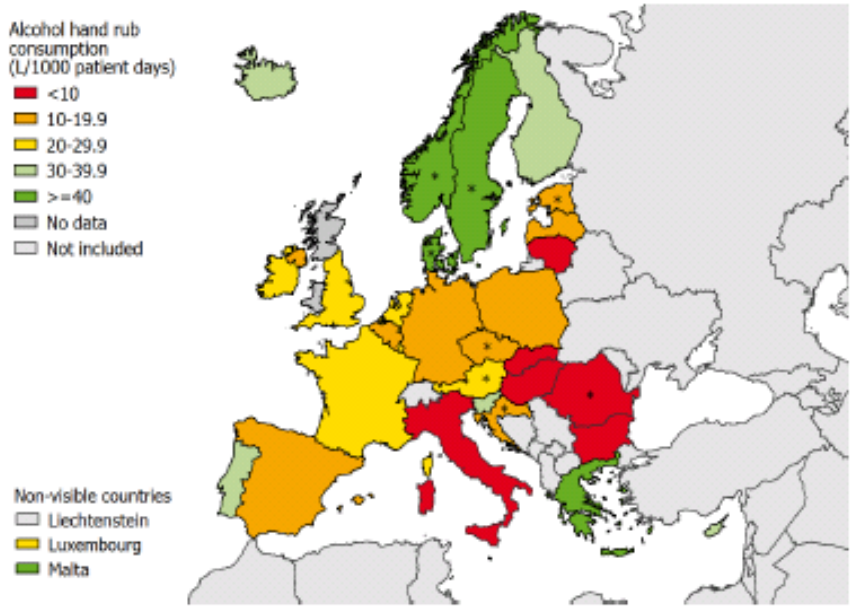

Figure 1. Median alcohol hand rub consumption (litres per 1000 patient-days) in acute care hospitals that participated in the ECDC point prevalence survey of HAIs and antimicrobial use, EU/EEA (data for 2010 or 2011).[22]

[20] World Health Organization (WHO). 2009. WHO guidelines on hand hygiene in health care. Retrieved from: http://www.who.int/gpsc/5may/tools/9789241597906/en/

[21] European Centre for Disease Prevention and Control. Point prevalence survey of healthcare associated infections and antimicrobial use in European acute care hospitals. Stockholm: ECDC; 2013. Retrieved from: http://ecdc.europa.eu/en/publications/Publications/healthcare-associated-infections-antimicrobial-use-PPS.pdf

Table 4. Antimicrobial activity and summary of properties of biocides used in hand hygiene.

Antiseptics	Gram-positive bacteria	Gram-negative bacteria	Viruses enveloped	Viruses non-enveloped	Myco-bacteria	Fungi	Spores
Alcohols	+++	+++	+++	++	+++	+++	-
Chloroxylenol	+++	+	+	±	+	+	-
Chlorhexidine	+++	++	++	+	+	+	-
Hexachlorophene[a]	+++	+	?	?	+	+	-
Iodophors	+++	+++	++	++	++	++	±[b]
Triclosan[d]	+++	++	?	?	±	±[e]	-
Quaternary ammonium compounds[c]	++	+	+	?	±	±	-

Antiseptics	Typical conc. in %	Speed of action	Residual activity	Use
Alcohols	60-70 %	Fast	No	HR
Chloroxylenol	0.5-4 %	Slow	Contradictory	HW
Chlorhexidine	0.5-4%	Intermediate	Yes	HR,HW
Hexachlorophene[a]	3%	Slow	Yes	HW, but not recommended
Iodophors	0.5-10 %)	Intermediate	Contradictory	HW
Triclosan[d]	(0.1-2%)	Intermediate	Yes	HW; seldom
Quaternary ammonium compounds[c]		Slow	No	HR,HW; Seldom; +alcohols

Good = +++, moderate = ++, poor = +, variable = ±, none = –
HR: handrubbing; HW: handwashing
*Activity varies with concentration.
[a] Bacteriostatic.
[b] In concentrations used in antiseptics, iodophors are not sporicidal.
[c] Bacteriostatic, fungistatic, microbicidal at high concentrations.
[d] Mostly bacteriostatic.
[e] Activity against *Candida* spp., but little activity against filementous fungi.
Source: adapted with permission from Pittet, Allegranzi & Sax, 2007.[479]

2.2.2. Biocidal products used for other hospital hygiene purposes

In addition to hand hygiene, biocides are widely used in hospitals and other healthcare settings for perioperative skin antisepsis, sterilisation and disinfection of medical and surgical equipment, and for environmental cleaning. Disinfectants kill or destroy microorganisms which may be present on the object or surface required to be "clean", i.e. disinfected with the aim of eliminating pathogenic microorganisms. The purpose of biocidal products is to prevent HAI associated with surgical and non-surgical operations through transfer of microorganisms in sterile compartments, or to prevent and control transmission of microorganisms between patients (e.g. hepatitis C, multidrug-resistant bacteria) and also indirectly via the environment.

[22] World Health Organization (WHO). 2009. WHO guidelines on hand hygiene in health care. Retrieved from: http://www.who.int/gpsc/5may/tools/9789241597906/en/

There is no single universal disinfectant which will kill all pathogenic organisms. Therefore the availability of a range of products with different modes of action and the selection of the most appropriate disinfectant for the required result is extremely important.[23]

Disinfection of medical and surgical equipment, including endoscopes

A variety of biocides are used for sterilisation and disinfection of equipment and of the environment in hospital and other healthcare facilities, and for perioperative skin antisepsis.[24]

Sterilisation is the process of elimination of all living microorganisms, including spores, and is accomplished by physical or chemical measures. It is used for equipment that is considered critical because of the high risk of infection if it is contaminated, such as but not limited to surgical instruments, vascular catheters and implants. Sterilisation is essential for the prevention of subsequent HAI when such equipment is used. Usually, sterilisation is accomplished by heat, however biocides are used for heat-sensitive items. Such biocides with sterilising action include ethylene oxide, hydrogen peroxide gas plasma and liquid sterilisers like preparations that include glutaraldehyde, peracetic acid, isopropanol, hypochlorous acid, hydrogen peroxide. For sterilisation, these chemicals are often used in combinations.

Disinfection refers to the elimination of most or all living microorganisms, but not of spores, and it usually involves the use of biocides. Disinfection is usually sufficient for semi-critical devices, i.e. equipment that comes in contact with mucous membranes. Such equipment includes endoscopes, anaesthesia equipment and mechanical ventilation equipment. The biocides used for this purpose include glutaraldehyde, peracetic acid, ortho-pthalaldehyde and peracetic acid.

There are no accurate data on the number of HAIs that are prevented by the use of disinfectants, as studies on the effect of using non-disinfected or non-sterile equipment would be considered unethical. However, given an estimated number of more than 50 million surgical operations in Europe every year,[25;26] and considering a conservative doubling of the average risk of HAI from 1 to 2% for various types of surgical intervention if no disinfection were applied, an estimated minimum of 500 000 of HAIs are prevented each year by disinfection only for patients undergoing surgical interventions.

For endoscopy, the rate of HAIs is reportedly very low (1 in 1.8 million procedures)[27]. However, reports of rates up to 6%[28] have been published and were often associated with

[23] Analysis of measures geared to the sustainable use of biocidal products, Final Report, 2015. Retrieved from: /CircaBC/SANTE/BPR - Public/Library/Study reports/Sustainable use/Sustainable use of Biocides - Final report.pdf

[24] Lippincott Williams & Wilkins. 2012. Hospital epidemiology and infection control. 4th ed.

[25] World Health Organisation Regional Office for Europe. European health for all database (HFA-DB) 2015. Retrieved from: http://data.euro.who.int/hfadb/

[26] Weiser TG, Regenbogen SE, Thompson KD, Haynes AB, Lipsitz SR, Berry WR, et al. 2008. An estimation of the global volume of surgery: a modelling strategy based on available data. Lancet.372(9633): 139-44.

[27] Schembre DB. 2000. Infectious complications associated with gastrointestinal endoscopy. Gastrointestinal Endoscopy Clinics of North America. 10(2):215-32.

inappropriately cleaned and decontaminated endoscopes[29]. According to Eurostat data[30], 873 000 bronchoscopies are performed each year in the EU. With an assumed rate of HAI of 6% associated with improperly disinfected endoscopes, and with >90% of such HAIs considered preventable, the number of HAIs prevented by disinfection of bronchoscopes can be estimated at 45 000 per year among patients undergoing bronchoscopy. At least similar numbers could be expected for gastrointestinal endoscopy.

Disinfection of hospital environment

Biocides are also used for environmental cleaning in hospitals and other healthcare facilities. Patient room surfaces (e.g., floor, bedrails, patient furniture) and non-critical equipment (e.g. blood pressure cuffs and stethoscopes) are disinfected with various biocides, including quaternary ammonium compounds, sodium hypochlorite and phenolic compounds. Environmental disinfection of patient rooms during hospitalisation and after discharge of the patient is a recommended measure for the prevention of infections by *Clostridium difficile*, *Staphylococcus aureus* and other pathogens is supported by a number of studies.[31] In the EU, the estimated annual number of cases of *Clostridium difficile* infection (CDI) is 124 000 and that of healthcare-associated meticillin-resistant *Staphylococcus aureus* (MRSA) infections is 179 000. Bundles of measures that include environmental disinfection have been shown to decrease incidence of CDI by up to 50%[32]. However, it is difficult to distinguish which if any part of this decrease is associated with specifically the use of disinfectants and there are also studies that failed to show a significant effect of surface disinfection.[33]

Skin disinfection

In addition, biocides (e.g. chlorhexidine, iodine compounds, alcohol-based solutions) are used for skin disinfection prior to surgical procedures as recommended by several organisations, including the Royal College of Surgeons of England[34] and the US Centers for Disease Control and Prevention (CDC).[35;36] Table 5 summarises the main disinfectant groups

[28] Gorse GJ, Messner RL. 1991. Infection control practices in gastrointestinal endoscopy in the United States: a national survey. Infect Control Hosp Epidemiol. 12(5):289-96.

[29] Kovaleva J, Peters FT, van der Mei HC, Degener JE.2013. Transmission of infection by flexible gastrointestinal endoscopy and bronchoscopy. Clin Microbiol Rev 26 (2):231-54.

[30] Eurostat. 2015. Surgical operations and procedures statistics. Retrieved from: http://ec.europa.eu/eurostat/statistics-explained/index.php/Surgical_operations_and_procedures_statistics

[31] Khanafer N, Voirin N, Barbut F, Kuijper E, Vanhems P. 2015. Hospital management of *Clostridium difficile* infection: a review of the literature. J Hosp Infect. 90(2):91-101.

[32] Gerding DN, Muto CA, Owens RC, Jr. 2008. Measures to control and prevent *Clostridium difficile* infection. Clin Infect Dis. 46 Suppl 1:S43-9.

[33] Dettenkofer M, Wenzler S, Amthor S, Antes G, Motschall E, Daschner FD. 2004. Does disinfection of environmental surfaces influence nosocomial infection rates? A systematic review. Am J Infect Control. 32(2):84-9.

[34] Leaper DJ, Orr C, Maung Z, White A. 2001. Inflammation and Infection: STEP 2000 Module II. Royal College of Surgeons of England: Blackwell Science

[35] Centers for Disease Control and Prevention. 2008. Guideline for disinfection and sterilization in healthcare facilities 2008. Retrieved from: http://www.cdc.gov/hicpac/pdf/guidelines/Disinfection_Nov_2008.pdf

[36] Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. 1999. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol. 20(4):250-78; quiz 79-80.

used in healthcare facilities for sterilisation or disinfection of medical equipment and for environmental disinfection

Table 5. Characteristics and uses of the main disinfectant groups used in hospitals and other healthcare facilities (adapted from WHO[37]).

Agent	Spectrum	Uses
Alcohol (including ethanol or isopropanol)	Active against bacteria, mycobacteria, fungi and viruses. Inactive against spores	Hand hygiene, disinfection of some non-critical items (e.g. oral thermometers and stethoscopes), disinfection of small surfaces
Chlorine compounds (mostly aqueous solution of sodium hypochorite – household bleach)	Active against bacteria, mycobacteria, fungi, viruses and spores	Disinfection of environmental surfaces (e.g. floors), spills and water systems
Glutaraldehyde	Very active against bacteria, mycobacteria, fungi, viruses and spores	High-level disinfection / sterilisation of heat-sensitive semicritical items (e.g. endoscopes)
Peracetic acid	Active against bacteria, mycobacteria, fungi, viruses and spores	Disinfection of endoscopes (in automated reprocessors or for manual processing)
Orthophthalaldehyde	Very active against bacteria, mycobacteria, fungi, viruses and spores	Disinfection of endoscopes
Hydrogen peroxide	Active against bacteria, mycobacteria, fungi, viruses and spores (less active than other compounds for Gram-positive bacteria and spores)	Cold sterilisation of heat-sensitive critical items. Combined with peracetic acid, for disinfection of hemodialyzers
Phenolics	Active against bacteria, mycobacteria, fungi, viruses and spores. Less active against viruses and inactive against spores	Disinfection of inanimate objects and surfaces
Quaternary ammonium compounds	Less active against Gram-negative bacteria, fungi and viruses and inactive against mycobacteria and spores	In combination with other compounds for disinfection of non-critical items and surfaces

2.2.3. Disinfection in community settings

There is no reliable information available on actual use of biocidal products in schools and day care settings but ECDC has commissioned a systematic literature review on the prevention of norovirus infection in schools and childcare facilities in 2013.[38] The report entails detailed information on recommendations for environmental cleaning and disinfection, mostly focusing on sodium hypochlorite but mentioning also the efficacy of other disinfectants against norovirus.

[37] WHO 2014. Safe management of wastes from health-care activities 2014. Retrieved from: http://apps.who.int/iris/bitstream/10665/85349/1/9789241548564_eng.pdf?ua=1

[38] European Centre for Disease Prevention and Control. 2013. Prevention of norovirus infection in schools and childcare facilities. Stockholm: ECDC. Retrieved from: http://ecdc.europa.eu/en/publications/Publications/norovirus-prevention-infection-schools-childcare-facilities.pdf

2.2.4. Vector control of mosquito-borne diseases (West Nile Fever, Dengue, Chikunguya and Malaria)

No vaccines are available to prevent West Nile fever and chikungunya in the EU. The first dengue vaccine has been recently approved in Mexico, Brazil and The Philippines. Prevention and control of these diseases is primarily based on the implementation of vector management measures and the interruption of human–vector contact. It often constitutes the first line of activity in case of epidemics of vector-borne diseases. To be effective, vector control programs require a strong organisational backbone relying on a previously defined plan, skilled technicians and operators, appropriate equipment, and sufficient financial resources. Chemical control is still the most important element in the integrated approach to vector control[39]. Vector management options include source reduction (reducing larval breeding sites by e.g. environmental management), application of larvicides and the use of adulticides (insecticides) in case of an outbreak.[40;41]

Most West Nile virus vector control experiences have been recently developed in the US, where ecological conditions are different from the EU and vector control is organised under a different regulatory frame. The extrapolation of information produced in North America to Europe might be limited because of the seemingly different epidemiology in the European region.

In the EU malaria control is based on early diagnosis and correct treatment of cases, and vector control using indoor residual spraying and treated bed nets. Several systematic reviews provide evidence that the implementation of these vector control measures prevents and controls the disease transmission and lowers the incidence in the population at risk.[42;43;44]

2.3. Expected impacts on transmissible diseases expected by the options to set criteria to identify ED substances

In the screening of biocidal active substances of the 44 disinfectants one, Iodine, was identified as a potential ED under Option 2, Option 3 Category I, and Option 4. Of the 49 pest control substances only one insecticide, Cypermethrin, was identified as a potential ED. Under Option 3 two substances used in disinfectants (DCCP and Gluteraldehyde) were classified in Category II of suspected ED. For insecticides the substances Abamectin, Clothianidin, Deltamethrin, Fipronil, Lambda-cyhalothrin, Pyriproxifen, Hydrogencyanide

[39] WHO. 2016. WHO Pesticide Evaluation Scheme (WHOPES) Geneva [cited 2016 02 February]. Retrieved from: http://www.who.int/whopes/en/

[40] Baldacchino F, Caputo B, Chandre F, Drago A, della Torre A, Montarsi F, et al. 2015. Control methods against invasive Aedes mosquitoes in Europe: a review. Pest Manag Sci. 71(11):1471-85.

[41] Bellini R, Zeller H, Van Bortel W. 2014. A review of the vector management methods to prevent and control outbreaks of West Nile virus infection and the challenge for Europe. Parasit Vectors. 7:323.

[42] Gamble CL, Ekwaru JP, ter Kuile FO. 2006. Insecticide-treated nets for preventing malaria in pregnancy. Cochrane Database of Systematic Reviews. (2):CD003755.

[43] Pluess B, Tanser FC, Lengeler C, Sharp BL. 2010. Indoor residual spraying for preventing malaria. Cochrane Database of Systematic Reviews. (4):CD006657.

[44] Lengeler C. 2004. Insecticide-treated bed nets and curtains for preventing malaria. Cochrane Database of Systematic Reviews. (2):CD000363.

and Permethrin were identified under Category II and Etofenprox and Imidacloprid under Category III (see results of the screening in Annex 5). It is important to note that the results of the screening should be very cautiously interpreted for the potential impact as it is not possible to judge how representative the screening results are within and across the product groups. For example, the screening did cover only 44 of the 266 active substance-product types in the main group of disinfectants. However, it is clear that the setting of ED criteria implies that some active substances used in biocidal products could be non-approved or approved under strict conditions. The results also indicate that the different options may result in different numbers of disinfectants or insecticides identified as ED. Critical impacts may occur if key substances for transmissible diseases would not be available and no appropriate alternatives could be found or developed.

Based on the current information it cannot be excluded neither properly estimated whether non-approval of key biocidal substances in relation to transmissible diseases will occur The BP Regulation provides the possibility, notwithstanding a chemical is identified as an ED, to authorise it with restrictions for a fixed time period in cases the substance is essential to prevent or control a serious danger to human health. However, at the moment no experience exists with the application of this derogation. Nevertheless, it can be assumed that a key substance to control a serious danger to human health, for example to stop local transmission of the dengue virus or malaria, would be approved under derogation for use in the relevant Member States. Under this consideration all Options 1 to 4 would have the same impact. Contrarily, it seems less likely that disinfectants identified as EDs would be approved because the use of these substances can be less directly linked to a specific human health threat. Nonetheless several substances remain available on the market, the non-approval of a substances used in disinfectants may have a health impact. As explained above, there is a need for wide spectrum of disinfectants as there is no single universal disinfectant which will kill all pathogenic microorganisms. The choice of a disinfectant depends on the situation: the surface or item to be disinfected and the risk of specific organisms being present. Some disinfectants can kill many different types of microorganisms, while others are more specific in the organisms they kill but are often preferred because, as disinfectants, they are non-corrosive and so will not damage the equipment being disinfected In Annex 14 it is indicated that the non-approval of active substances in the EU will probably not trigger automatically innovation for replacing these by other substances, even if it is noted that disinfectants are a growing market and thus some innovation may be expected to occur in this commercially interesting market segment (see Figure 2).

Notwithstanding the above described high uncertainties it can be assumed that the impact on transmissible diseases would be associated with the number of chemicals that would be identified as EDs, which are likely to be non-approved. Although it is important to stress that no linear relationship can be considered between the number of active substances available and the efficacy of tools to manage transmissible diseases. The application of derogations in the BP Regulation could make available to professional users biocides to minimise the risk of spread of these diseases, this will be not the case for consumers. In any case, it cannot be excluded that also for professional users the number of biocides may decrease, even if derogations may be granted for some substances identified as ED. The ranking of the four

options can be done with the option having the most number of chemicals identified as EDs performing the worst as in theory less biocidal substances would be available. Thus Option 4 would be expected to have the least impact compared to options 2 3, and 1, i.e. 4 > 2/3 > 1. options A, B and C were not evaluated as these are not relevant for biocidal products.

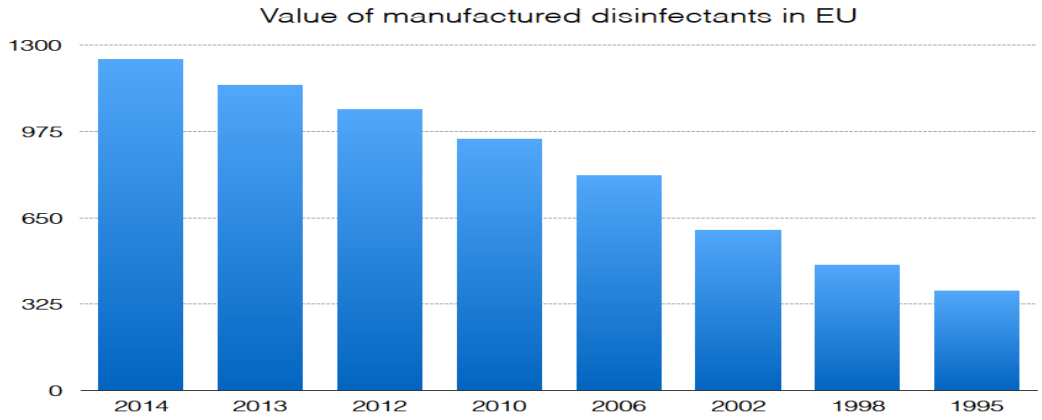

Figure 2. Value of manufacture disinfectants (millions Euro); data of Eurostat (PRODCOM database).

3. FOOD SAFETY (CONTAMINATION OF FOOD BY MYCOTOXINS)

The EU legislation aims to ensure a high level of food safety via an integrated approach which covers all relevant areas "from the farm to the fork" and improve the effective functioning of the internal market. The implementation of this approach involves having effective control systems to ensure compliance with EU safety and quality standards, which include chemical safety because of the role chemical substances, play in food production and processing. The benefits of using chemicals in food production and processing have, on the other hand, to be balanced with potential risks for the health of the food consumer due to side effects and residues of these chemicals. That is why, for instance, for the traces pesticides leave in treated food products, the EU legislation[45] asks for setting maximum residue levels (MRLs), which are applicable also for substances identified as endocrine disruptors used in plant protection products (PPP). Similarly, for active substances contained in biocidal products limits should be established where the use of these substances in the environment of food production or food processing, or in direct contact with food, may involve a risk for human health. Annexes 15 (Food supply and international trade) and 9 (Human health – Hormone related diseases) provide details on the MRL setting for PPP and its potential impacts.

[45] Regulation (EC) No 396/2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC OJ L 70

However, a number of chemical substances may be present in the environment as pollutants. These contaminants may be unintentionally present in raw materials used in food production. Union food legislation aims at the reduction of contaminants in accordance with the high level of consumer protection that is required in Article 152 of the Treaty establishing the European Community. The legislation on contaminants is based on scientific advice and the principle that contaminant levels shall be kept as low as can be reasonably achieved following good working practices. Maximum levels have also been set for certain contaminants (e.g. mycotoxins) in order to protect public health. To achieve this high level of health protection for the consumer, a risk analysis procedure that is based on sound scientific evaluation and takes into account other factors – such as the feasibility of control – underpins Community legislation.

Mycotoxins are produced during storage or plant growth and have an important impact on human health. As their occurrence is affected by the use of PPP, they are considered as one criterion for the assessment of potential impacts on human health in the framework of this impact assessment.

3.1. Threats, risks and costs of mycotoxins

Mycotoxins are a group of chemicals produced by fungi species (molds) and represent one of the most important categories of biologically produced natural toxins relative to health[46]. For example, the World Health Organisation[47] estimated that there were 22,000 cases of aflatoxin-related cancer (hepatocellular carcinoma).

These colorless, tasteless and odorless toxins are produced during storage or plant growth.[48] Aflatoxins, ochratoxins, trichothecenes, zearalenone, fumonisins, tremorgenic toxins, Deoxynivalenol (DON), and ergot alkaloids are the mycotoxins of greatest health and economic importance. Mycotoxins do not decompose easily in the body of the animals, so they can also endanger the health of consumers by their presence in food of animal origin (milk, meat, butter, cheese, eggs). The economic impact of mycotoxins concern loss of human and animal life, increased health care and veterinary costs, reduced livestock production, disposal of contaminated foods and feeds, and investments to prevent mycotoxin occurrence.[48]

No detailed data are available on the economic impact in the EU. The total mycotoxin – related losses to agriculture in the US are calculated as high USD 1,4 billion annually[49]. For

[46] Mycotoxins are capable of having acute toxic, carcinogenic, mutagenic, teratogenic, immunotoxin, and oestrogenic effects in man and animals, for example aflatoxin B1 have been shown to be genotoxic i.e. can damage DNA and cause cancer.

[47] Gibb et al. 2010. WHO estimates of the global and regional disease burden of four foodborne chemical toxins. Food Research 4: 1393.

[48] Hussein S. Hussein, Jeffrey M. Brasel. 2001. Toxicity, metabolism, and impact of mycotoxins on humans and animals. Toxicology 167, p 101.

[49] Vardon, P., McLaughlin, C, Nardinelli, C. 2003. Potential economic costs of mycotoxins in the United States. In: Council for Agricultural Science and Technology (CAST). Mycotoxins: Risks in Plant, Animal,and Human Systems, Task Force Report No. 139: Ames, IA, 2003.

the Philippines, Thailand and India the total social costs of aflatoxin were estimated at USD 900 million (market losses USD 200 million, livestock losses USD 200 million and health losses USD 500 million)[50]. Lack of information on animal health (e.g. animal illnesses and productivity losses due to low-level exposures) makes the evaluation of economic impacts of mycotoxins in animal feed charged with uncertainty[51]. In a recent review, it was estimated that 25% of the world's crops may be contaminated with mycotoxins.[48] Therefore, taking into account the worldwide contamination of many foods and feeds with mycotoxins, probably the occurrence of mycotoxins leads to significant economic impacts.

In the public consultation in 2015 it was indicated that the loss of PPP would undoubtedly lead to significant yield reductions, and to an increase in the occurrence of mycotoxins, especially in grain. The potential impacts on food safety were emphasised.

3.2. The occurrence of mycotoxins in the EU

In 2003 EU-experts concluded that *Fusarium* mycotoxins are widely distributed in the food chain in the EU[52] (see Table 6 and Table 7). The major sources are products made from cereals, in particular wheat and corn.

In the EU the presence of mycotoxins in food and feed is monitored. The Rapid Alert System for Food and Feed (RASFF) was put in place to provide food and feed control authorities with a tool to exchange information. RASFF notifications report on risks identified in food or feed that is placed on the market. Each year several hundred notifications occur for mycotoxins (see Table 8), mostly for aflatoxins in imported products (peanuts, pistachios and dried figs). Several RASFF notifications relate to aflatoxins in maize produced in EU regions. Mycotoxins can be considered a concern in the EU as it is one of the main hazard categories notified. Interestingly, the mycotoxin zearalenone is a potent endocrine disruptors commonly found on several foods and feeds in temperate regions worldwide.[53]

Each year academic, governmental and commercial organisations provide to the European Food Safety Authority (EFSA) analytical results on chemical contaminants in food and feed. Mycotoxins is one of the groups reported.

The provided data in Table 9 shows that mycotoxins are detected in many samples of food and feed in the EU and can be considered currently a concern in the EU.

[50] Lubulwa, A.S.G., Davis, J.S., 1994. Estimating the social costs of the impacts of fungi and aflatoxins in maize and peanuts. In: Stored Product Protection: Proceedings of the 6th International Working Conference on Stored-product Protection, Highley, E., Wright, E.J., Banks, H.J., Champ, B.R., Eds. CAB International, Zallingford, UK: pp 1017-1042.

[51] Wu, F. 2007. Measuring the economic impacts of Fusarium toxins in animal feeds. Animal Feed Science and Technology 137: 363-374.

[52] Report of experts participating in Task 3.2.10, Collection of occurrence data of Fusarium toxins in food and assessment of dietary intake by the population of EU Member States (2003). Retrieved from: http://ec.europa.eu/food/fs/scoop/task3210.pdf

[53] Zinedine, A. et al. 2007. Review on the toxicity, occurrence, metabolism, detoxification, regulations and intake of zearalenone: an oestrogenic mycotoxin. Food Chem Toxicolo 45(1): 1-18.

Table 6. Overview on Fusarium toxin occurrence data (2003)[52]

Fusarium toxin	Countries	Number of samples	Positive samples
Type B trichothecenes			
Deoxynivalenol	11	11 022	57 %
Nivalenol	7	4 166	16 %
3-Acetyldeoxynivalenol	6	3 721	8 %
15-Acetyldeoxynivalenol	3	1 954	20 %
Fusarenon X	3	1 872	10 %
Type A trichothecenes			
T-2 Toxin	8	3 490	20 %
HT-2 Toxin	6	3 032	14 %
T-2 Triol	2	1 389	6 %
Neosolaniol	2	1 323	1 %
Diacetoxyscirpenol	3	1 886	4 %
Monoacetoxyscirpenol	1	853	1 %
Verrucarol	1	121	0%
Zearalenone	9	5 018	32 %
Fumonisins			
Fumonisin B_1	9	3 863	46 %
Fumonisin B_2	6	1 010	42 %
Fumonisin B_3	1	239	36 %
	Sum:	**44 959**	

Table 7. Summary of food groups most frequently contaminated with Fusarium mycotoxins (2003)[52]

Fusarium toxin	Main food items/food groups contaminated (percentage of positive samples)
Type B trichothecenes	
Deoxynivalenol	corn (89 %), wheat* (61 %)
Nivalenol	corn (35 %), oats (21 %), wheat*(14 %)
3-Acetyldeoxynivalenol	corn (27 %), wheat*(8%)
Type A trichothecenes	
T-2 Toxin	corn (28 %), wheat (21 %), oats (21 %)
HT-2 Toxin	oats (41 %), corn (24 %), rye** (17 %)
Zearalenone	corn (79 %), corn milling fractions (51 %), corn based products (53%); wheat (30 %), wheat milling fraction (24 %), wheat based products (11 %); baby food (23 %)
Fumonisins	
Fumonisin B_1	corn (66 %), corn flour (79 %), corn based products (31 %), corn flakes (46 %); wheat (79 %)
Fumonisin B_2	corn (51 %)

* Wheat and wheat flour ** Rye and rye flour

Table 8. The Rapid Alert System for Food and Feed (RASFF) - Notifications on mycotoxins in food and feed[54].

Substance	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Aflatoxins	839	946	801	705	902	368	649	585	484	341
Deoxynivalenol (DON)				10	4	3	2	11	4	8
Fumonins	14	2	15	9	2	1	3	4	4	7
Ochratoxin A	27	42	54	30	20	27	34	35	32	54
Patulin		6	7		3					
Zearalenon			1	6	2					
Total mycotoxins	880	996	878	760	933	669	688	635	528	410
Total notifications RASFF	5562	7170	6840	7354	3099	3322	3358	3812	3516	3205

[54] European Commission. 2016. DG SANTE Website Directorate-General for Health and Food Safety: http://ec.europa.eu/food/safety/rasff/reports_publications/index_en.htm

Table 9. Occurrence of mycotoxins in agricultural products of EU-origin in the years 2004-2014 (EFSA – Extract of the EFSA database on Collection on Contaminant Occurrence Data[55])

Type of mycotoxin	Commodity	Number of	Number of samples	Mean (µg/kg)	Median (µg/kg)	P95 (µg/kg)	Maximum allowed
Aflatoxin B1	barley	235	225	0,0	0,0	0,0	2,0
	Corn	943	681	3,2	0,0	16,2	2,0
	Oats	142	142	0,0	0,0	0,0	2,0
	wheat	562	538	0,0	0,0	0,0	2,0
	Almond	634	490	1,2	0,0	1,5	8,0
	Pistachios	522	419	5,9	0,0	16,4	8,0
	Peanuts	725	641	0,4	0,0	0,2	2,0
	dried figs	533	436	1,7	0,0	6,7	6,0
Aflatoxins	barley	87	72	0,3	0,0	1,8	4,0
	Corn	320	231	1,0	0,0	2,7	4,0
	Oats	15	15	0,0	0,0	0,0	4,0
	wheat	215	188	0,2	0,0	1,4	4,0
	Almond	101	87	0,6	0,0	2,4	10,0
	Pistachios	90	70	1,5	0,0	10,7	10,0
	Peanuts	222	207	0,1	0,0	0,5	4,0
	dried figs	206	170	2,3	0,0	6,2	10,0
Ochratoxin A	barley	498	438	0,7	0,0	1,1	3,0
	Corn	272	234	0,3	0,0	1,3	3,0
	Oats	221	189	10,6	0,0	3,0	3,0
	wheat	1463	1280	0,1	0,0	0,5	--
	Almond	92	85	0,1	0,0	0,2	--
	Pistachios	117	109	0,2	0,0	0,4	--
	Peanuts	65	49	0,8	0,0	1,4	--
	dried figs	320	219	3,9	0,0	10,2	--
Deoxynivalenol	barley	1706	1145	126,4	0,0	500,0	750,0
	Corn	1209	639	261,4	0,0	1170,5	750,0
	Oats	615	342	4669,3	0,0	756,0	750,0
	wheat	3236	1428	199,0	33,2	900,8	750,0
Zearalenone	barley	2498	1777	8,7	0,0	33,0	75,0
	Corn	3258	1545	64,3	5,0	270,0	100,0
	Oats	1029	815	8,7	0,0	41,2	75,0
	wheat	8932	5637	16,3	0,0	61,0	75,0
Fumonisin B1	Corn	1517	708	499,6	33,4	2353,6	--
Fumonisin B2	Corn	1542	1001	153,7	0,0	825,7	--
Total Fumonisins	Corn	1980	1295	289,0	0,0	1410,2	1000,0

[55] EFSA. 2016. European Food Safety Authority. Summary of the 2014 data collection on contaminant occurrence data. Published 21 January 2016. Retrieved from: http://www.efsa.europa.eu/en/supporting/pub/954e

Table 10. Occurrence of mycotoxins in imported agricultural products (non-EU-origin) in the years 2004-2014 (EFSA – Extract of the EFSA database on Collection on Contaminant Occurrence Data[56])

Type of mycotoxin	Commodity	Number	Number	Mean	Median	P95	Maximum
Aflatoxin B1	barley	11	10	0,1	0,0	0,6	2,0
	corn	159	141	1,6	0,0	1,4	2,0
	oats	0	0				2,0
	wheat	87	73	0,0	0,0	0,2	2,0
	almond	2877	2334	7,8	0,0	1,8	8,0
	pistachios	11870	9653	2,3	0,0	5,2	8,0
	peanuts	5423	4373	20,7	0,0	4,9	2,0
	dried figs	6266	4812	1,4	0,0	3,9	6,0
Aflatoxins	barley	0	0				4,0
	corn	4	3	0,1	0,0	0,2	4,0
	oats	0	0				4,0
	wheat	1	1	0,0	0,0	0,0	4,0
	almond	1505	1272	1,2	0,0	2,1	10,0
	pistachios	9047	7366	2,4	0,0	5,1	10,0
	peanuts	2080	1776	3,3	0,0	5,7	4,0
	dried figs	3753	2932	2,0	0,0	6,6	10,0
Ochratoxin A	barley	3	3	0,0	0,0	0,0	3,0
	corn	38	37	0,0	0,0	0,0	3,0
	oats	1	0	200,0	200,0	200,0	3,0
	wheat	35	18	0,8	0,0	4,4	--
	almond	147	140	0,0	0,0	0,0	--
	pistachios	171	155	0,6	0,0	0,7	--
	peanuts	1176	1142	0,1	0,0	0,0	--
	dried figs	981	676	3,8	0,0	8,2	--
Deoxynivalenol	barley	4	3	28,5	0,0	97,0	750,0
	corn	66	53	25,0	0,0	182,5	750,0
	oats	5	2	10017,8	39,0	40010,0	750,0
	wheat	87	69	35,5	0,0	76,2	750,0
Zearalenone	barley	2	2	0,0	0,0	0,0	75,0
	corn	95	72	13,7	0,0	73,6	100,0
	oats	0	0				75,0
	wheat	41	41	0,0	0,0	0,0	75,0
Fumonisin B1	corn	164	36	1170,3	312,5	5411,4	--
Fumonisin B2	corn	167	53	352,0	74,1	1405,0	--
Total Fumonisins	corn	61	29	247,3	49,0	944,0	1000,0

[56] EFSA. 2016. European Food Safety Authority. Summary of the 2014 data collection on contaminant occurrence data. Published 21 January 2016. Retrieved from: http://www.efsa.europa.eu/en/supporting/pub/954e

3.3. Protection of citizens, animals and the environment in the EU from mycotoxins

To protect humans and animals from the dangerous effects of mycotoxins, the European Commission has set, based on scientific advice, maximum levels in food and feed products for several mycotoxins.[57;58] It is important to underline that the same legislation applies whether food or feed are imported in the EU or produced in the EU.

In order to avoid or reduce the presence of mycotoxins in food and feed, the most effective way is to prevent fungal infestation of plant material, but even the best management of agricultural strategies cannot totally eradicate mycotoxin contamination.[59] A number of methods are available to reduce the occurrence of mycotoxins, which are briefly detailed below.

3.3.1. Agronomical measures

Contamination by mycotoxins depends on both climate and cropping system.[60] Crop rotation and tillage are recommended to control plant contamination with *Fusarium* spp., but these agricultural practices are not always recognised as efficient.[59] It is interesting to note that several studies indicate that, notwithstanding the absence of applying PPP in organic farming, that the levels of mycotoxins in organic and non-organic products are similar.[61;62] This may be also related to plant varieties, as plant breeding can provide varieties that are more resistant to spoilage and mycotoxin formation. This method can be considered as the best solution for disease control.[59]

3.3.2. Chemical plant protection products

Chemical PPP are applied to control diseases, and this disease reduction then may lead to a reduction in mycotoxin production. However, it is important to note that most PPP used on crops were primarily designed to control diseases and associated reductions in crop yield, and not for their impact in reducing mycotoxin formation.[63] In 1999 the Scientific Committee on Plants concluded that there was insufficient evidence that pesticides play a major role in

[57] Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs. Retrieved from: http://ec.europa.eu/food/safety/chemical_safety/contaminants/legislation/index_en.htm.

[58] The presence of contaminants in feed is controlled by EC Directive 2002/32. Retrieved from: http://ec.europa.eu/food/food/animalnutrition/contaminants/index_en.htm.

[59] Jean Pierre Jouany. 2007. Methods for preventing, decontaminating and minimizing the toxicity of mycotoxins in feeds. Animal Feed Science and Technology 137: 342–362

[60] A. Champeil, J.F. Fourbet, T. Dore, L. Rossignol. 2004. Influence of cropping system on Fusarium head blight and mycotoxin levels in winter wheat. Crop Protection 23:531–537, p 531.

[61] Vanova et al. 2008. The content of Fusarium mycotoxins, grain yield and quality of winter wheat cultivars under organic and convential cropping systems. Plant Soil Environ. 54: 395-402.

[62] Edwards, S.G. 2009. Fusarium mycotoxin content of UK organic and convential barley. Food Additives and Contaminants 26: 1185-1190.

[63] Belli, N., et al. 2007. Effect of chemical treatments on ochratoxigenic fungi and common mycobiota of grapes. Journal of Food Protection 70: 157-163.

preventing or inhibiting the production of mycotoxins by toxicogenic fungi[64]. Currently azole fungicides have been reported to be the most effective active substances in the control of *Fusarium* species and in the reduction of the main mycotoxins that occur in cereal grain, such as DON[65]. *Fusarium* ear rot is a severe and worldwide disease of maize[66]. Treatments with fungicides applied in combination with an insecticide, significantly reduced the mycotoxin fumonisin occurrence in maize.[59] In an advice to the Food Standards Agency[67] the efficacy of PPP to control mycotoxins in the UK was reviewed since the publication of the report of the Scientific Committee on Plants. It was concluded that, based on fifteen studies, there is a strong body of evidence that fungicide application does reduce DON formation in wheat. It was also concluded there is good evidence that insecticides reduce the levels of fumonisins in maize. The advice further stated that the results of studies into the effects of PPP on DON in barley were less conclusive and other mycotoxin and crop combinations have received relatively little attention of scientists (for example, T2 and HT2 toxins in wheat, barley and oats, DON in maize, ochratoxin in grapes).

3.3.3. Plant protection products based on microorganisms action

Several bacterial species have shown the ability to inhibit fungal growth and production of aflatoxins under laboratory conditions. Microbial antagonists or competitors can be sprayed on plants at the flowering stage to eradicate or limit the growth of toxin producing fungi. For example, *Bacillus subtilis* can inhibit the growth of fungi during their endophytic growth phase.[59;67] However, biological control appears not to give good control in real field conditions because it is difficult to bring the bacterial cells to the fungal infection sites on commodities under field conditions.[68]

3.4. Expected impacts on presence of mycotoxins based on the screening results

It is clear that the use of PPP in certain crop-mycotoxin combinations contributes to limit the contamination of crops with fungi and consequently the occurrence of mycotoxins in crops grown in the EU. In comparing the options outlined in this impact assessment it is key to consider from a health perspective whether a possible reduced range of available

[64] See Scientific Committees on the European Commission website: http://ec.europa.eu/food/fs/sc/scp/out56_en.html

[65] V. Scarpino, A. Reyneri, M. Sulyok, R. Krska and M. Blandino. 2015. Effect of fungicide application to control *Fusarium* head blight and 20 Fusarium and Alternaria mycotoxins in winter wheat (*Triticum aestivum* L.). World Mycotoxin Journal. 8 (4): 499-510.

[66] Filippo De Curtis, Vincenzo De Cicco, Miriam Haidukowski, Michelangelo Pascale, Stefania Somma, Antonio Moretti. 2011. Effects of agrochemical treatments on the occurrence of Fusarium ear rot and fumonisin contamination of maize in Southern Italy. Field Crops Research 123. 161–169, p 161.

[67] Food Standards Agency (FSA) report from a preliminary study carried out by the FSA. R. Massey. 2012. "The likely effects of reduced pesticide usage on mycotoxin levels in food".

[68] K.R.N. Reddy, N.I. Farhana, B. Salleh and C.A.F. Oliveira. 2010. Microbiological Control of Mycotoxins: Present Status and Future Concerns. in. A Mendez-Vilas (ed) Current Research, technology and Education Iopics in Applied Microbiology and Microbial Biotechnology. FORMATEX 2010.

fungicide/insecticide products is likely to lead to increased exposure of consumers to mycotoxins.

The screening of PPP for endocrine disrupting properties resulted in a varying number of PPP identified under the four options (see Annex 5). In all the options PPP were identified belonging to the group of azoles (for example, cyproconazole, tebuconazole, tetraconazole, see Table 3 in Annex 5). This group of fungicides is considered to be important for *Fusarium* control in the EU. Depending on the option, azoles would be impacted between 5% and 35%. Option 4 identified both the lowest number of PPP as EDs and the lowest number of substances belonging to the group of azoles (see Figure 3 and Table 3 in Annex 5).

Table 11. Factors influencing the fungal contamination of crops and the occurrence of mycotoxins in food and feed

PRE-HARVEST	**POST-HARVEST**
Environmental conditions related to storage (temperature, humidity)	Environmental conditions in the field (temperature, humidity)
Biological control	Biological control
Chemical control	Chemical control
Plant breeding	
Agronomical measures (crop rotation, soil tillage)	

It is not possible to indicate whether the loss of one or more PPP, including substances belonging to the group of azoles, will lead to higher levels of contamination of crops and consequently higher levels of mycotoxins in food and feed in the future as many factors influence the occurrence of mycotoxins (see Table 11). In addition, the uncertainties, based on the available information, exclude the possibility to determine the potential impact of the loss of one of more substances contained in PPP. The impact for mycotoxins will firstly depend on whether alternative chemicals are or will be available, assuming the identified substance will not be allowed to be made available on the EU market, to replace the identified substance. An analysis of the identified substances under each option points out that substances in the same group of PPP remain available to manage fungi (see Annex 5, Table 2 analysing the outcome of screening for groups of PPP). However, it is unclear whether these alternatives are equally effective to control the fungi producing mycotoxins and whether the efficacy will be reduced in the short term because of the development of resistance (see Annex 13). Biological control measures may become available to control the fungi producing mycotoxins, but it has to be noted that up to now the efficacy of biological control measures is limited and are not applied in practice. Therefore, it is unclear whether it would be possible, and commercially interesting, to develop effective biocontrol products on the short or long term that could replace chemical control. More promising alternatives appear using and breeding plant cultivars limiting the development of mycotoxin producing fungi and agronomical measures.

In conclusion, it cannot be excluded that farmers in the EU will be negatively impacted by the different options because they will have less effective means to control mycotoxin producing fungi and, therefore, products may not comply with legal levels of mycotoxins for food (and these products cannot be placed on the EU market). As a consequence, it cannot be excluded that public and animal health will be negatively impacted by the different options as food and feed may contain higher levels of mycotoxins.

In addition, as indicated earlier mycotoxins are a worldwide problem. This is also emphasised by RASFF-data showing that notifications concern mostly imported products (Table 8). According to RASFF the most notified products are peanuts, pistachios and dried figs. Data on trade values show (Table 12) that these products involve large markets.

Exporting countries will need to comply with lower MRLs of chemical residues for the substances identified as EDs, as a direct consequence of implementation of legal requirements (see Annex 8 on Horizontal issues, and Annex 15 on trade). At the same time, products found to contain mycotoxins above the legal level cannot be placed on the EU market. These two requirements may represent in certain cases a trade-off, since some PPP may be needed to control mycotoxin producing fungi. However, no information is available on the PPP that are used in exporting countries and the availability of alternatives for controlling mycotoxins in crops, as this depends also on the country or region.

It is thus clear that contamination of food or feed with mycotoxins or with residues above legal set MRLs for PPP can lead to trade impacts. A study estimated in 2001 that lowering the aflatoxin standard in the EU would have a negative impact on African exports of cereals, dried fruits and nuts to Europe and result in a USD 670 million loss per year to Africa.[69] It can be concluded that, depending on the availability of chemical and non-chemical alternatives for these PPP in the exporting countries, it will be more or less difficult for exporting countries to prevent mycotoxin contamination of their products and to maintain their markets in the EU. So, it cannot be excluded that an impact will occur on trade flows associated to the contamination of products with mycotoxins. It is important to note that the compliance process also can result in competitive advantage for some suppliers and contribute to more sustainable and profitable trade over the long term.[70]

The impact of the four options in relation to mycotoxins depends on many factors and includes large elements of uncertainty. It could be concluded that the likelihood of having an impact on farmers, trade and/or health will be probably higher if an option results in in a high number of substances identified as EDs and/or more substances are identified belonging to a group of PPP relevant for the control of fungi producing mycotoxins. Although it is important to stress that no linear relationship can be considered between the number of active substances available and reduced levels of contamination of crops by fungi. This implies that

[69] Otsuki, T, Wilson, J.S., Sewadeh, M. 2001. Saving two in a billion/ quantifying the trade effect of European Food Safety standards on African exports. Food Policy 26 (5): 495-514

[70] World Bank. 2005. Food safety and Agricultural Health Standards. Challenges and Opportunities for Developing Country Exports. Report No. 31207 of the World Bank, Washington DC, USA. Retrieved from: http://siteresources.worldbank.org/INTRANETTRADE/Resources/Topics/Standards/standards_challenges_synthesisreport.pdf

Option 4 appears relatively the best option in relation to control mycotoxin contamination of food and feed, followed by Option 2 and Option 3 Category I, and finally by Option 1, i.e. 4 > 2/3 > 1. Regarding regulatory decision making, Option C performs better than Options B and A, i.e. C > B > A.

Table 12. Trade value of almonds, pistachios, dried figs, cashew nuts, hazelnuts, chestnuts, macadamia nuts and Brazil nuts in the EU in 2014.

VALUE OF IMPORTED NUTS AND DRIED FIGS 2014 - THOUSAND EUR

REGION/PRODUCT	ASIA	EUROPE	NORTH AMERICA	AFRICA	LATIN AMERICA	MIDDLE EAST	OCEANIA
Almonds	€7,910	€1,778	€1,189,494	€9,367	€1,352	€2,515	€113,158
Pistachios	€1,730	€13,099	€393,939	€45	€450	€180,767	€0
Dried figs	€34	€102,864	€52	€248	€36	€530	€0
Cashew nut	€472,694	€453	€1,814	€31,055	€31,819	€21	€129
Hazelnuts	€136,697	€621,012	€4,370	€96	€22,709	€5	€121
Chestnuts	€4,489	€38,015	€0	€118	€1,152	€0	€8
Macadamia nuts	€1,503	€0	€1,585	€39,256	€3,346	€5	€13,897
Brazil Nut	€410	€95	€83	€0	€81,900	€2	€0

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COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annex 11 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

{COM(2016) 350 final}
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ANNEX 11

ENVIRONMENT

Contents

This Annex focuses on the assessment of potential impacts, which build on the results of the screening study explained in Annexes 3 to 5. The results of the screening do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation. The methods and results presented in this Annex are to be interpreted as an estimation of the potential impacts.

Annexes 8 to 15 describe the impacts expected when implementing the criteria to identify EDs (Options 1 to 4) under the current regulatory framework (Option A). In addition, it was assessed whether these expected impacts would remain the same or not under consideration of different regulatory implementations (Options B and C, only applicable to the PPP Regulation). The analyses of the impacts described in these Annexes translate into the "performance" of the options, which is one of the input parameters to the MCAs (Annex 6 and 7).

The MCAs results are not concluding on any preferred option for setting scientific criteria to identify endocrine disruptors, but aim at providing additional information to decision makers with regards to the potential impacts expected when implementing the criteria, after those would have been selected on the basis of science (two MCAs were performed: Options 1 to 4 under the current regulatory context, and Options A compared to Options B and C).

At a preliminary stage of the impact assessment it was anticipated that Option C should be discarded, nevertheless it was maintained for the analysis of the impacts for methodological reasons (see Section 4.2.3 of the main report and Annexes 6 and 7). Option C only applies to the PPP Regulation.

1. INTRODUCTION

The use of chemicals may cause environmental effects. That is why EU legislation concerning the placing on the market of plant protection products[1] (PPP) and biocidal products[2] (BP) provides that any PPP or BP may only be authorised for placing on the market and use when it is supported by a sound scientific risk assessment which includes consideration of environmental risk. Risk assessment considers the hazard of a substance and the exposure levels to which humans and the environment are exposed to. Risk is assessed by comparing safety thresholds based on hazard data (hazard assessment) with exposure levels (exposure assessment).

Endocrine disruption is a relatively recent way of looking at the toxicity of chemicals, which aims at understanding the mode of action, i.e. how chemicals lead to the adverse effects observed. Most of the adverse effects that may be produced by endocrine disruptors (ED) on the environment are however already considered by the EU legislation since several years and accordingly regulatory actions have been taken in the past. Concerns about the uncertainty regarding the extent of exposure to chemical pollutants in the environment, and the effects that they might have, were discussed at the Weybridge workshop on EDs in 1996[3]. One of the main conclusions reached at the meeting was that for wildlife, few cases within the EU were known where effects could be clearly ascribed to EDs. In 2001, an international workshop[3] on EDs was held in Aronsborg (Bålsta) Sweden and it concluded that further research on the topic was needed both for human health and wildlife, including development of test methods and testing strategies, besides up-to-date databases with information on EDs.

The impact on the environment of the different options setting criteria to identify EDs is analysed in the subsections below with the aim to rank the policy options proposed in this impact assessment. Some general considerations on endocrine disruption given in Annex 9 (Human Health – Hormone related diseases) are applicable also to this section. In addition, it needs to be considered that it is so far not possible to identify robust and reliable environmental impact indicators in relation to ecosystem services or species level effects, as concluded in a recent study carried out for the European Commission[4], which concluded that the indicators that could be developed for the environment were limited inter alia because of the lack of monitoring data.

[1] Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309.

[2] Regulation (EU) No 528/2012 of the European Parliament and of the Council concerning the making available on the market and use of biocidal products. OJ L 167/1.

[3] Workshop "The Impact of Endocrine Disruptors on Human Health and Wildlife", Weybridge UK, 2-4 December 1996. Retrieved on: http://ec.europa.eu/environment/chemicals/endocrine/documents/reports_en.htm

[4] Risk and Policy Analysts (RPA) et al. 2015. Study on the Calculation of the Benefits of Chemical Legislation on Human Health and the Environment, Final report for DG Environment, March 2016, Loddon, Norfolk, UK

2. CHEMICAL QUALITY OF WATER

PPP are in general expected to enter the environment from diffuse routes by a variety of mechanisms. Contrarily, for biocidal products an important source for potential contamination of the environment is the effluent from sewage treatment plants.[5]

As mentioned above, both the PPP Regulation and the BP Regulation require a scientific environmental risk assessment, which includes the aquatic compartment, including both surface water and groundwater. For both cases, the predicted environmental concentrations derived from the use of a particular PPP or BP need to be calculated, based on the expected uses.

Concerning **groundwater,** particular conditions apply. Point 3(10) of Annex II to Regulation (EC) No 1107/2009 on PPP establishes that "*An active substance shall only be approved where it has been established for one or more representative uses that … the predicted concentration of the active substance or of metabolites, degradation or reaction products in groundwater complies with the respective criteria of the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6)".* Regulation (EC) No 1107/2009 further states in Article 4(3)(b) that *"a plant protection product, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use, shall……have no immediate or delayed harmful effects on groundwater".* In practice, this means that an active substance cannot be approved if its estimated concentration in groundwater exceeds the limit of 0.1µg/L (maximum permissible level in drinking water). This also applies to all the relevant metabolites and breakdown products that may be produced from degradation of the active substance. A metabolite is considered relevant when there is a reason to assume it has intrinsic properties comparable to the parent substance in terms of its biological target activity, or that it poses a higher or comparable risk to organisms than the parent substance or that it has certain toxicological properties that are considered unacceptable.[6,7]

As regards **drinking water,** Article 4(3)(b) of Regulation (EC) No 1107/2009 also mentions that *"a plant protection product, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use, shall……have no immediate or delayed harmful effects on human health, including that of vulnerable groups, or animal health, directly or indirectly or through drinking water (taking into account substances resulting from water treatment)".*

Considering this requirement for groundwater and drinking water, which does not depend on how criteria to identify EDs will look like, it is expected that the chemical quality of groundwater and drinking water will not be affected by the different options for criteria to

[5] Hecker, M. and Henner, H. 2011. Endocrine disruptor screening: regulatory perspectives and needs. Environmental Sciences Europe 23:15. doi:10.1186/2190-4715-23-15

[6] European Commission Guidance Document on the Assessment of the Relevance of Metabolites In Groundwater of Substances Regulated Under Council Directive 91/414/EEC. Retrieved on: http://ec.europa.eu/food/plant/pesticides/guidance_documents/docs/wrkdoc21_en.pdf

[7] Article 3(32) of Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309

identify EDs. In fact, it is expected that the current regulatory system based on risk assessment will ensure in any case that substances approved as PPP (and their relevant metabolites) will be present in groundwater and drinking water, at levels not exceeding 0.1µg/L if PPP are used correctly, taking into account any necessary restrictions to mitigate any possible risk of leaching to groundwater.

With respect to chemical quality of **surface water,** the PPP Regulation foresees that a risk assessment is carried out by comparing toxicity thresholds of key organisms with exposure values (PEC, predicted environmental concentration) according to relevant guidance documents[8]. As a consequence, low quantities of PPP may be acceptable in surface water, if it is demonstrated that these levels do not pose any risk to the relevant environmental species (e.g. aquatic organisms). This implies that the chemical quality of surface water may be affected only up to an extent which does not cause negative effects on aquatic organisms.

The approval of active substances and authorisation of BP under the BP Regulation is, like for PPP, based on a risk assessment. The main difference with PPP is the attention for the marine aquatic environment because of the use of wood preservatives and antifoulings. Applicants have to submit detailed information for active substances and BP concerning the environment (see in particular Points 9, 10 and 11 of Annex II and Annex III of the BP Regulation). Guidance is available regarding how to fulfil the information requirements and how to evaluate applications in order to protect the environment. The Guidance covers, inter alia, assessment of effects for the freshwater and marine aquatic compartments;[9] emission scenarios to estimate the potential release to the environment of active substances from BP or treated articles.[10]

For all kind of chemicals, including PPP and BP, the Water Framework Directive (Directive 2000/60/EC) allows to assess quality of water bodies via evaluation of:

1) "good chemical status" of water bodies (defined in terms of compliance with all the quality standards established for chemical substances at European level);

2) “good ecological status” of water bodies (defined in terms of quality of the biological community, the hydrological characteristics and the chemical characteristics).

As regards the "good chemical status" of water bodies, lists of “priority substances” and priority hazardous substances” are identified based on their toxicological profile and are periodically monitored in the EU water bodies. “Priority substances” include substances with ED properties. The values compiled are aimed at providing information which would inform regulatory decision makers on particular substances, and if applicable, take the necessary measures to remedy undesired levels of substances. In some cases, substances (or their

[8] For instance: EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2013. Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. EFSA Journal 2013;11(7):3290, 268 pp. doi:10.2903/j.efsa.2013.3290.

[9] ECHA 2015. European Chemical Agency. Guidance on the Biocidal Products Regulation. Volume IV Environment – Part B Risk Assessment (active substances) Retrieved on: http://echa.europa.eu/documents/10162/15623299/bpr_guidance_ra_vol_iv_part_b_en.pdf

[10] ECHA 2016. Emission scenario documents. Retrieved from: http://echa.europa.eu/fr/guidance-documents/guidance-on-biocides-legislation/emission-scenario-documents

metabolites) in the water can derive from different sources and it is not always easy to identify the most appropriate action to reduce substance levels in the environment.

Both for PPP and BP, if we compared the different options for criteria to identify EDs only considering the *chemical* quality of the groundwater, drinking water and surface water, the options would be ranked in terms of the number of substances identified, i.e. the higher the number of substances removed from the market the better the chemical status of the waters (option 1 > 2/3 > 4). This is an approach, which does not consider that some of these levels of chemicals would actually pose no risk to aquatic organisms.

Regarding options for regulatory decision making, Options A and B would rate equally assuming that both would lead to chemical qualities which would pose no risk to organisms, and both options would rate better than Option C. In other words, the options would perform A/B > C and this performance has been considered for all MCA-scenarios with exception of scenario 5 "aim: exposure zero" (see Annex 7).

This MCA-scenario "aim: exposure zero" was developed in order to perform a sensitivity analysis on the performance of the options. It assessed the performance of the options based on a different assumption: the higher the number of substances removed from the market, the better the performance of the options with respect only to exposure (no consideration of risk assessment) for the environment. Similarly, regarding options A to C, the assessment under this scenario was based on the number of correctly identified ED substances which will not be approved. As Option A would take from the market (non-approval) more substances identified as EDs than Options B or C, it would perform the best with respect only to exposure (no consideration of risk assessment) for the environment. The options under this scenario consequently perform as A > B > C.

3. WILDLIFE VERTEBRATE POPULATIONS

3.1. Evidence on possible association between ED exposure and wildlife population declines

The possibility that the current decline in some wildlife populations may be at least partially due to exposure to EDs in the environment have been raised in international reports on the topic. The WHO-UNEP 2012 report "Science of Endocrine Disrupting Chemicals"[11] suggests an association between chemicals with ED properties and wildlife population declines.

The report indicates that the decline is due to a number of factors including overexploitation, loss of habitat, climate change and chemical contamination. However, the authors of the report state that, given their understanding of EDs and of their effects on the reproductive system, it is likely that declines in the numbers of some wildlife populations (raptors, seals and snails) have occurred because of the effects of chemicals (DDT, PCBs and tributyltin, respectively) on these species. They stress that evidence for EDs as a cause of these

[11] Bergman Å, Heindel J, Jobling S, Kidd KA, Zoeller RT. 2012. eds. State of the science of endocrine disrupting chemicals, Geneva: United Nations Environment Programme and the World Health Organization, 2013. Retrieved from: http://unep.org/pdf/9789241505031_eng.pdf

population declines has increased in 2012 relative to 2002, because of the population recoveries following restrictions on the use of these chemicals. The report acknowledges that an endocrine mechanism for current wildlife declines is *probable*, but not proven. It also concludes that:

- EDs with mechanisms of action similar to the chemicals mentioned above are *suspected* to also be a factor contributing to declines seen in wildlife species today.
- Demonstrating a clear link between endocrine effects in individuals and population declines or other effects will always be challenging, because of the difficulty in isolating effects of chemicals from the effects of other stressors and ecological factors

The 2012 report of the European Environmental Agency[12] on EDs points out that there is evidence of reproductive and developmental harm linked to impairments in endocrine function in a number of wildlife species, particularly in environments that are contaminated by cocktails of chemicals that are in everyday use. Laboratory studies show that the reproductive systems of a broad range of vertebrate species (e.g. polar bears and fish) and some invertebrate species (e.g. snails, oysters and insects) are susceptible to ED chemicals, and that foetal/early exposure of animal models to these chemicals can reproduce the pathogenesis seen in some populations. According to the authors, in some fish species, the evidence linking exposure to chemicals with reproductive disorders and dysfunction is strong. According to the report it is clear that examples exist of male and female reproductive dysgenesis and of thyroid hormone disruption in some wildlife classes that can be linked, quite convincingly, to EDs exposure, although the report acknowledges that causation is difficult to prove.

Most if not all the evidence brought forward in the WHO-UNEP 2012 report refer to substances which are not anymore on the market (e.g. DDT, DDD, DDE, dicofol, atrazine, dibromochloropropane, lindane, tributyltin, hexachlorobenzene, carbaryl, vinclozolin, procymidone and fenitrothion, triphenyltin and triclosan) or they are not PPP or BP (e.g. PCBs, flame retardants, dioxins, mercury). A similar situation can be noted for the report of the EEA[12] as the report refers to PPP active substances that are not anymore allowed to be placed on the market (e.g. atrazin, diazinon, alachlor, vinclozolin, dieldrin, chlordane, dicofol, methoxychlor, nonylphenol ether, polyoxyethyleneglycol, nonylphenol ethoxylate, fenarimol and methoprene).

The conclusions of the WHO-UNEP 2012 report have been criticised in the public literature for misinterpreting the available evidence and for methodological issues.[13,14] According to Lamb et al., the WHO-UNEP 2012 report does not accurately reflect the original articles which are cited as the two most prominent examples of evidence of ED in wildlife (link

[12] EEA Technical Report No 2/2012, The impacts of endocrine disrupters on wildlife, people and their environments – The Weybridge+15 (1996–2011) report. Retrieved on: www.eea.europa.eu/publications/the-impacts-of-endocrine-disrupters

[13] Lamb et al. 2014. Critical comments on the WHO-UNEP state of the science of endocrine disrupting chemicals – 2012. Regulatory toxicology and pharmacology 69(1): 22-40. doi:10.1016/j.yrtph.2014.02.002

[14] Lamb et al. 2015. Comments on the opinions published by Bergman et al. (2015) on Critical comments on the WHO-UNEP state of the science of endocrine disrupting chemicals (Lamb et al. 2014). Regulatory toxicology and pharmacology 73(3): 754-757. doi:10.1016/j.yrtph.2015.10.029

between DDT and bird population and between tributyltin and snail population): according to Lamb et al., the authors of the original works concluded that the lack of data on both exposure and effects in these organisms did not allow firm conclusions. E.g. according to Lamb et al. a review[15] on the possible link between tributyltin (TBT) and snail population decrease indicated inter alia the lack of agreement among researchers on the mechanism for induction of effects and the fact that female masculinisation by TBT or triphenyltin (TPT) has been confirmed in the laboratory in only a small fraction of species affected (7.5% or 20 species confirmed out of 268 total species examined). All these uncertainties were not indicated in the evidence reported on the topic in the WHO-UNEP 2012 report.

Lamb et al. do not agree with the conclusion of the WHO-UNEP 2012 report that *an endocrine mechanism for wildlife declines is probable but not conclusive.* They also state that it would be more appropriate to conclude that the evidence for an endocrine mechanism is hypothetical, rather than probable, particularly given the fact that for the two best known examples for wildlife declines, DDT and TBT, an endocrine mechanism, while possible, is only one of many potential factors that may be contributing to the observed population dynamics. Hecker and Henner[16] indicated that many studies have been conducted to describe potential EDs in wild and laboratory animals, but few studies have attempted to explore the ecological relevance of the exposure to endocrine active chemicals under field conditions.

Other scientists[17] criticise the WHO-UNEP 2012 report (some of them ex-chair of European Commission Scientific Committees). They support the critics of Lamb et al. 2014 and further state: "*the 2002 WHO/ICPS report demanded that a review of all data on endocrine disruption had to be appropriately performed according to the well-established principles of data evaluation. This was not adequately performed in the WHO/UNEP report of 2012 and is also missing in the Zoeller et al.'s (2014) article.*

Finally, other critics[18,19] to the WHO-UNEP 2012 report regarded more general methodological issues, such as the existence and relevance of low-dose effects and non-monotonic dose-response curves for EDs (among these authors, some were members of European Agencies Scientific Committees).

The Kortenkamp report[20] provides an overview on the ED effects in different animal species. In fish, effects of EDs on reproductive endpoints are well documented both in the field and

[15] Titley-O'Neal, C.P., Munkittrick, K.R., and MacDonald, B.A., 2011. The effects of organotin on female gastropods. Journal of Environmental Monitoring. 13: 2360-2388. DOI: 10.1039/C1EM10011D

[16] Hecker, M. and Henner, H. 2011. Endocrine disruptor screening: regulatory perspectives and needs. Environmental Sciences Europe 23:15

[17] Autrup, H., Barileb, F. A., Blaauboerc, B. J., Degend, G. H., Dekant, W.,, Dietrich, D., Domingog, J. L., Gorih G. B., Greim, H., Hengstlerd, J. G., Kacewj, S., Marquardtk, H., Pelkonenl, O., Savolainenm, K., and Vermeulenn, N. P. 2015. Principles of Pharmacology and Toxicology also Govern Effects of Chemicals on the Endocrine System. Toxicol Sci. 2015 Jul;146(1):11-5.

[18] Testai, E., Galli, C.L., Dekant, W., Marinovich, M., Piersma, A.H., Sharpe, R.M., 2013. A plea for risk assessment of endocrine disrupting chemicals. Toxicology, http://dx.doi.org/10.1016/j.tox.2013.07.018

[19] Borgert, C. J., Baker, S. P., and Matthews, J. C. 2013. Potency matters: thresholds govern endocrine activity. Regul. Toxicol. Pharmacol., 67, 83–88.

[20] Kortenkamp, A., Martin, O., Faust, M., Evans, R., McKinlay, R., Orton, F., Rosivatz, E., 2011. State of the art assessment of endocrine disrupters. Final Report. Retrieved from: http://ec.europa.eu/environment/chemicals/endocrine/pdf/sota_edc_final_report.pdf

the laboratory; in amphibians, EDs have been shown to affect reproductive and thyroid endpoints; in marine mammals, ED has not been studied in great detail, but there are strong indications that endocrine related endpoints have been affected by persistent organic pollutants (POPs) in wild populations; in birds, abnormalities of the reproductive tract, thyroid function and hormonally sensitive behavioural endpoints have been reported in the wild and can be induced in the laboratory with model EDs and hormones; in reptiles, ED remains a largely unexplored area of research and is not covered by the assays currently validated; in invertebrates, knowledge of endocrinology and how it is affected by EDs is largely confined to arthropods and molluscs.

Similarly to the WHO-UNEP 2012 report, also in the Kortenkamp report, the evidence reported in favour of a link between exposure to EDs and adverse effect in the environment is limited to substances which are not PPP or BP. In the rare cases, where the effect in a wild species is linked to a specific PPP or BP, these substances happen to be not anymore on the EU market since years (Table 1).

Table 1. Pesticides mentioned as EDs in the WHO-UNEP 2012 report but already removed from the EU market based on Directive 91/414/EC and Directive 79/117/EC[21]

ACTIVE SUBSTANCE	NON-APPROVED SINCE	CLASS OR USE
hexachlorobenzene	2004/1979*	fungicide
tributylin (3AS)	2002	fungicide
atrazine	2004	herbicide
terbufos	2002	insecticide
trichlorfon	2007	insecticide
mirex	2004	insecticide
coumpahos	1993	insecticide
permethrin	2000	insecticide
heptachlor epoxide	2004/1979*	metabolite heptachlor***
chlordane	2004/1979*	organochlorine insecticide
4,4'-DDE	1993**	organochlorine insecticide
DDT	2004/1979*	organochlorine insecticide
dicofol	1979	organochlorine insecticide
dieldrin	2004/1979*	organochlorine insecticide
endosulfan	2005	organochlorine insecticide
heptachlor	2004/1979*	organochlorine insecticide
lindane	2000	organochlorine insecticide
methoxychlor	2002	organochlorine insecticide
nonachlor (trans and cis chlordane)	2004	organochlorine insecticide
toxaphene (campechlor)	1979	organochlorine insecticide
fonofos	2002	organophosphate insecticide
phorate	2002	organophosphate insecticide
phorate	2002	organophosphate insecticide
oxychlordane	2004	metabolite chlordane ***
*= non-approved in principle in 1979, with few exceptional uses left on the market		
**= not on the EU market since at least 1993: were never notified for assessment under the EU review program		
***= date of non-approval equivalent of the one of the parent compound		

[21] Council Directive 79/117/EEC of 21 December 1978 prohibiting the placing on the market and use of plant protection products containing certain active substances. OJ L 33, 8.2.1979, p. 36–40 (DA, DE, EN, FR, IT, NL). Available on: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:31979L0117

3.2. Consideration of vertebrate and invertebrate populations

A reasonably complete suite of standardised assays for testing the effects of EDs is available for the oestrogenic, androgenic, thyroid and steroidogenic modalities in mammals and fish, with fewer tests for birds and amphibians.[8] For invertebrates, standardised mechanistic assays are not yet available as OECD testing guidelines, mainly due to poor current understanding of endocrinology in most invertebrates understanding, which differs from the one of vertebrates., and the lack of screening endpoints specifically related to ED.

Therefore, the screening of chemicals performed as a supportive study for this IA focused on vertebrate wildlife species.

As a consequence, considering the current state of knowledge, the evidence compiled in this IA focusses on impacts related to potential associations between exposure to EDs and adverse effects limited to human health and wild vertebrate species. However, effects on invertebrates are also assessed, including effects on reproduction, before approval or authorisation of PPP and BP (see next section).

3.3. Environmental risk assessment in the context of approval of active substances used in PPP and BP and rating of the options for identifying ED criteria

As mentioned in Section 1 of this Annex, it needs to be considered that it is so far not possible to identify robust and reliable environmental impact indicators in relation to ecosystem services or species level effects,[4] which implies that robust conclusions are difficult to extract. Nevertheless, protection of the environment remains a priority, as it is a mayor objective in the PPP and BP Regulations, and thus guides this impact assessment. Protection of the environment is therefore analysed under consideration of the current regulatory decision making under the PPP and BP Regulations.

As mentioned already in other sections of this IA report, PPP and BP are among the strictest regulated chemicals worldwide.[22;23] The legislation requires that the substances be deemed hazardous until proven otherwise, and the burden of proof lies with the applicant requiring an authorisation to place the substance on the EU market to provide the scientific information needed to evaluate the possible risk.[24] Only substances present on the positive list can be used in PPP or BP placed on the EU market, if applicable with restrictions in use, provided they also pass the second step of national authorisation of the formulated products.

The EU legislation in place also implies that both PPP and BP are among the most "data rich" regulated product groups in the EU. Under both regulations, a detailed list of data

[22] Article 1.4 of Regulation (EC) no 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309.

[23] Article 1.1 of Regulation (EU) no 528/2012 of the European Parliament and of the Council concerning the making available on the market and use of biocidal products. OJ L 167/1.

[24] These are elements of the precautionary principle, see Communication from the Commission on the precautionary principle, COM(2000) 1 final. Retrieved from: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52000DC0001

requirements[25;26] is specified and has to be submitted by the applicant before any approval of the active substance or authorisation of a product containing the approved substances can be considered. These core data requirements, in particular under the PPP regulation, include testing of several non-target species which cover several ecological compartments (earthworms, algae, fish, aquatic and terrestrial arthropods including bees, birds, mammals, terrestrial plants). These tests cover, in most of the cases, reproductive effects, and may include also early-life studies, full-life-cycle, multi-generation tests or more complex semi-field studies if so required. It could be thus concluded that effects on wildlife species, in terms of potential reproductive effects which may be potentially relevant for population effects, are already covered by the PPP Regulation. In addition, tests which would cover ED endpoints have been added recently to the data requirements. For BP the studies should also, if appropriate, address the potential effects on sensitive taxa or species in the marine environment that contains key taxa that are not present in freshwater environment (e.g. Echinodermata).

Further, recent trends in environmental risk assessment may be considered, as for instance the application of the ecosystem service concept[27], The Economics of Ecosystems and Biodiversity (TEEB)[28], which would also cover effects on biodiversity. The European Food Safety Authority concluded that in general environmental risk assessment should be based on effects on populations rather than for individuals.[29]

Confirming this trend it should be mentioned that also under REACH[30] it was recognised that the information on selected species may still be a poor predictor of impacts at the ecosystem level.

Confirming the fact that the current EU regulatory system already addresses EDs, is the fact that most of the evidence presented in the WHO-UNEP 2012 report for pesticides with ED properties related wildlife effects, is concerning substances that are not anymore approved in the EU as PPP or BP for many years (e.g. DDT, vinclozolin, methoxychlor, terbutyltin) (see Table 1).

[25] Regulations EU 283/2013 and EU 284/2013, setting data requirements for active substances and for PPP, respectively; Communications 2013/C 95/01 and 2013/C 95/02, detailing the list of test methods and guidance documents for active substances and for PPP, respectively.

[26] Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products. Official Journal of the European Union, L 167, 27 June 2012. doi:10.3000/19770677.L_2012.167.eng

[27] EFSA Panel on Plant Protection Products and their Residues (PPR); Scientific Opinion on the development of specific protection goal options for environmental risk assessment of pesticides, in particular in relation to the revision of the Guidance Documents on Aquatic and Terrestrial Ecotoxicology (SANCO/3268/2001 and SANCO/10329/2002). EFSA Journal 2010;8(10):1821. [55 pp.] doi:10.2903/j.efsa.2010.1821. Available online: www.efsa.europa.eu/efsajournal.htm

[28] See The economics of ecosystems and biodiversity (TEEB) website: http://www.teebweb.org/

[29] European Food Safety Authority; Application of systematic review methodology to food and feed safety assessments to support decision making. EFSA Journal 2010; 8(6):1637. doi:10.2903/j.efsa.2010.1637.

[30] Assessing the health and environmental impacts in the context of socio-economic analysis under REACH. Final Report- Part 1: Literature review and recommendations. March 2011. Prepared for the European Commission, Directorate-General for Environment. Available at: http://echa.europa.eu/documents/10162/13580/reach_sea_part1_en.pdf.

Regarding biocides, for instance, ***triclosan***, a disinfectant identified as a substance with ED properties in the 2012 WHO/UNEP report, is not approved in the EU as an active substance to be used in BP (product-types 1, 2, 7 and 9) since 2014 and 2016, respectively.[31]

Triclosan is an antibacterial active ingredient for use in disinfectants and preservatives. It may also have virucidal and fungicidal activity. In the WHO-UNEP 2012 report, it is mentioned that triclosan disrupts steroidogogenic enzymes involved in the production of testosterone and estrogen, which could lead to reduced reproductive success in both males and females. The 2012 WHO/UNEP report indicated that there is growing number of studies from the open literature showing potential problems with triclosan concerning ED. It is pointed out to postpone the assessment on ED properties until the currently on-going evaluation under REACH has been finalised[32].

Regarding biocides, the situation may be more complex due to the possibility to consider socio economic factors. An interesting example is ***creosote,*** a wood preservative identified as biocidal substance with potential ED properties under option 1. Creosote is a distillate of coal tars and it is a complex mixture of hundreds of distinct compounds, including bi- and polycyclic aromatic hydrocarbons. It is used for biocidal treatment of timber as wood preservative by vacuum-pressure impregnation (product type 8). Creosote was approved in 2013[33]: it contains PBT constituents and it is classified as carcinogenic category 2, thus fulfilling the exclusion criteria under the BP Regulation. However, it was approved based on the assessment report which concluded that there are no realistic alternatives. Also the results of the public consultation on this active substance indicated that there would be severe economic and practical consequences if creosote treated wood cannot be used in infrastructure built for telephone communications and railway connections. The approval specifies that BP containing creosote may only be authorised for uses where no appropriate alternatives are available.

As illustrated in the previous paragraphs, several substances have been non-approved in the EU, sometimes since years, or approved subject to strict conditions in recent years, demonstrating the regulatory system in the EU succeeds in protecting the environment.

As a consequence, it can be assumed, based on available scientific evidence from EU agencies and scientific committees,[34;35] that a regulatory decision making based on a risk assessment would protect environment in a similar way as a hazard approach.

Option B Option B only applies to the PPP Regulation. The derogations to the non-approval of active substances, currently mainly hazard-based, would be updated in light of new scientific evidence (e.g. recent scientific opinions of EFSA , Scientific Committee SCHER ,

[31] Commission Implementing Decision of 24 April 2014 (2014/227/EU) and of 27 January 2016 (2016/110/EU)
[32] For further information see the decision on substance evaluation for Triclosan. Retrieved from: http://echa.europa.eu/documents/10162/13628/corap_sev1_222-182-2_dec_final_public_2710_en.pdf
[33] Commission Directive 2011/71/EU
[34] EFSA Scientific Committee; Scientific Opinion on the hazard assessment of endocrine disruptors: scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing effects mediated by these substances on human health and the environment. EFSA Journal 2013;11(3):3132. [84 pp.] doi: 10.2903/j.efsa.2013.3132.
[35] Scientific Committee on Consumer Safety (SCCS) Memorandum on Endocrine Disruptors. Retrieved from: http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_009.pdf

expert meeting in Berlin) to risk based derogations. While the general hazard approach for EDs would be maintained, the derogations would be based on a stronger risk component compared to the current situation. Amendments to the Annexes, via Regulatory Procedure with Scrutiny (RPS) are foreseen in Regulation (EC) No 1107/2009 taking into account current scientific and technological knowledge (cf. Article 78 of the PPP Regulation). This option is therefore feasible within the remit of the mandate of the Commission as it does not imply changes by ordinary legislative procedure to the basic act.

The inclusion of socio-economic considerations (Option C) may consider a risk/benefit analysis and protect the environment to a less extent. This option would request a modification via ordinary legislative procedure of the current PPP Regulation.

Option 1 is not able to identify EDs relevant for the environment. There is indeed a scientific consensus that interim criteria are not fit for correctly identifying EDs since they are unable to detect an ED mode of action. They detect many false positives because the interim criteria identify EDs even when no ED mode of action is present. They also detect many false negatives, as shown by the limited overlap between substances identified under option 1 (interim criteria) and option 2 (WHO definition). This overlap is visible in Fig 2 of the main report and in Table 1 of Annex A5.

As a consequence, the performance of options would be 2/3/4 > 1 and A/B > C, respectively. These performances of the options have been considered for all MCA-scenarios with exception of the MCA-scenarios "aim: exposure zero".

In order to perform a sensitivity analysis on the performance of the options, the MCA-scenario "aim: exposure zero" was developed. It assessed the performance of the options considering a different assumption only based on exposure considerations: the higher the number of active substances identified as EDs, the better the performance of the option with respect to exposure (without consideration of any risk assessment) for the environment.. As a consequence, within this scenario, the options performed as follows: 2/3 > 4 > 1. Regarding Options A to C, the assessment was based on the number of correctly identified ED substances which will not be approved. As Option A would take from the market (non-approval) more substances identified as EDs than Options B or C, it is assumed that it would perform the best with respect to exposure. Under this scenario, the options consequently perform as follows: A > B > C, only based on exposure.

4. ANIMAL WELFARE

Animal testing is required on a standard basis to assess the safety of active substances and PPP and BP, to both humans and the environment. Also the potential of chemicals to disrupt endocrine functions relies on a large number of *in vivo* tests, i.e. tests using live animals[36].

[36] Only in vivo can absorption, distribution, metabolism and excretion of a chemical be accounted for. The impacts of ED on wildlife, people and their environments – The Weybridge+15 (1996–2011) report: europa.eu/publications/the-impacts-of-endocrine-disrupters.

With increasing testing demands and requirements the number of rats, mice, fish and frogs needed for generating the relevant data will grow[37].

The EU legislation in place tries to reduce as much as possible the use of animals for scientific purposes (see Sections below). In addition, the European Commission, trade associations and companies are cooperating via the European Partnership for Alternative Approaches to Animal Testing (EPAA) to accelerate the development, validation and acceptance of alternative approaches to animal use in regulatory testing. The overall aim is the replacement, reduction and refinement (3Rs) of animal use in regulatory testing[38]. However, for the purpose of identifying EDs, it is likely that *in vivo* animal testing cannot be avoided completely, as in accordance with the WHO/IPCS definition (2002), an ED is defined as "*an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects* ***in an intact organism****, or its progeny, or (sub)populations*".

It is thus expected that the four options may thus have an effect on animal testing. Therefore they will be assessed on the basis of the number of animal tests they would trigger: for the purpose of the multi-criteria analysis, it was assumed that the more animal tests an option implies, the worst performing it is.

Further, in the public consultation (See Annex 2) it was also indicated that evidence coming from *in vivo* testing is required in order to identify an ED. This is applicable for all options; however, for Option 3, additional animal tests would be needed to clarify the status of the active substances found in the Categories II and III. This would imply the use of more animals to generate data.

It was also pointed out that the ED criteria would involve large numbers of test animals to provide data which would not add any additional understanding to the toxicological behaviour of the chemicals that already have extensive data packages. Further, for some areas it would be difficult in the future to differentiate between a potential ED and an ED, for instance for substances registered solely for use in cosmetic products due to the ban on animal testing for cosmetic ingredients (effective since 2013).

Despite the on-going additional efforts launched at various levels, the replacement of animal test methods by alternative *in vitro* or *in silico* methods in relation to complex toxicological endpoints is considered to be scientifically challenging. However, another respondent to the public consultation stressed that the definition of EDs should be flexible enough to allow for use of alternative methods to *in vivo* tests. Limiting the definition to evidence only provided by animal testing would preclude adoption of approaches that could minimise or eliminate the use of animals.

It was also pointed out that the protection of humans and wildlife from the effects of EDs should not lead to the addition of new tests to what is already an exhaustive testing strategy. Non-animal test methods should be promoted in order to produce safety data relevant to

[37] Hecker, M. and Henner, H. 2011. Endocrine disruptor screening: regulatory perspectives and needs. Environmental Sciences Europe 23:15

[38] EPAA. 2016. European Partnership for Alternative Approaches to Animal Testing website. Retrieved from: http://ec.europa.eu/growth/sectors/chemicals/epaa/index_en.htm

humans and to replace animal studies currently in use. Tests on vertebrates should be undertaken as a last resort.

4.1. Provisions in relation to Animal Testing in EU legislation

4.1.1. General provisions

The protection and welfare of animals is an area covered by a wide range of EU legislation.

Article 13 of the Treaty on the Functioning of the European Union states that "*In formulating and implementing the Union's agriculture, fisheries, transport, internal market, research and technological development and space policies, the Union and the Member States shall, since animals are sentient beings, pay full regard to the welfare requirements of animals, while respecting the legislative or administrative provisions and customs of the Member States relating in particular to religious rites, cultural traditions and regional heritage*."

The use of animals for scientific purposes has been covered by EU legislation since 1986. Directive 2010/63/EU[39] on the protection of animals used for scientific purposes (replacing Directive 86/609/EEC) entered in effect on the January 1, 2013. The directive strengthens the legislation and improves the welfare of those animals which still need to be used. The principle of the 'Three Rs' (to Replace, Reduce and Refine the use of animals) is clearly stated.

This Directive widens the scope of animal testing and includes foetuses of mammalian species in their last trimester of development and cephalopods, as well as animals used for the purposes of basic research, higher education and training. It lays down minimum standards for housing and care, regulates the use of animals through a systematic project evaluation requiring inter alia assessment of pain, suffering distress and lasting harm caused to the animals. It requires regular risk-based inspections and improves transparency through measures such as publication of non-technical project summaries and retrospective assessment. The development, validation and implementation of alternative methods is promoted through measures such as establishment of a EU reference laboratory for the validation of alternative methods supported by laboratories within Member States and requiring Member States to promote alternative methods at national level.

4.1.2. Plant Protection Products Regulation

The PPP Regulation[40], which regulates the placing on the market of PPP, aims to reduce animal testing to the maximum.

Animals are used in the assessment of the safety of active substances and PPP, to both humans and the environment, as required by the Regulation. Although alternative test

[39] Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes, OJ L 276, 20.10.2010

[40] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC, OJ L309,24.11.2009

methods have reduced the reliance on animal testing and the number of animals involved, computer simulation and *in vitro* methods cannot yet replicate the complexity or reaction of a living creature.

Article 62 (1) of the Regulation states that: "*Testing on vertebrate animals for the purposes of this Regulation shall be undertaken only where no other methods are available. Duplication of tests and studies on vertebrates undertaken for the purposes of this Regulation shall be avoided in accordance with paragraphs 2 to 6*."

Animal testing on vertebrate animals should therefore be minimised (cf. also Article 7 (d) and Article 33 (3) (c); but also Regulation EU 283/2013 setting data requirements for active substances[41]) and undertaken only as a last resort. There should not be duplication of tests and data sharing is promoted: "*The prospective applicant and the holder or holders of the relevant authorisations shall make every effort to ensure that they share tests and studies involving vertebrate animals. The costs of sharing the test and study reports shall be determined in a fair, transparent and non-discriminatory way. The prospective applicant is only required to share in the costs of information he is required to submit to meet the authorisation requirements.*" (Article 62 (3) of the PPP Regulation).

The PPP Regulation also includes several recitals and articles that refer to the development and promotion of alternative methods and the importance of replacing animal studies. For instance, Recital 11 of the Regulation states that "*The development of non-animal test methods should be promoted in order to produce safety data relevant to humans and to replace animal studies currently in use*."

In addition, the PPP Regulation stipulates the standard data requirements[35] which have to be submitted in all cases.

4.1.3. Biocidal Products Regulation

The BP Regulation[42], which regulates the placing on the market and the use of BP, aims at minimising animal testing as far as possible.

One aim of the regulation is to avoid unnecessary testing on animals (cf. article 62 of the BP Regulation: "*In order to avoid animal testing, testing on vertebrates for the purposes of this Regulation shall be undertaken only as a last resort. Testing on vertebrates shall not be repeated for the purposes of this Regulation*"). Therefore, before carrying out any tests on animals, companies need to send an inquiry to the European Chemicals Agency (ECHA) to find out whether the same test or study has already been conducted and submitted under EU biocides legislation. If such information exists, companies are required to share the data. The owner of the data and the applicant seeking to rely on this data for a purpose under the BP Regulation must negotiate and come to a mutually acceptable arrangement. In absence of an agreement on sharing of vertebrate animal studies between the data owner and the prospective

[41] Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, OLJ L93, 3.4.2013

[42] Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products, OJ L167,27.6.2012

applicant, the Agency may allow the use of the studies by the prospective applicant without prejudice to the decision on the compensation made by national courts.

Annex II of the BP Regulation (information requirements for active substances) also refers to Directive 86/609/EEC on the protection of animals used for scientific purposes as it requires that "*Tests performed should comply with the relevant requirements of protection of laboratory animals, set out in Directive 2010/63/EU of the European Parliament and the Council of 22 September 2010 on the protection of animals used for scientific purposes (2) and in the case of ecotoxicological and toxicological tests, good laboratory practice, set out in Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their application for tests on chemical substances (3) or other international standards recognised as being equivalent by the Commission or the Agency. Tests on physico-chemical properties and safety-relevant substance data should be performed at least according to international standards.*"[42]

In addition, the BP Regulation requires information to be submitted as part of the application for the approval of an active substance (Article 6 of the BP Regulation) or for the authorisation of a BP (Article 20 of the BP Regulation).

4.2. Expected impacts on animal testing by the options presented in this impact assessment

While recognising that animal testing is still needed to ensure the protection of human health and the environment, EU legislation sets very high animal welfare standards for such testing and requires that whenever possible this testing is replaced, reduced and refined.

None of the options for criteria to identify EDs will succeed in avoiding animal testing. On the contrary, some options may actually trigger further animal testing, which is a reason of concern for several respondents to the public consultation who specifically called for the development and use of methods that do not rely on animal testing in order to produce safety data.

Option 1 (interim criteria) is based on Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures (CLP Regulation): in order for an applicant to prove that an active substance is not carcinogenic category 2, toxic for reproduction category 2, and does not have toxic effects on the endocrine organs, studies, mostly based on animal tests, will need to be provided.

Options 2, 3 and 4 are all based on the WHO/IPCS definition which implies the need for evidence from experimental *in-vivo* animal studies to support the claim that a substance has/has not the capacity to cause endocrine-mediated adverse effects in humans or wildlife populations. These options make it difficult to identify an ED based only on *in vitro* testing.

Furthermore, Option 3 (WHO/IPCS definition + additional categories) would potentially trigger even more animal testing. If an active substance would be categorised as a suspected

ED or an endocrine active substance (Categories II and III of Option 3), the applicant may need to provide additional studies (most probably based on animal testing) to prove that the substance should not be categorised. Applicant would be requested to do so by authorities for clarification or, alternatively, they may provide the data in order to demonstrate that the substance should not be considered a suspected ED or an endocrine active substance to avoid "negative flagging" (substances placed in Categories II and III could be subject to misinterpretation).

Looking at the animal tests which may be triggered by the different options, Option 3 is considered as performing worse that the Options 1, 2, and 4. The latter are based on standard data requirements under the PPP and BP legislation, while Category III may trigger additional animal testing without direct regulatory consequences. The options are thus performing 1/2/4>3.

With regards to Options A to C, no difference in terms of animal tests required is expected because the data requirements under the PPP Regulation and BP Regulation are set. The fact that the decision on the approval of a substance is taken mainly based on hazard or based on risk, or that socio economic elements can be taken into consideration, is not expected to affect the data requirements for a dossier. Therefore, in terms of animal welfare, all options are performing the same: A/B/C.

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PART 13/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annexes 12 and 13 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

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ANNEX 12

SECTORIAL COMPETITIVENESS: EU AGRICULTURE

Contents

This Annex focuses on the assessment of potential impacts, which build on the results of the screening study explained in Annexes 3 to 5. The results of the screening do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation. The methods and results presented in this Annex are to be interpreted as an estimation of the potential impacts.

Annexes 8 to 15 describe the impacts expected when implementing the criteria to identify EDs (Options 1 to 4) under the current regulatory framework (Option A). In addition, it was assessed whether these expected impacts would remain the same or not under consideration of different regulatory implementations (Options B and C, only applicable to the PPP Regulation). The analyses of the impacts described in these Annexes translate into the "performance" of the options, which is one of the input parameters to the MCAs (Annex 6 and 7).

The MCAs results are not concluding on any preferred option for setting scientific criteria to identify endocrine disruptors, but aim at providing additional information to decision makers with regards to the potential impacts expected when implementing the criteria, after those would have been selected on the basis of science (two MCAs were performed: Options 1 to 4 under the current regulatory context, and Options A compared to Options B and C).

At a preliminary stage of the impact assessment it was anticipated that Option C should be discarded, nevertheless it was maintained for the analysis of the impacts for methodological reasons (see Section 4.2.3 of the main report and Annexes 6 and 7). Option C only applies to the PPP Regulation.

1. Agriculture in the EU

Agriculture plays an important role in the EU: it supplies nutritious and high quality food to the 508.2 million Europeans[1], but also jobs. The farming and food sectors together provide 7% of all jobs and generate 6% of European gross domestic product[2].

The EU is the largest wine and olive oil producer in the world. It is also one the largest producers of cereals at global level (the harvested production of cereals, including rice, in the EU-28 was estimated to be around 334.2 million tonnes in 2014). The EU is a major actor in the international trade of agricultural product as it is a leading exporter (mostly processed and high-value-added products).[3]

According to the Agriculture, forestry and fishery statistics - 2014 edition[4], there were 12.2 million farms in the EU-28 in 2010, with the vast majority of these (96.9%) classified as family farms[5]. Altogether, their utilised agricultural area (UAA) encompassed 176 million hectares (ha), or 1.76 million km². The land used by farms in the EU-28 accounted for approximately 40% of the total land area.

Around four fifths (80.3% in 2010) of all farms in the EU-28 had less than 10 hectares of utilised agricultural area, and together these smaller farms cultivated some 12.2% (of the utilised agricultural area. By contrast, only 5.9% of the farms in the EU-28 cultivated 50 hectares or more of land for agricultural purposes, however, these larger farms collectively cultivated 66.6% of the total utilised agricultural area.[4]

In addition, based on the "Annual Working Unit per holding" which gives the number of full-time equivalent jobs per holding for different farm size categories, nowhere in the EU can we find agricultural holdings with more than 250 employees. Even in the highest size class of holdings (100 ha and more) the highest number of full-time equivalent jobs per holding is 20.5 AWU/holding (Slovenia). The idea that larger holdings are more likely to employ several people than smaller holdings is therefore not verified.

As a consequence, if the definition for SMEs "less than 250 employees" is applied[6], all agricultural holdings qualify as SMEs and it can be assumed that the higher the impacts on

[1] EUROSTAT, News release 124/2015, 10 July 2015. Retrieved from: http://ec.europa.eu/eurostat/documents/2995521/6903510/3-10072015-AP-EN.pdf/d2bfb01f-6ac5-4775-8a7e-7b104c1146d0

[2] European Commission. 2014. The European Union explained. Agriculture - The EU's common agricultural policy (CAP): for our food, for our countryside, for our environment. Retrieved from: http://europa.eu/pol/pdf/flipbook/en/agriculture_en.pdf

[3] EUROSTAT, Statistics explained. Agricultural production – Crops. Retrieved from: http://ec.europa.eu/eurostat/statistics-explained/index.php/Agricultural_production_-_crops#Further_Eurostat_information

[4] EUROSTAT. 2015. Agriculture, forestry and fishery statistics, 2014 edition. Retrieved from: http://ec.europa.eu/eurostat/documents/3217494/6639628/KS-FK-14-001-EN-N.pdf/8d6e9dbe-de89-49f5-8182-f340a320c4bd, (p 12)

[5] According to the FAO definition, the term 'family farm' is used to refer to any farm under family management where 50 % or more of the regular agricultural labour force was provided by family workers.

[6] Definition of an SME according to tool 19 of the better regulation toolbox: http://ec.europa.eu/smart-regulation/guidelines/tool_19_en.htm "Businesses can be characterised as Small and Medium Enterprises (SMEs) by looking at the number of employees: micro companies have 0-9 employees, small companies have 10-49 employees, medium-sized companies have 50-249 employees while large companies have 250 or more employees."

farmers, the more difficult it will be for them to cope with these impacts as they are all SMEs. These difficulties might translate into loss of revenues, the need to change agricultural production, loss of jobs in the farming sector, etc.

Table 1. Distribution of holdings and utilised agricultural area by size and class (UAA), EU, 2005 and 2010

Size classes in hectares	Number of holdings			Utilised agricultural area		
	EU-27		EU-28	EU-27		EU-28
	2005	2010	2010	2005	2010	2010
	(thousands)			(thousand hectares)		
Total	14 482	12 015	12 248	171 996	174 499	175 815
	(% share within total) (1)			(% share within total) (1)		
0	2.0	2.2	2.1	0.0	0.0	0.0
> 0 to < 2	48.3	46.9	47.0	3.0	2.4	2.4
2 to < 5	21.2	20.1	20.2	5.6	4.4	4.4
5 to < 10	10.9	10.9	10.9	6.4	5.2	5.3
10 to <20	7.1	7.5	7.5	8.4	7.3	7.3
20 to < 30	2.8	3.1	3.1	5.8	5.3	5.3
30 to < 50	2.9	3.3	3.3	9.3	8.8	8.8
50 to < 100	2.8	3.3	3.2	16.4	15.9	15.9
100 or more	2.0	2.7	2.7	45.2	50.9	50.7

(1) Shares may not sum to 100 % due to rounding.
Source: Eurostat (online data code: ef_kvaareg)

Table 2. AWU/holding, 2010 (Calculations done by DG AGRI on the basis of data from Eurostat)

GEO/AGR AREA	Total	Zero ha	Less than 2 ha	From 2 to 4.9 ha	From 5 to 9.9 ha	From 10 to 19.9 ha	From 20 to 29.9 ha	From 30 to 49.9 ha	From 50 to 99.9 ha	100 ha or over
Belgium	1,44	1,21	1,22	1,17	1,16	1,34	1,45	1,54	1,74	2,12
Bulgaria	1,10	1,17	0,88	1,27	1,58	1,83	2,13	2,10	2,70	7,65
Czech Repu	4,72	16,00	1,05	1,46	1,14	1,31	1,49	1,66	2,37	17,40
Denmark	1,24	1,98	2,63	1,54	0,47	0,56	0,69	0,86	1,28	2,90
Germany (u	1,82	3,98	1,64	1,57	0,88	1,14	1,46	1,72	2,07	4,60
Estonia	1,28	7,47	0,62	0,59	0,68	0,76	0,88	1,10	1,29	6,24
Ireland	1,18	2,00	0,67	0,64	0,79	1,00	1,18	1,36	1,59	1,93
Greece	0,59	1,38	0,31	0,67	0,94	1,18	1,34	1,48	1,69	2,06
Spain	0,90	1,14	0,52	0,59	0,78	1,03	1,19	1,31	1,62	2,75
France	1,51	1,71	0,73	0,83	1,12	1,41	1,57	1,67	1,80	2,32
Croatia	0,79	5,22	0,44	0,81	1,14	1,52	2,02	1,94	2,23	9,13
Italy	0,59	0,96	0,29	0,53	0,80	1,09	1,38	1,64	2,06	3,24
Cyprus	0,48	1,65	0,25	0,71	1,15	1,80	2,08	2,21	2,73	4,17
Latvia	1,02	2,09	0,45	0,65	0,83	1,06	1,28	1,53	1,77	4,88
Lithuania	0,73	11,92	0,38	0,48	0,64	0,92	1,15	1,27	1,64	5,90
Luxembourg	1,68	1,00	0,65	1,44	1,86	1,29	1,08	1,33	1,77	2,52
Hungary	0,73	0,66	0,50	0,79	0,97	1,21	1,38	1,57	2,01	8,84
Malta	0,39	0,68	0,31	0,78	1,30	2,25	0,00	:	:	:
Netherlands	2,24	3,07	2,22	2,09	2,06	2,07	2,06	2,08	2,56	4,11
Austria	0,76	0,37	0,38	0,40	0,63	0,85	1,04	1,20	1,31	1,46
Poland	1,26	1,49	0,73	1,04	1,41	1,73	1,98	2,11	2,20	5,92
Portugal	1,19	2,36	0,98	1,10	1,25	1,55	1,83	2,17	2,49	3,44
Romania	0,42	0,20	0,29	0,62	0,89	1,21	1,52	1,77	2,16	5,41
Slovenia	1,03	1,26	0,57	0,85	1,19	1,61	1,99	2,37	2,82	20,50
Slovakia	2,29	2,16	0,61	0,72	0,85	1,04	1,00	1,40	1,94	16,95
Finland	0,94	1,35	1,75	0,48	0,43	0,55	0,80	1,06	1,43	2,07
Sweden	0,80	1,32	1,48	0,34	0,38	0,48	0,61	0,78	1,16	2,34
United King	1,43	1,17	1,29	1,08	0,74	0,84	1,06	1,19	1,56	2,63
EU-28	0,81	0,68	0,41	0,73	1,01	1,26	1,42	1,56	1,82	3,62
EU-27	0,81	0,68	0,41	0,73	1,01	1,26	1,42	1,55	1,82	3,61
EU-15	0,94	1,42	0,44	0,67	0,86	1,09	1,29	1,48	1,78	2,81
EU-N12	0,72	0,47	0,40	0,78	1,17	1,53	1,76	1,87	2,11	7,84
EU-N13	0,72	0,47	0,40	0,78	1,17	1,53	1,77	1,88	2,11	7,86

2. of plant protection products (PPP)

The use of PPP plays an important role in EU agricultural production. Farmers use PPP to ensure less weed and pest damage to crops and a consistent yield. Therefore, as the availability of PPP is expected to be impacted by the future endocrine disruptors (EDs) criteria as these might result in the non-approval of substances, farmers are one of the main stakeholders that will be impacted as they use PPP for their production.

There are three main types of PPP:

- fungicides[7]: used for the control of fungi.
- herbicides[7]: used for the control of unwanted plants or weeds.
- insecticides[7]: used for the control of insects.

In the EU, since the 90s, PPP are regulated products that need to be authorised before being placed on the market (Regulation (EC) No 1107/2009, which replaced Directive 91/414/EC). This pre-market approval system is considered as one of the strictest worldwide: any PPP must be authorised before it can be placed on the market and used. Only PPP which contain active substances placed on a "positive list" can be authorised for use in the EU, if the use has been considered not to cause adverse effects on human or animal health or unacceptable effects on the environment.

The EU pesticides database[8] on active substances summarises the active substances assessed so far (both approved and not approved). Currently, there are 482 active substances approved on the EU market which can be used in PPP and which include low risk substances and microorganisms: 147 fungicides, 123 herbicides, 98 insecticides, and 114 other type (e.g. repellent, rodenticide, attractant, etc.) (Figure 1).

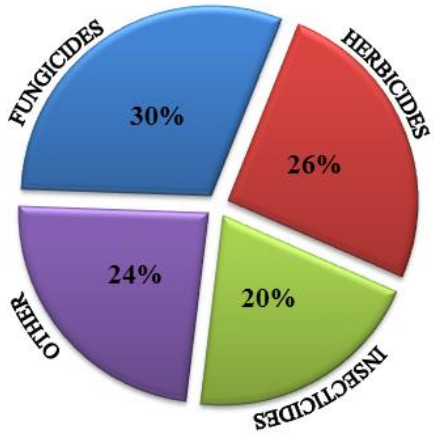

Figure 1. Approved active substances to be used in PPP in the EU, by 01/01/2016.

[7] Stephenson G.R., Ferris I.G., Holland P.T., Nordberg M., 2006. Glossary of terms relating to pesticides (IUPAC Recommendations 2006), Pure Appl. Chem., Vol. 78, No. 11, pp. 2075–2154. doi:10.1351/pac200678112075. Retrieved from: http://www.iupac.org/publications/pac/2006/pdf/7811x2075.pdf

[8] EU pesticides database on active substances. Available on: http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.selection&language=EN

3. Assessment of potential impacts on agriculture

In the public consultation carried out in the context of this impact assessment (IA) (September 2014 to January 2015) many farmers and agricultural producers responded. In total 488 web-based and 33 email responses were received from agricultural producers/farmers.

About 57% of web-based responses submitted on behalf of an organisation came from agricultural producers/farmers. A high proportion of those who answered expressed concerns about the potential disappearance of key PPP and the high yield losses that would result from this. They also mentioned the linked resistance problem, i.e. if only a few similar types of PPP remain available, the development of resistance of diseases to these products will take place faster and more frequently, creating a problem for agricultural production. In addition, they mentioned the fact that there might be no suitable substitutes for some of the substances that may no longer be available.

Given the feedback received from farmers and the importance of agriculture for the EU, the criteria illustrated under section 3.2 were chosen to compare how the different options (1 to 4 and A to C) would impact the competitiveness of EU agriculture.

All criteria are based in first instance on the results of the screening study (see Annex 5) and consider the impacts derived from the regulatory consequences (a non-approval of the active substance in the worst case) on other aspects. The results of the screening were filtered for other "cut off" criteria 1) none of the substances identified as ED were classified or to be classified as M1 nor persistent in the environment (see Annex 5), 2) substances which are classified or to be classified as C1, or R1 were flagged and not considered for the assessment of the impacts on agriculture. In this way, substances which are already having regulatory consequences under Regulation (EC) No 1107/2009 under consideration of other "cut off" criteria are not double counted.

The assessment focused on PPP used in agriculture (including horticulture), while forestry and amenity areas were not considered. A series of additional data have been considered for this assessment. In section 3.1 below, the additional data used and the selected criteria are briefly described. In first instance the analysis will be used to assess the performance of options 1 to 4. Options A to B are linked to the decision making, with Option C affecting less active substances than B and A in all cases.

3.1. Additional Data used for the assessment

In order to carry out the analysis of the impacts on EU agriculture, the following datasets and information sources have been used.

1) EU Pesticide Database

The EU Pesticide Database[8] has been used to obtain information on active substances. For each active substance the database also indicates to which sub-group of pesticides it belongs (e.g. herbicide, fungicide, or insecticide).

2) Data supplied by Member States (MS)

The PPP Application Management System (PPPAMS) was developed by the European Commission to support MS in fulfilling their legal obligations under Regulation (EC) No 1107/2009, notably Article 57(1) and (2). The objectives of the PPPAMS are harmonisation of the formal requirements for application of PPP, streamline mutual recognition of authorisations to speed up time to market, improve the management of the evaluation process for authorisation of PPP, and deliver correct and timely information on authorised or withdrawn PPP to stakeholders.

The process on building up the PPPAMS is on-going. In its context, in June 2015 and in order to compile data for the IA, the European Commission sent a request to MS to provide information on existing authorisations of PPP and their use at national level for the IA. This data should be kept available by MS according to article 57 of Regulation (EC) 1107/2009.

Complete datasets on existing authorisations of PPP and their use at national level were available by 1 January 2016 for Estonia, Germany, Austria, Belgium, the Netherlands, Czech Republic, Slovenia, and Greece[9]. With exception of Estonia representing the Northern zone and Greece representing the Southern zone, all other data are from the Central zone.

The data were processed by the Commission services. After receiving the data from the MS (in most of the cases, the data were provided in their national language), they were checked by the Commission services to ensure conformity with a common language (EPPO codes for crops and pests).[10] However, a final quality check by the corresponding MS has not been done yet.

3) Eurostat data

Regulation (EC) No 1185/2009 requests MS to submit data on sales and use of pesticides to the Commission (Eurostat). This regulation also provides that for confidentiality reasons the Commission aggregates the data before publication.

The data on sales of actives substances for the following 11 MS that have agreed to the disclosure of the documents in an earlier case (GestDem 2015/2182) was available for the assessment: Belgium, Bulgaria, Czech Republic, Denmark, Finland, France, Italy, Luxembourg, Malta, Slovenia and Sweden. After assessing the data for these 11 MS, it was analysed if they correlate with the data for EU 27 based on the complete set of data. However, as Regulation 1185/2009 does not allow the Commission to produce any statistics on active substance level, the annex containing these data is kept separate and confidential (Annex 13).

[9] According to Regulation (EC) 1107/2009, there are three zones in the EU. The following MS belong to:
Zone A (North): Denmark, Estonia, Latvia, Lithuania, Finland, Sweden;
Zone B (Centre): Belgium, Czech Republic, Germany, Ireland, Luxembourg, Hungary, Netherlands, Austria, Poland, Romania, Slovenia, Slovakia, United Kingdom;
Zone C (South): Bulgaria, Greece, Spain, France, Italy, Cyprus, Malta, Portugal

[10] European and Mediterranean Plant Protection Organization (EPPO) Global Database. Available on: https://gd.eppo.int/

3.2. Selection of Criteria

(a) Number of PPP that would be affected

Because of the two step approach of the EU legislation concerning PPP (approval of active substances at EU level, authorisation of PPP uses at national level) there may be more or less PPP uses authorised at EU level for each active substance, and this may also vary across MS.

In order to assess the number of PPP that would be affected, a "worst case scenario" is used as a starting point: PPP active substances that would be identified as ED would not be approved and would therefore no longer be available on the EU28 market for use in PPP. The application of derogations, which would actually reduce the impacts, under the provisions of negligible exposure or Article 4.7 of Regulation 1107/2009 are assumed to apply equally (in the same proportion) to all options and therefore not considered to play a role for a relative ranking of the options. They were as a consequence not considered for the purposes of simplification.

For each non-approved active substance at EU level, the number of PPP authorisations at national level that would be affected has been assessed. It is assumed that the higher the number of PPP that would potentially disappear from the market, the higher the likely impacts for farmers. As mentioned before, farmers are considered SMEs. Since evidence to quantitatively assess the impacts in terms of yield losses of the potential disappearance of one single substance is lacking, a more detailed analysis of the agricultural impacts could not be carried out.

The potential disappearance of certain PPP active substances, and consequently of certain PPP, may result in the rising production prices of some crops and agriculture commodities. This might be passed on to consumers who may find it difficult to manage any significant increase in food prices and may reduce their consumption of fresh products. It might also result in a change of diet for consumers (they could for instance consume more substitute products).

Consumption expenditure "*is what people, acting either individually or collectively, spend on goods and services to satisfy their needs and wants. A household's economic well-being can be expressed in terms of its access to goods and services. The more that can be consumed, the higher the level of economic well-being, though the relationship between the two is not a linear one. Measuring consumption expenditure might, therefore, be a way of measuring economic well-being*." [11]

There are different household consumption habits across the EU; culture, income, weather, household composition, economic structure and degree of urbanisation are all factors that can have an impact on habits in each MS.[11]

In national accounts, the final consumption expenditure of households *"is the biggest component of the expenditure approach to GDP. Its evolution allows an assessment of*

[11] EUROSTAT. 2013. Statistics explained. Household consumption expenditure - background. Available on: http://ec.europa.eu/eurostat/statistics-explained/index.php/Household_consumption_expenditure_-_background

purchases made by households, reflecting changes in wages and other incomes, but also in employment and in savings behaviour."[11]

According to Eurostat, in 2012 food represented on average 16% of household expenditure in the EU 27. Bread and cereals, meat, fish and dairy products represented on average 17%, 25%, 3 % and 19 % of household expenditure on food respectively for 2012.[12]

- Oils and fats, fruits, vegetables and potatoes as well as other food products represent on average 5%, 20% and 12% of household expenditure for food respectively.[12]
- Bread and cereals therefore represented on average 2.72% of household expenditure in 2012 in the EU 27.[12]
- Fruits, vegetables and potatoes represented on average 3.2% of household expenditure in 2012 in the EU 27.[12]

It can be assumed that the higher the impact on agricultural production resulting from the potential loss of some PPP, the higher the likelihood of having impacts on the end consumer.

(b) Crops affected

Based on the available MS data, the number of crops for which PPP authorisations would be affected has been identified. This assessment was done at genus level[13] due to the fact that this level of information was considered as the most reliable and consistent one given the data collected. It is assumed that the longer the list of crops concerned by the disappearance of certain active substances, the higher the impacts for EU agriculture and farmers will be.

This criterion is considered important because some of the main problems with losing part of the PPP portfolio are an increased risk of yield losses due to pests and fungi where there is no other effective PPP available, and an increased risk of pests developing resistance to PPP due to reduced number of alternatives (this is discussed under the third criterion). Farmers might react in different ways to these impacts: they could either go out of business or might decide to change crops. The price of their products might also increase and this could eventually impact end consumers (see previous section).

(c) Existence of alternatives / risk of resistance of pests (see Annex 10)

Regulation (EC) No 1185/2009 classifies the active substances by chemical class. In order to carry out an analysis on the existence of alternatives (both chemicals and micro-organisms falling under Regulation (EC) No 1107/2009), in a first step, the proportion of active substances identified as ED under each of the options by chemical class and major group (fungicide, herbicide, insecticide) was calculated.

[12] EUROSTAT. 2012. Statistics explained. Comparative price levels for food, beverages, and tobacco. Available on: http://ec.europa.eu/eurostat/statistics-explained/index.php/Comparative_price_levels_for_food,_beverages_and_tobacco

[13] "A genus is a principal taxonomic category that ranks above species and below family, and is denoted by a capitalized Latin name, e.g. Leo. " Retrieved from http://www.oxforddictionaries.com/definition/english/genus

It is assumed that the higher the percentage of chemical class affected, the lower the number of alternatives existing. It is acknowledged that for some crops, only one particular active substance is effective/efficient and therefore its loss might lead to higher impacts for the crop production than the data shown. However, the level of detail and of reliability of additional data at the disposal of the Commission did not allow for a more detailed analysis.

It is assumed that the lower the number of alternatives existing for a crop/pest, the higher the potential risks of resistance appearance in pests are. This could decrease sustainability of agriculture as farmers would not have at their disposal a wide range of PPP to make it possible to select and rotate products that are appropriate for the crop/pest situation, avoiding thus resistance development through repeated use of the same active substances. This aspect is important from an agricultural point of view, as recognised by on-going international activities focusing on this topic and done by the European and Mediterranean Plant Protection Organisation (EPPO[14]) and the Food and Agriculture Organisation of the United Nations (FAO).

Other crop management methods (e.g. resistant varieties) are not mentioned in this analysis because they can vary significantly from one MS to another, depending on the climatic/agronomic and the market expectation in a given MS. Therefore, no general conclusion for a particular crop could be drawn, however the analysis is considered suitable to illustrate a general outcome.

Similar calculations were performed for the volumes of sales of these active substances for 11 MS[15] for which Eurostat data were available for the years 2011; 2012 and 2013. The analysis and results of these data is kept as confidential due to the provisions of Regulation (EC) No 1185/2009 (Annex 13).

3.3. Expected impacts of the different options on agricultureResults of the screening

The substances identified as ED under any of the options considered for the screening are listed below in Table 3.

The substances identified as EDs in the screening were filtered for other "cut off" criteria 1) none of the substances identified as ED were classified or to be classified as M1 nor persistent in the environment (see Annex 5), 2) substances which are classified or to be classified as C1, or R1 were flagged and not considered for the impacts on agriculture.

Figure 2 summarises the number of active substances identified as ED under each of the four options with regulatory consequences by PPP major group (excluding substances which are also classified as C1 or R1, or substances being identified as candidate for substitution because of persistency) as follows:

[14] EPPO 2015. PP 1/213 (4) Resistance risk analysis. Bulletin OEPP/EPPO Bulletin (2015) 45 (3), 371–387 ISSN 0250-8052. DOI: 10.1111/epp.12246.

[15] An average was calculated for the years 2011;2012;2013 for the following MS: BE, BG, CZ, DK, FI, FR, IT, LU, MT, SE, SI

- under Option 1, 13.6% of the fungicides, 13% of the herbicides, and 3% of the insecticides currently on the market would be non-approved;
- under Option 2 and 3 Category I, these percentages are reduced to 8.8%, 7.3% and 4.1%, respectively;
- under Option 4, fungicides and herbicides are further reduced to 4% and 0.8 %, while the percentage for insecticides remains as for Option 2 and Option 3.

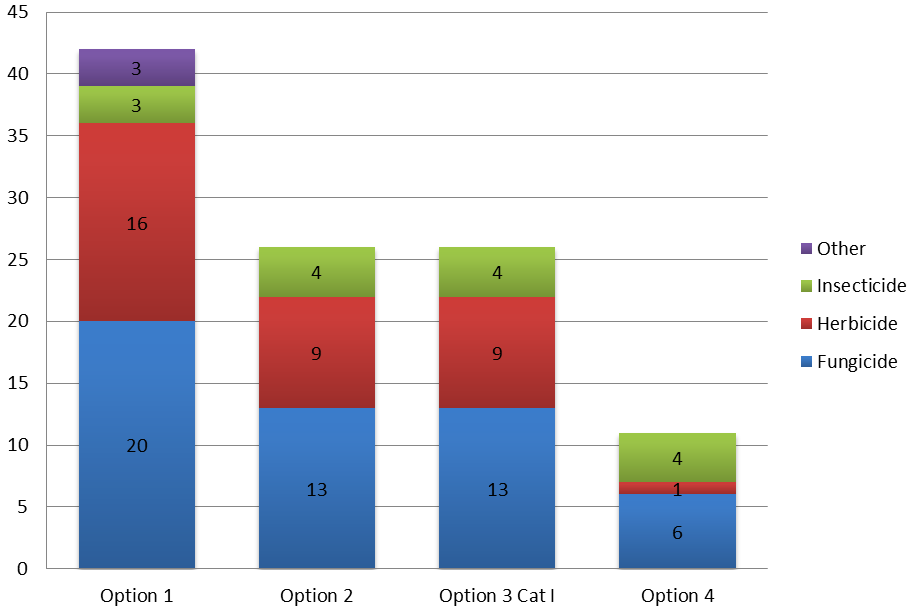

Figure 2. Number of substances identified as ED by PPP major group excluding substances which are also C1 or R1

Table 3. Active substances currently approved for their use in PPP identified as ED under the different options (excluding substances which are also C1, R1):

Option 1 (42)	Option 2 and 3 Category I (26)	Option 4 (11)
1-Naphthylacetamide	2,4-D	8-hydroxyquinoline
1-Naphthylacetic acid	8-hydroxyquinoline	Cypermethrin
8-hydroxyquinoline	Boscalid	Fenamidone
Abamectin	Cypermethrin	Flubendiamide
Benthiavalicarb	Desmedipham	Malathion
Bromoxynil	Fenamidone	Mancozeb
Captan	Flubendiamide	Metiram
Chlorotoluron	Iprodione	Pendimethalin
Cycloxydim	Lenacil	Spirodiclofen
Cymoxanil	Malathion	Tetraconazole
Dazomet	Mancozeb	Ziram
Dimoxystrobin	Maneb	
Fenbuconazole	Metiram	
Fenpropimorph	Myclobutanil	
Fluazifop-P-butyl	Oxadiazon	
Fluazinam	Pendimethalin	
Flupyrsulfuron-methyl	Propyzamide	
Halosulfuron methyl	Spirodiclofen	
Hymexazol	Tebuconazole	
Indolylbutyric acid	Tepraloxydim	
Ipconazole	Tetraconazole	
Isoproturon	Thiophanate-methyl	
Isopyrazam	Thiram	
Isoxaflutole	Tralkoxydim	
Maneb	Triflusulfuron	
Metam	Ziram	
Metconazole		
Metribuzin		
Myclobutanil		
Prochloraz		
Profoxydim		
Prothioconazole		
Pymetrozine		
Quinoclamine		
Quizalfop-P		
Spirotetramat		
Spiroxamine		
Tebuconazole		
Tembotrione		
Tepraloxydim		
Thifensulfuron-methyl		
Triadimenol		

3.4. Number of PPP that would be affected

Figure 3 indicates the number of PPP that would potentially be affected[16] at national level following the non-approval of the active substances that would be identified as ED under the different options at EU level. Table 7 to Table 14 provide details of the number of PPP authorisations by active substance for the eight MS for which data was available.

One authorised product at national level could contain several active substances identified as ED. This is the reason why the total number of authorisations per option may differ from the sum of occurrences for the active substances under the same option.

It is assumed that the higher the number of PPP that will potentially disappear from the market, the higher the likely impacts for farmers. In addition, it is also assumed that the impact on SMEs would be higher, as farmers are mainly SMEs. Intuitively, one would think that the higher the number of actives substances identified as ED, the higher the number of PPP authorisations that would be affected. Such an assumption would lead to Option 1 (the one identifying the highest number of active substances as ED) being the one performing the worst but the evidence available for the 8 MS which provided data did not confirm this in most of the cases. Figure 3Figure 3 summarises the number of PPP that would be affected per option for all the MS for which data was available. Table 4 illustrates the performance of the options for each MS analysed and the overall performance.

In all analysed MS, Option 4 is the one performing the best as it would lead to the potential disappearance of the lowest number of PPP. The second best option is Option 1 (interim ED) for all countries, except for the Czech Republic and the Netherlands, as it is the one that would lead to the potential disappearance of the second lowest number of PPP. The third best option is Option 2 and Option 3 Category I. In summary, Option 4 performs better than Option 1, which performs better than Option 2 and 3, i.e. 4 > 1 > 2/3.

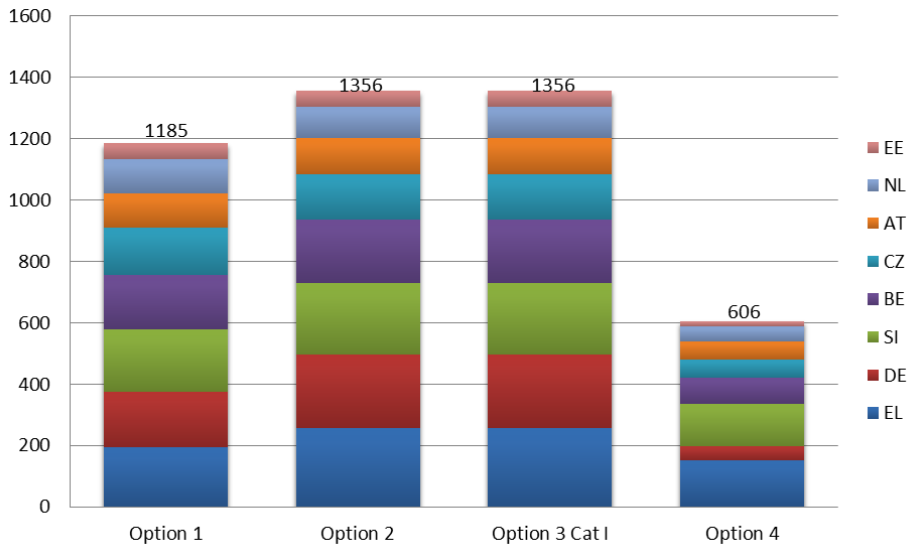

Figure 3. Number of PPP that would be affected under Option 1, Option 2, Option 3 Category I, and Option 4, divided by MS.

[16] PPP affected imply PPP authorisations affected at MS level.

Table 4. Ranking of options - criterion I: No of PPP affected

RANKING OF OPTIONS CRITERION I

Zone	Member State	Performance	No of PPP affected		
			Option 1	Option 2 and 3 Category I	Option 4
Northern	ESTONIA	4>1/2/3	51	51	18
Central	GERMANY	4>1>2/3	179	240	47
Central	AUSTRIA	4>1>2/3	112	121	58
Central	SLOVENIA	4>1>2/3	204	233	136
Central	CZECH REPUBLIC	4>2/3>1	154	146	59
Central	BELGIUM	4>1>2/3	178	206	88
Central	NETHERLANDS	4>2/3>1	112	101	49
Southern	GREECE	4>1>2/3	195	258	151
-	**Total (8 MS)**	**4>1>2/3**	**1185**	**1356**	**606**

3.5. Crops affected

The information on the crops affected in each of the MS for which data is available is given at genus[17] level in Table 15 to Table 22 at the end of this annex.

It can be assumed that the longer the list of crops concerned by the disappearance of certain active substances, the higher the impacts for EU agriculture and farmers will be. Intuitively, one would think that the higher the number of actives substances identified as ED, the higher the number of crops that would be affected. Such an assumption would lead to Option 1 (the one identifying the highest number of active substances as ED) being the one performing the worst but the evidence available for the 8 MS which provided data did not confirm this in most of the cases. For certain crops, no or very few possibilities will remain to control pests and diseases with pesticides. The yields could be reduced. In all these potential cases, end consumers would also be affected (see remarks on consumers in Section 3.2 (b)).

In all these MS, Option 4 is the one performing the best as it would affect the lowest number of crops at genus level.

For all the countries for which data is available, except for Austria and the Netherlands, the second best option is Option 1 (interim ED) as it is the one that would affect the second lowest number of crops at genus level and the third best option is Option 2 and Option 3 category I. In summary, Option 4 performs better than Option 1, which performs better than Option 2 and 3, i.e. 4 > 1 > 2/3

[17] For further information on what each genus refers to the European and Mediterranean Plant Protection Organization (EPPO) Global Database, available on: https://gd.eppo.int/

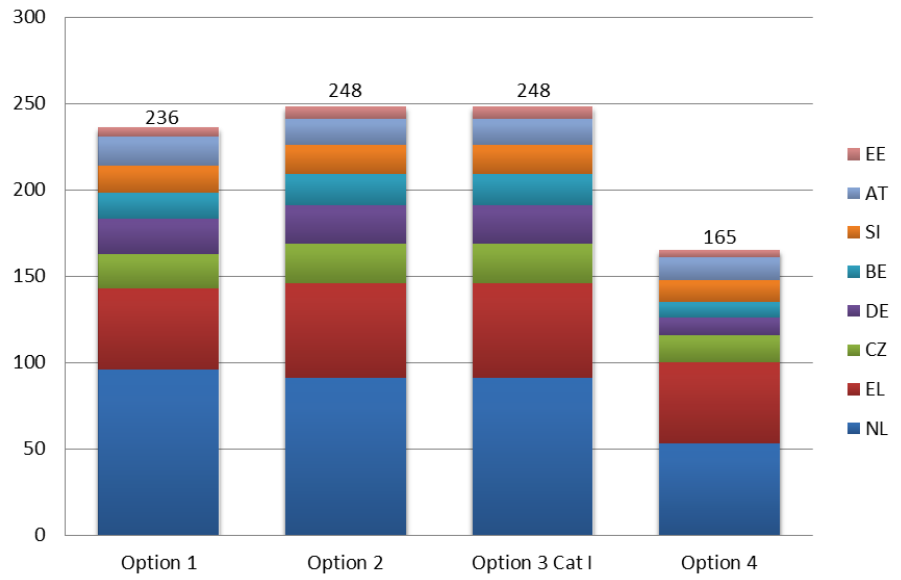

Figure 4. Number of crops (genus level) that would be affected under Option 1, Option 2, Option 3 Category I, and Option 4, divided by MS.

Table 5. Ranking of options - criterion II: No of crops (genus level) affected

RANKING OF OPTIONS CRITERION II

Zone	Member State	Performance	No of crops affected (genus level)		
			Option 1	Option 2 and 3 Category I	Option 4
Northern	ESTONIA	4>1>2/3	5	7	4
Central	GERMANY	4>1>2/3	20	22	10
Central	AUSTRIA	4>2/3>1	17	15	13
Central	SLOVENIA	4>1>2/3	16	17	13
Central	CZECH REPUBLIC	4>1>2/3	20	23	16
Central	BELGIUM	4>1>2/3	15	18	9
Central	NETHERLANDS	4>2/3>1	96	91	53
Southern	GREECE	4/1>2/3	47	55	47
	TOTAL (8 MS)	4>1>2/3	**236**	**248**	**165**

3.6. Existence of alternatives and the risk of resistance of pests

In order to carry out an analysis on the existence of alternatives (both chemicals and micro-organisms falling under Regulation (EC) No 1107/2009), in a first step, the chemical classes that would be affected by the potential non approval of the active substances identified as EDs under the different options were assessed. Chemical classes are defined in Annex III to Regulation 1185/2009, as last updated by Commission Regulation No 656/2011.

This information was first analysed in terms of percentage of active substances that would be affected per chemical class and major group (e.g. herbicides, fungicides, and insecticides) – Table 6 based on the number of active substances that would be identified as ED.

It is assumed that the higher the percentage of chemical class affected, the lower the number of alternatives existing. It is acknowledged that for some crops, only one particular active substance is effective/efficient and therefore its loss might lead to higher impacts for the crop production than the data shown. However, the level of detail and of reliability of additional data at the disposal of the Commission did not allow for a more detailed analysis.

It is assumed that the lower the number of alternatives existing for a crop/pest, the higher the potential risks of resistance appearance in pests are. This could decrease sustainability of agriculture as farmers would not have at their disposal a wide range of PPP to make it possible to select and rotate products that are appropriate for the crop/pest situation, avoiding thus resistance development through repeated use of the same active substances.

Other crop management methods (e.g. resistant varieties) are not mentioned in this analysis because they can vary significantly from one MS to another, depending on the climatic/agronomic and the market expectation in a given MS. Therefore, no general conclusion for a particular crop could be drawn because a method that is valid for one crop in a given MS is not necessarily valid for the same crop in another MS.

Similar calculations were performed for the volumes of sales of these active substances for 11 MS[18] for which Eurostat data was available for the years 2011; 2012 and 2013. An average was calculated for the three years and used as a basis for the analysis. Further, the correlation of the average volume of sales for the years 2011; 2012 and 2013 and the whole EU 27 was calculated to assess whether the trends observed for the 11 MS were valid for the EU27.

When looking at the percentage of each chemical class identified as EDs during the screening, the data show for instance that for a total of four active substances belonging to the cyclohexanedione herbicides chemical class being on the market, under Option 1, 75% of them would be affected. Under Option 2 and Option 3 Category 1, 50% of them would be affected and under Option 4, this chemical class would not be affected at all. The lowest impact for this chemical class would therefore be under Option 4 as it would not be affected at all.

Figure 5 indicates the percentage of chemical class affected per option, based on the number of active substances. Option 1 (interim ED criteria) is the one affecting the chemical classes the most heavily. It has the highest number of occurrences where it would affect between 67 and 100% of a given chemical class. It has the highest number of occurrences where it would affect between 34 and 66% of a given chemical class. The same trend is observed for chemical classes affected in a proportion going from 0 to 33%. Option 1 is therefore the worst performing option under this criterion as it implies that there would be fewer alternatives available on the market to control pests.

Option 4 (WHO definition and inclusion of potency as element of hazard characterisation) would be the best performing one under this criterion as it would affect the lowest number of chemical classes. Besides, even within the chemical classes it would affect, it would affect them to a lower degree: there are no cases in which Option 4 affects between 67 and 100% of

[18] An average was calculated for the years 2011;2012;2013 for the following MS: BE, BG, CZ, DK, FI, FR, IT, LU, MT, SE, SI

a chemical class. There are only 5 cases in which Option 4 affects between 34 and 66% of a chemical class and only 4 cases in which it affects a chemical class between 0 and 33%.

Similar calculations were performed for the volumes of sales of these active substances for 11 MS[19] for which Eurostat data was available for the years 2011; 2012 and 2013. They are reported in a confidential annex (Annex 13) due to the provisions of Regulation (EC) No 1185/2009. The results of this annex confirm the same trend.

Option 4 is the one affecting the less heavily the chemical classes, even when looking at the average volumes of sales for the years 2011; 2012 and 2013 in the 11 MS.

To summarise, the performance of the four options would be 4 > 2/3 > 1.

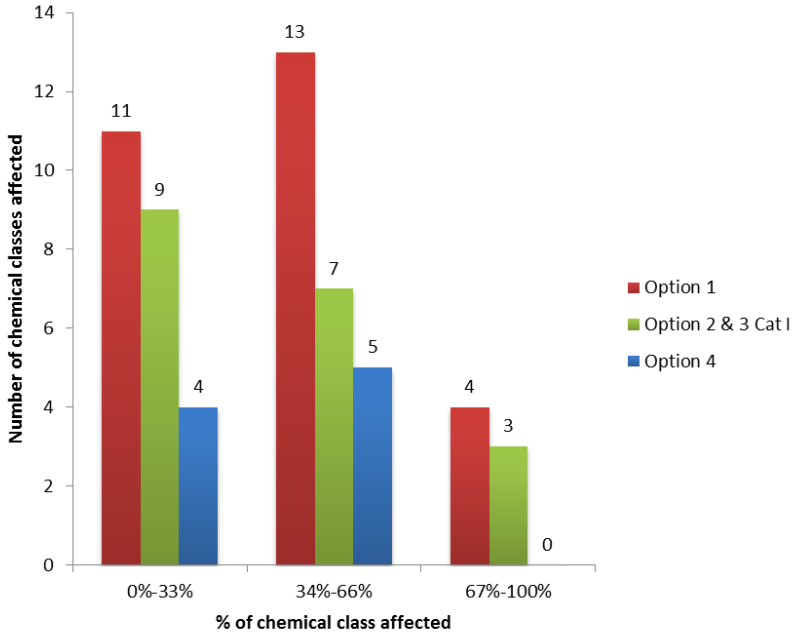

Figure 5.[20] How many chemical classes and to which extent each of the options (in percentages) affects the PPP chemical classes, based on the number of active substances identified as EDs

[19] An average was calculated for the years 2011;2012;2013 for the following MS: BE, BG, CZ, DK, FI, FR, IT, LU, MT, SE, SI

[20] Figure 5 is a graphical explanation of Table 6. Each bar represents the share of identified EDs within the chemical class, i.e. to which extent a chemical class is affected by the options. If there are two active substances in a chemical class and one of them is identified as an ED it would mean that 50% of the chemical class is affected and will be counted in the bin 34%-66%. This is calculated for each chemical class for each option. The aggregated result is presented in the graph. The higher the bar, the more chemical classes are affected to that certain extent (bin).

Table 6. Percentage of each chemical class[21] identified as EDs during the screening performed in the framework of this IA for each of the four options.

	Chemical class	Approved AS	Option 1	Option 2 and 3 Category I	Option 4
FUNGICIDES	ALIPHATIC NITROGEN FUNGICIDES	2	50%		
	AMIDE FUNGICIDES	7	14%	14%	
	ANILIDE FUNGICIDES	13	8%		
	BENZIMIDAZOLE FUNGICIDES	3		33%	
	CARBAMATE FUNGICIDES	3	33%		
	CONAZOLE FUNGICIDES***	20	35%	15%	5%
	DICARBOXIMIDE FUNGICIDES	1		100%	
	DINITROANILINE FUNGICIDES	1	100%		
	DITHIOCARBAMATE FUNGICIDES	6	17%	83%	50%
	IMIDAZOLE FUNGICIDES	3		33%	33%
	MORPHOLINE FUNGICIDES	3	33%		
	OXAZOLE FUNGICIDES	2	50%		
	PHTHALIMIDE FUNGICIDES	2	50%		
	QUINOLINE FUNGICIDES	2	50%	50%	50%
	STROBILURINE FUNGICIDES	7	14%		
	UNCLASSIFIED FUNGICIDES	13	8%		
HERBICIDES	AMIDE HERBICIDES	8		13%	
	ANILIDE HERBICIDES	6	17%		
	ARYLOXYPHENOXY- PROPIONIC HERBICIDES	10	20%		
	BIS-CARBAMATE HERBICIDES	3		33%	
	CARBAMATE HERBICIDES***	1			
	CYCLOHEXANEDIONE HERBICIDES	4	75%	50%	
	DINITROANILINE HERBICIDES	3		33%	33%
	ISOXAZOLE HERBICIDES	2	50%		
	NITRILE HERBICIDES	1	100%		
	PHENOXY HERBICIDES	7		14%	
	SULFONYLUREA HERBICIDES	21	10%	5%	
	TRIAZINONE HERBICIDES	2	50%		
	TRIAZOLE HERBICIDES***	1			
	TRIKETONE HERBICIDES	3	33%		
	UNCLASSIFIED HERBICIDES***	8	13%	13%	
	URACIL HERBICIDES	1		100%	
	UREA HERBICIDES***	5	40%		
INSECTICIDES	INSECTICIDES PRODUCED BY	5	20%		
	ORGANOPHOSPHORUS INSECTICIDES	9		11%	11%
	PYRAZOLE (PHENYL-) INSECTICIDES	5		20%	20%
	PYRETHROID INSECTICIDES	13		8%	8%
	PYRIDINE INSECTICIDES	2	50%		
	PYRIDYLMETHYLAMINE INSECTICIDES***	3			
	TETRONIC ACID INSECTICIDES	2		50%	50%
	UNCLASSIFIED INSECTICIDES-ACARICIDES	27	4%		
OTHER	OTHER PHYSIOLOGICAL PLANT GROWTH	9	33%		
	OTHER SOIL STERILANTS	3	67%		
	RODENTICIDES***	5			

(Chemical classes identified with *** include substances identified as ED, which are falling under the "cut-off" criteria and were excluded from the calculation of the percentages).

[21] as defined in Regulation EC No 1185/2009

3.7. Performance of options A to C for all criteria related to EU agriculture

While all options applied under the current legislative framework in the PPP sector (Option A) may lead to an impact on agriculture because of a decision making based mainly on hazard, Option B would allow proportionate decision making based on more risk elements and would thus have less impact on agriculture than Option A. Option C would allow consideration of socio-economic aspects during the regulatory decision making, which is so far the case only for limited derogations of reduced scope. Thus, the options would perform this way: C>B>A.

3.8. Tables - Number of PPP that would be affected

Tables 7 to 14 provide information on which active substances will be affected under each option and how many authorisations they have in each MS for which data was available. The number of authorisations per active substance is listed as 'occurrences per active substances (AS)'. Note that the total number of authorisations per option may differ from the sum of occurrences because one authorisation may contain more than one active substance. The order of the tables is:

- Table 7 Estonia
- Table 8 Germany
- Table 9 Austria
- Table 10 Slovenia
- Table 11 Czech Republic
- Table 12 Belgium
- Table 13 Netherlands
- Table 14 Greece

Table 7. Number of PPP authorisations that would be affected in Estonia[22].

ESTONIA					
Option 1		**Option 2 & 3 Category I**		**Option 4**	
Authorisations	**51**	**Authorisations**	**51**	**Authorisations**	**18**
Active Substance	Occurrences per AS	Active Substance	Occurrences per AS	Active Substance	Occurrences per AS
Tebuconazole	15	Tebuconazole	15	Mancozeb	9
Prothioconazole	10	Mancozeb	9	Pendimethalin	6
Prochloraz	5	Boscalid (formerly nicobifen)	7	Cypermethrin	2
Fluazinam	5	2,4-D	7	Fenamidone	1
Metconazole	5	Pendimethalin	6		
Fenpropimorph	4	Cypermethrin	2		
Spiroxamine	2	Thiophanate-methyl	1		
Metribuzin	2	Desmedipham	1		
Dimoxystrobin	2	Iprodione	1		
Pymetrozine	1	Thiram	1		
Abamectin (aka avermectin)	1	Fenamidone	1		
Isoproturon	1				
Chlorotoluron	1				
Triadimenol	1				
Fluazifop-P	1				
Cycloxydim	1				

[22] One authorised product at national level could contain several active substances identified as ED. This is the reason why the total number of authorisations per option may differ from the sum of occurrences for the active substances under the same option.

Table 8. Number of PPP authorisations that would be affected in Germany[22].

GERMANY					
Option 1		**Option 2 & 3 Category I**		**Option 4**	
Authorisations	**179**	**Authorisations**	**240**	**Authorisations**	**47**
Active Substance	Occurrences per AS	Active Substance	Occurrences per AS	Active Substance	Occurrences per AS
Tebuconazole	39	2,4-D	102	Mancozeb	21
Bromoxynil	18	Tebuconazole	39	Pendimethalin	9
Prothioconazole	16	Mancozeb	21	Cypermethrin	5
Fluazinam	11	Propyzamide	14	Tetraconazole	5
Thifensulfuron-methyl	10	Pendimethalin	9	Metiram	4
Cymoxanil	10	Myclobutanil	8	Fenamidone	2
Myclobutanil	8	Boscalid (formerly nicobifen)	8	Spirodiclofen	1
Chlorotoluron	8	Desmedipham	6		
Abamectin (aka avermectin)	8	Thiophanate-methyl	5		
Prochloraz	8	Tetraconazole	5		
Isoproturon	7	Cypermethrin	5		
Fenpropimorph	7	Thiram	5		
Metribuzin	6	Metiram	4		
Isopyrazam	5	Triflusulfuron	3		
Metconazole	4	Fenamidone	2		
Flupyrsulfuron-methyl (DPX KE 459)	4	Maneb	2		
Triadimenol	4	Iprodione	2		
Spiroxamine	4	Lenacil	1		
Captan	3	Spirodiclofen	1		
Maneb	2				
Benthiavalicarb	2				
Dimoxystrobin	2				
Quinoclamine	2				
Tembotrione	2				
Cycloxydim	1				
Fluazifop-P	1				
Hymexazol	1				
Spirotetramat	1				
Pymetrozine	1				
Isoxaflutole	1				

Table 9. Number of PPP authorisations that would be affected in Austria[22].

AUSTRIA					
Option 1		**Option 2 & 3 Category I**		**Option 4**	
Authorisations	**112**	**Authorisations**	**121**	**Authorisations**	**58**
Active Substance	Occurrences per AS	Active Substance	Occurrences per AS	Active Substance	Occurrences per AS
Cymoxanil	21	2,4-D	38	Mancozeb	33
Fluazinam	11	Mancozeb	33	Cypermethrin	11
Prochloraz	11	Cypermethrin	11	Pendimethalin	8
Metribuzin	9	Desmedipham	9	Ziram	2
Spiroxamine	8	Pendimethalin	8	Metiram	2
Captan	8	Myclobutanil	7	Malathion	1
Myclobutanil	7	Lenacil	4	Spirodiclofen	1
Bromoxynil	6	Thiram	4		
Isoproturon	4	Triflusulfuron	3		
Tembotrione	4	Metiram	2		
Quizalofop-P	3	Ziram	2		
Isoxaflutole	3	Spirodiclofen	1		
Cycloxydim	3	Maneb	1		
Ipconazole	2	Malathion	1		
Fluazifop-P	2				
Fenpropimorph	2				
Spirotetramat	2				
Isopyrazam	2				
Dimoxystrobin	1				
Dazomet	1				
Pymetrozine	1				
Hymexazol	1				
Maneb	1				

Table 10. Number of PPP authorisations that would be affected in Slovenia[22].

SLOVENIA					
Option 1		**Option 2 & 3 Category I**		**Option 4**	
Authorisations	**204**	**Authorisations**	**233**	**Authorisations**	**136**
Active Substance	Occurrences per AS	Active Substance	Occurrences per AS	Active Substance	Occurrences per AS
Tebuconazole	49	Mancozeb	73	Mancozeb	73
Thifensulfuron-methyl	18	Tebuconazole	49	Pendimethalin	22
Captan	15	Pendimethalin	22	Tetraconazole	13
Metribuzin	15	Thiram	16	Metiram	11
Triadimenol	10	Tetraconazole	13	Spirodiclofen	9
Cycloxydim	9	Metiram	11	Ziram	8
Dazomet	9	Spirodiclofen	9		
Tembotrione	8	Propyzamide	8		
Fluazinam	8	Ziram	8		
Prochloraz	7	Boscalid (formerly nicobifen)	8		
Pymetrozine	6	Tepraloxydim	5		
Chlorotoluron	6	Thiophanate-methyl	5		
Fenbuconazole	6	Iprodione	4		
Fenpropimorph	5	Myclobutanil	2		
1-Naphthylacetamide (1-NAD)	5				
Tepraloxydim	5				
Isoproturon	4				
Abamectin (aka avermectin)	4				
Metconazole	3				
Quinoclamine	3				
Cymoxanil	3				
Indolylbutyric acid	3				
Myclobutanil	2				
Isoxaflutole	1				

Table 11. Number of PPP authorisations that would be affected in Czech Republic[22].

CZECH REPUBLIC					
Option 1		**Option 2 & 3 Category I**		**Option 4**	
Authorisations	**154**	**Authorisations**	**146**	**Authorisations**	**59**
Active Substance	Occurrences per AS	Active Substance	Occurrences per AS	Active Substance	Occurrences per AS
Tebuconazole	42	Tebuconazole	42	Mancozeb	28
Cymoxanil	19	Mancozeb	28	Pendimethalin	16
Prothioconazole	13	Pendimethalin	16	Tetraconazole	5
Isoproturon	12	2,4-D	14	Cypermethrin	4
Thifensulfuron-methyl	9	Desmedipham	11	Fenamidone	3
Metribuzin	9	Thiram	6	Metiram	2
Prochloraz	8	Tetraconazole	5	Ziram	1
Fluazinam	7	Cypermethrin	4	Malathion	1
Spiroxamine	7	Thiophanate-methyl	4		
Bromoxynil	7	Propyzamide	4		
Fenpropimorph	6	Fenamidone	3		
Captan	4	Myclobutanil	3		
Metconazole	4	Lenacil	2		
Isopyrazam	3	Metiram	2		
Myclobutanil	3	Iprodione	2		
Triadimenol	3	Triflusulfuron	2		
Isoxaflutole	3	Ziram	1		
Tembotrione	2	Malathion	1		
Dimoxystrobin	2				
Ipconazole	2				
Benthiavalicarb	2				
Pymetrozine	1				
Hymexazol	1				
Spirotetramat	1				
Quinoclamine	1				
Dazomet	1				

Table 12. Number of PPP authorisations that would be affected in Belgium[22].

BELGIUM					
Option 1		**Option 2 & 3 Category I**		**Option 4**	
Authorisations	**178**	**Authorisations**	**206**	**Authorisations**	**88**
Active Substance	Occurrences per AS	Active Substance	Occurrences per AS	Active Substance	Occurrences per AS
Cymoxanil	31	Mancozeb	44	Mancozeb	44
Prothioconazole	20	2,4-D	38	Cypermethrin	16
Tebuconazole	18	Tebuconazole	18	Flubendiamide	11
Fluazinam	17	Cypermethrin	16	Pendimethalin	9
Prochloraz	10	Desmedipham	13	Tetraconazole	4
Isoproturon	9	Flubendiamide	11	Fenamidone	3
Myclobutanil	8	Propyzamide	10	Metiram	1
Metribuzin	7	Pendimethalin	9	Spirodiclofen	1
Abamectin (aka avermectin)	6	Iprodione	9		
Captan	6	Myclobutanil	8		
Thifensulfuron-methyl	6	Thiram	7		
1-Naphthylacetamide (1-NAD)	6	Boscalid (formerly nicobifen)	6		
Fenpropimorph	5	Tetraconazole	4		
Isopyrazam	4	Oxadiazon	3		
Tembotrione	4	Lenacil	3		
Spiroxamine	4	Fenamidone	3		
Profoxydim	3	Thiophanate-methyl	2		
Quinoclamine	3	Maneb	2		
Triadimenol	3	Tepraloxydim	2		
Isoxaflutole	3	Spirodiclofen	1		
Bromoxynil	3	Metiram	1		
Tepraloxydim	2				
Dimoxystrobin	2				
Maneb	2				
Hymexazol	1				
Ipconazole	1				
Benthiavalicarb	1				
Spirotetramat	1				
Pymetrozine	1				
Dazomet	1				
Cycloxydim	1				

Table 13. Number of PPP authorisations that would be affected in the Netherlands[22].

NETHERLANDS					
Option 1		**Option 2 & 3 Category I**		**Option 4**	
Authorisations	**112**	**Authorisations**	**101**	**Authorisations**	**48**
Active Substance	Occurrences per AS	Active Substance	Occurrences per AS	Active Substance	Occurrences per AS
Cymoxanil	17	Mancozeb	29	Mancozeb	29
Tebuconazole	15	Tebuconazole	15	Pendimethalin	9
Abamectin (aka avermectin)	13	2,4-D	12	Flubendiamide	3
Fluazinam	8	Pendimethalin	9	Cypermethrin	3
Metribuzin	7	Boscalid (formerly nicobifen)	8	Spirodiclofen	2
Captan	7	Propyzamide	6	Fenamidone	2
Prochloraz	7	Iprodione	5	Metiram	1
Dazomet	6	Flubendiamide	3		
Bromoxynil	5	Cypermethrin	3		
1-Naphthylacetamide (1-NAD)	4	Maneb	3		
Pymetrozine	3	Thiram	3		
Profoxydim	3	Spirodiclofen	2		
Maneb	3	Fenamidone	2		
Thifensulfuron-methyl	2	Lenacil	1		
Metam (incl. -potassium and -sodium)	2	Metiram	1		
Isopyrazam	2				
Isoproturon	2				
Tembotrione	2				
Benthiavalicarb	2				
Cycloxydim	1				
Hymexazol	1				
Spirotetramat	1				
Quinoclamine	1				

Table 14. Number of PPP authorisations that would be affected in Greece[22.]

GREECE					
Option 1		**Option 2 & 3 Category I**		**Option 4**	
Authorisations	**195**	**Authorisations**	**258**	**Authorisations**	**151**
Active Substance	Occurrences per AS	Active Substance	Occurrences per AS	Active Substance	Occurrences per AS
Tebuconazole	28	Mancozeb	77	Mancozeb	77
Cymoxanil	27	Pendimethalin	29	Pendimethalin	29
Abamectin (aka avermectin)	23	Tebuconazole	28	Cypermethrin	27
Myclobutanil	22	Cypermethrin	27	Metiram	6
Captan	18	Myclobutanil	22	Ziram	5
Metam (incl. -potassium and -sodium)	8	2,4-D	15	Fenamidone	3
Fluazinam	7	Iprodione	15	Tetraconazole	3
Bromoxynil	7	Boscalid (formerly nicobifen)	8	Flubendiamide	1
Metribuzin	7	Metiram	6	Spirodiclofen	1
1-Naphthylacetamide (1-NAD)	6	Maneb	6		
Maneb	6	Ziram	5		
Triadimenol	5	Desmedipham	4		
Prochloraz	4	Tetraconazole	3		
Thifensulfuron-methyl	4	Thiram	3		
Profoxydim	3	Fenamidone	3		
Isoxaflutole	3	Propyzamide	3		
Prothioconazole	2	Thiophanate-methyl	2		
Tembotrione	2	Spirodiclofen	1		
Spiroxamine	2	Lenacil	1		
Hymexazol	2	Flubendiamide	1		
Benthiavalicarb	2				
Fenpropimorph	2				
Halosulfuron methyl	1				
Fenbuconazole	1				
Cycloxydim	1				
Spirotetramat	1				
Pymetrozine	1				
Dazomet	1				

3.9. Tables - Number of crops that would be affected (genus level)

Tables 15 to 22 provide information on which crops (genus level) would be affected under each option in each MS for which data was available. The EPPO database[23] can be used to see what species are represented within the genera. The order of the tables is the following:

- Table 15 Estonia
- Table 16 Germany
- Table 17 Austria
- Table 18 Slovenia
- Table 19 Czech Republic
- Table 20 Belgium
- Table 21 Netherlands
- Table 22 Greece

Table 15. Number of crops (genus level) affected in Estonia.

ESTONIA					
Option 1		**Option 2 and 3 Category I**		**Option 4**	
1BEAG	Beta	1BEAG	Beta	1SOLG	Solanum
1BRSG	Brassica	1BRSG	Brassica	1TRFG	Trifolium
1GLXG	Glycine	1FRAG	Fragaria	1TRZG	Triticum
1SOLG	Solanum	1SOLG	Solanum	1TULG	Tulipa
1TRZG	Triticum	1TRFG	Trifolium	**TOTAL**	**4**
TOTAL	**5**	1TRZG	Triticum		
		1TULG	Tulipa		
		TOTAL	**7**		

[23] https://gd.eppo.int/

Table 16. Number of crops (genus level) affected in Germany.

GERMANY					
Option 1		**Option 2 and 3 Category I**		**Option 4**	
1ALLG	Allium	1AATG	Actaea	1AVEG	Avena
1BEAG	Beta	1ALLG	Allium	1BRSG	Brassica
1BRSG	Brassica	1AVEG	Avena	1FRAG	Fragaria
1CUMG	Cucumis	1BEAG	Beta	1HUMG	Humulus
1FOEG	Foeniculum	1BRSG	Brassica	1SECG	Secale
1HORG	Hordeum	1CUUG	Cucurbita	1SIPG	Silphium
1HUMG	Humulus	1FOEG	Foeniculum	1SOLG	Solanum
1LACG	Lactuca	1FRAG	Fragaria	1TRZG	Triticum
1MABG	Malus	1HORG	Hordeum	1TTLG	Triticosecale
1PIBG	Pisum	1HUMG	Humulus	1VITG	Vitis
1PYUG	Pyrus	1MABG	Malus	**TOTAL**	**10**
1QUEG	Quercus	1MLSG	Melissa		
1ROSG	Rosa	1PARG	Petroselinum		
1SECG	Secale	1ROSG	Rosa		
1SOLG	Solanum	1SECG	Secale		
1SORG	Sorghum	1SIPG	Silphium		
1TRZG	Triticum	1SOLG	Solanum		
1TTLG	Triticosecale	1TRZG	Triticum		
1VITG	Vitis	1TTLG	Triticosecale		
1ZEAG	Zea	1VICG	Vicia		
TOTAL	**20**	1VITG	Vitis		
		1ZEAG	Zea		
		TOTAL	**22**		

Table 17. Number of crops (genus level) affected in Austria.

AUSTRIA					
Option 1		**Option 2 and 3 Category I**		**Option 4**	
1AGARG	Agaricus	1ALLG	Allium	1ALLG	Allium
1ALLG	Allium	1ASPG	Asparagus	1ASPG	Asparagus
1BEAG	Beta	1BEAG	Beta	1BRSG	Brassica
1BRSG	Brassica	1BRSG	Brassica	1CICG	Cichorium
1CICG	Cichorium	1CICG	Cichorium	1CPSG	Capsicum
1FRAG	Fragaria	1CPSG	Capsicum	1HORG	Hordeum
1HORG	Hordeum	1HORG	Hordeum	1MABG	Malus
1HUMG	Humulus	1HUMG	Humulus	1SOLG	Solanum
1MABG	Malus	1MABG	Malus	1TRZG	Triticum
1PAPG	Papaver	1SOLG	Solanum	1TTLG	Triticosecale
1PHSG	Phaseolus	1TRZG	Triticum	1VICG	Vicia
1SECG	Secale	1TTLG	Triticosecale	1VITG	Vitis
1SOLG	Solanum	1VICG	Vicia	1ZEAG	Zea
1TRZG	Triticum	1VITG	Vitis	**TOTAL**	**13**
1VICG	Vicia	1ZEAG	Zea		
1VITG	Vitis	**TOTAL**	**15**		
1ZEAG	Zea				
TOTAL	**17**				

Table 18. Number of crops (genus level) affected in Slovenia.

SLOVENIA					
Option 1		**Option 2 and 3 Category I**		**Option 4**	
1APUG	Apium	1ALLG	Allium	1APUG	Apium
1AVEG	Avena	1APUG	Apium	1BRSG	Brassica
1BRSG	Brassica	1BRSG	Brassica	1CUMG	Cucumis
1HORG	Hordeum	1CICG	Cichorium	1DAUG	Daucus
1MABG	Malus	1CUMG	Cucumis	1HORG	Hordeum
1MISG	Miscanthus	1DAUG	Daucus	1MABG	Malus
1PHSG	Phaseolus	1HORG	Hordeum	1PIBG	Pisum
1PRNG	Prunus	1MABG	Malus	1PRNG	Prunus
1PYUG	Pyrus	1PHSG	Phaseolus	1PYUG	Pyrus
1SECG	Secale	1PIBG	Pisum	1SOLG	Solanum
1SOLG	Solanum	1PRNG	Prunus	1TRZG	Triticum
1SPQG	Spinacia	1PYUG	Pyrus	1VITG	Vitis
1TRZG	Triticum	1SOLG	Solanum	1ZEAG	Zea
1TTLG	Triticosecale	1TRZG	Triticum	**TOTAL**	**13**
1VITG	Vitis	1TTLG	Triticosecale		
1ZEAG	Zea	1VITG	Vitis		
TOTAL	**16**	1ZEAG	Zea		
		TOTAL	**17**		

Table 19. Number of crops (genus level) affected in Czech Republic.

CZECH REPUBLIC					
Option 1		**Option 2 and 3 Category I**		**Option 4**	
1ANUG	Annona	1ALLG	Allium	1ALLG	Allium
1AVEG	Avena	1ARHG	Arachis	1BEAG	Beta
1BEAG	Beta	1AVEG	Avena	1BRSG	Brassica
1BRSG	Brassica	1BEAG	Beta	1CPSG	Capsicum
1CAUG	Carthamus	1BRSG	Brassica	1HORG	Hordeum
1CPSG	Capsicum	1CPSG	Capsicum	1MABG	Malus
1DAUG	Daucus	1DAUG	Daucus	1MEUG	Melilotus
1HELG	Helianthus	1HORG	Hordeum	1PHLG	Phleum
1HORG	Hordeum	1HOTG	Houttuynia	1PIUG	Pinus
1HUMG	Humulus	1LACG	Lactuca	1ROSG	Rosa
1LACG	Lactuca	1LIUG	Linum	1SECG	Secale
1MABG	Malus	1MABG	Malus	1SOLG	Solanum
1PAPG	Papaver	1MEUG	Melilotus	1TRZG	Triticum
1PRNG	Prunus	1PHLG	Phleum	1TTLG	Triticosecale
1SECG	Secale	1PIUG	Pinus	1VITG	Vitis
1SLYG	Silybum	1PRNG	Prunus	1ZEAG	Zea
1TRZG	Triticum	1ROSG	Rosa	**TOTAL**	**16**
1TTLG	Triticosecale	1SECG	Secale		
1VITG	Vitis	1SOLG	Solanum		
1ZEAG	Zea	1TRZG	Triticum		
TOTAL	**20**	1TTLG	Triticosecale		
		1VITG	Vitis		
		1ZEAG	Zea		
		TOTAL	**23**		

Table 20. Number of crops (genus level) affected in Belgium.

BELGIUM					
Option 1		**Option 2 and 3 Category I**		**Option 4**	
1AOYG	Astrocaryum	1BEAG	Beta	1CLKG	Cladium
1BEAG	Beta	1BRSG	Brassica	1PYUG	Pyrus
1BRSG	Brassica	1CLKG	Cladium	1ROSG	Rosa
1HORG	Hordeum	1IUNG	Juncus	1SOLG	Solanum
1LIUG	Linum	1PIBG	Pisum	1TRZG	Triticum
1MABG	Malus	1PRNG	Prunus	1VICG	Vicia
1PAVG	Pastinaca	1PYUG	Pyrus	1VITG	Vitis
1PIBG	Pisum	1RHEG	Rheum	1VLLG	Valerianella
1PYUG	Pyrus	1ROSG	Rosa	1ZEAG	Zea
1ROSG	Rosa	1SCVG	Scorzonera	**TOTAL**	**9**
1SOLG	Solanum	1SOLG	Solanum		
1TRZG	Triticum	1SPQG	Spinacia		
1VITG	Vitis	1TRZG	Triticum		
1VLLG	Valerianella	1VALG	Valeriana		
1ZEAG	Zea	1VICG	Vicia		
TOTAL	**15**	1VITG	Vitis		
		1VLLG	Valerianella		
		1ZEAG	Zea		
		TOTAL	**18**		

Table 21. Number of crops (genus level) affected in the Netherlands.

THE NETHERLANDS					
Option 1		**Option 2 and 3 Category I**		**Option 4**	
1ALLG	Allium	1AAOG	Aconitum	1AAOG	Aconitum
1AMYG	Amaryllis	1ABGG	Arum	1ABGG	Arum
1ANHG	Ananas	1ALLG	Allium	1ALLG	Allium
1ANMG	Anemone	1ANRG	Anthriscus	1APUG	Apium
1AODG	Anisodontea	1ANUG	Annona	1ASPG	Asparagus
1ASPG	Asparagus	1AOYG	Astrocaryum	1BRSG	Brassica
1ASTG	Aster	1APUG	Apium	1CEAG	Ceanothus
1AVEG	Avena	1ARWG	Armoracia	1CHYG	Chrysanthemum
1BEAG	Beta	1ASPG	Asparagus	1CICG	Cichorium
1BELG	Bellis	1AVEG	Avena	1CPSG	Capsicum
1BOUG	Bougainvillea	1BEAG	Beta	1CUMG	Cucumis
1BRSG	Brassica	1BRSG	Brassica	1CUUG	Cucurbita
1CEMG	Cestrum	1CEAG	Ceanothus	1CVBG	Cupressus
1CEOG	Celosia	1CHYG	Chrysanthemum	1DAUG	Daucus
1CHYG	Chrysanthemum	1CICG	Cichorium	1ECHG	Echinochloa
1CICG	Cichorium	1CIEG	Cicer	1ERUG	Eruca
1CING	Cinnamomum	1CITG	Citrullus	1ESAG	Escallonia
1CITG	Citrullus	1CPSG	Capsicum	1FESG	Festuca
1CLDG	Calendula	1CRYG	Carum	1FOEG	Foeniculum
1CLVG	Clematis	1CUMG	Cucumis	1FRAG	Fragaria
1CMUG	Calophyllum	1CUNG	Calluna	1HECG	Helichrysum
1CNKG	Convallaria	1CUUG	Cucurbita	1HSTG	Hosta
1CPSG	Capsicum	1CVBG	Cupressus	1IRIG	Iris
1CUMG	Cucumis	1DAUG	Daucus	1IRISG	Iris
1CUNG	Calluna	1DING	Dianthus	1LACG	Lactuca
1CUUG	Cucurbita	1ECHG	Echinochloa	1LGNG	Lagenaria
1CVOG	Crocus	1ERUG	Eruca	1LILG	Lilium
1DAHG	Dahlia	1ESAG	Escallonia	1LOLG	Lolium
1DAUG	Daucus	1EUOG	Euonymus	1LUPG	Lupinus
1DING	Dianthus	1FESG	Festuca	1MABG	Malus
1DORG	Doronicum	1FOEG	Foeniculum	1OEOG	Oenothera
1EYOG	Euryops	1FRAG	Fragaria	1PAOG	Paeonia
1FATG	Fatsia	1GLAG	Gladiolus	1PAVG	Pastinaca
1FESG	Festuca	1HECG	Helichrysum	1PHSG	Phaseolus
1FRAG	Fragaria	1HELG	Helianthus	1PIBG	Pisum
1GADG	Gardenia	1HORG	Hordeum	1PIPG	Piper
1GEBG	Gerbera	1HSTG	Hosta	1POAG	Poa
1GLAG	Gladiolus	1HUMG	Humulus	1PYUG	Pyrus
1GLXG	Glycine	1HYAG	Hyacinthus	1RBIG	Rubia
1HEEG	Hedera	1IRIG	Iris	1RHEG	Rheum
1HELG	Helianthus	1IRISG	Iris	1RHOG	Rhododendron
1HEOG	Heliotropium	1LACG	Lactuca	1ROSG	Rosa
1HORG	Hordeum	1LGNG	Lagenaria	1SCVG	Scorzonera
1HYAG	Hyacinthus	1LILG	Lilium	1SJNG	Senna
1HYEG	Hydrangea	1LIUG	Linum	1SOLG	Solanum
1IRIG	Iris	1LOLG	Lolium	1TRZG	Triticum
1IRISG	Iris	1LUPG	Lupinus	1TTLG	Triticosecale
1KANG	Kalanchoe	1MABG	Malus	1TULG	Tulipa
1LACG	Lactuca	1MEDG	Medicago	1VIBG	Viburnum
1LANG	Lantana	1MUAG	Mauritia	1VICG	Vicia
1LAVG	Lavandula	1OEOG	Oenothera	1VITG	Vitis
1LILG	Lilium	1OLVG	Olea	1XCHG	Xerochrysum
1LIUG	Linum	1PAOG	Paeonia	1ZEAG	Zea

THE NETHERLANDS					
Option 1		**Option 2 and 3 Category I**		**Option 4**	
1LOLG	Lolium	1PARG	Petroselinum	**TOTAL**	**53**
1MABG	Malus	1PAVG	Pastinaca		
1MUAG	Mauritia	1PHSG	Phaseolus		
1NARG	Narcissus	1PIBG	Pisum		
1NRIG	Nerine	1PIPG	Piper		
1OLVG	Olea	1POAG	Poa		
1OSPG	Osteospermum	1POPG	Populus		
1PARG	Petroselinum	1PRNG	Prunus		
1PELG	Pelargonium	1PYUG	Pyrus		
1PEUG	Petunia	1RAPG	Raphanus		
1PHSG	Phaseolus	1RBIG	Rubia		
1PIBG	Pisum	1RHEG	Rheum		
1PIPG	Piper	1RHOG	Rhododendron		
1POPG	Populus	1RIBG	Ribes		
1PRIG	Primula	1ROSG	Rosa		
1PRNG	Prunus	1RUBG	Rubus		
1PYUG	Pyrus	1SCVG	Scorzonera		
1RANG	Ranunculus	1SECG	Secale		
1RAPG	Raphanus	1SING	Sinapis		
1RHOG	Rhododendron	1SJNG	Senna		
1RIBG	Ribes	1SOLG	Solanum		
1ROSG	Rosa	1SPQG	Spinacia		
1RUBG	Rubus	1TOPG	Tropaeolum		
1SALG	Salvia	1TRFG	Trifolium		
1SCVG	Scorzonera	1TRZG	Triticum		
1SECG	Secale	1TTHG	Trichosanthes		
1SENG	Senecio	1TTLG	Triticosecale		
1SING	Sinapis	1TULG	Tulipa		
1SJNG	Senna	1VACG	Vaccinium		
1SOLG	Solanum	1VALG	Valeriana		
1SPQG	Spinacia	1VIBG	Viburnum		
1SQFG	Spathiphyllum	1VICG	Vicia		
1TNCG	Tanacetum	1VIGG	Vigna		
1TOPG	Tropaeolum	1VISG	Viscum		
1TRZG	Triticum	1VITG	Vitis		
1TTLG	Triticosecale	1XCHG	Xerochrysum		
1TULG	Tulipa	1ZEAG	Zea		
1VACG	Vaccinium	1ZIPG	Ziziphus		
1VICG	Vicia	**TOTAL**	**91**		
1VIGG	Vigna				
1VIOG	Viola				
1VITG	Vitis				
1ZEAG	Zea				
TOTAL	**96**				

Table 22. Number of crops (genus level) affected in Greece.

GREECE					
Option 1		**Option 2 and 3 Category I**		**Option 4**	
1AFEG	Anethum	1ABMG	Abelmoschus	1ABMG	Abelmoschus
1ALLG	Allium	1AFEG	Anethum	1AFEG	Anethum
1APUG	Apium	1ALLG	Allium	1ALLG	Allium
1ARHG	Arachis	1APUG	Apium	1APUG	Apium
1ARTG	Artemisia	1ARHG	Arachis	1ARHG	Arachis
1ASPG	Asparagus	1ASPG	Asparagus	1ASPG	Asparagus
1AVEG	Avena	1ATIG	Actinidia	1AVEG	Avena
1BARG	Barbarea	1AVEG	Avena	1BEAG	Beta
1BEAG	Beta	1BEAG	Beta	1BRSG	Brassica
1BRSG	Brassica	1BRSG	Brassica	1CICG	Cichorium
1CICG	Cichorium	1CICG	Cichorium	1CIDG	Citrus
1CIDG	Citrus	1CIDG	Citrus	1CIEG	Cicer
1CITG	Citrullus	1CIEG	Cicer	1CITG	Citrullus
1CNSG	Consolida	1CITG	Citrullus	1CORG	Coriandrum
1CPSG	Capsicum	1CORG	Coriandrum	1CPSG	Capsicum
1CUMG	Cucumis	1CPSG	Capsicum	1CUMG	Cucumis
1CUUG	Cucurbita	1CSNG	Castanea	1CUUG	Cucurbita
1CYDG	Cydonia	1CUMG	Cucumis	1CYLG	Corylus
1CYLG	Corylus	1CUUG	Cucurbita	1CYUG	Cynara
1CYUG	Cynara	1CYDG	Cydonia	1DAUG	Daucus
1DAUG	Daucus	1CYLG	Corylus	1FOEG	Foeniculum
1DING	Dianthus	1CYUG	Cynara	1FRAG	Fragaria
1EIOG	Eriobotrya	1DAUG	Daucus	1GLXG	Glycine
1FRAG	Fragaria	1DING	Dianthus	1GOSG	Gossypium
1GLXG	Glycine	1EIOG	Eriobotrya	1HELG	Helianthus
1GOSG	Gossypium	1FOEG	Foeniculum	1HORG	Hordeum
1HORG	Hordeum	1FRAG	Fragaria	1IUGG	Juglans
1IUGG	Juglans	1GLXG	Glycine	1LACG	Lactuca
1LACG	Lactuca	1GOSG	Gossypium	1LENG	Lens
1LEPG	Lepidium	1HELG	Helianthus	1LTHG	Lathyrus
1MABG	Malus	1HORG	Hordeum	1MABG	Malus
1NIOG	Nicotiana	1IUGG	Juglans	1NIOG	Nicotiana
1OLVG	Olea	1LACG	Lactuca	1PARG	Petroselinum
1ORYG	Oryza	1LENG	Lens	1PHSG	Phaseolus
1PHSG	Phaseolus	1LTHG	Lathyrus	1PIBG	Pisum
1PIBG	Pisum	1MABG	Malus	1PRNG	Prunus
1PRNG	Prunus	1NIOG	Nicotiana	1PYUG	Pyrus
1PYUG	Pyrus	1OLVG	Olea	1RAPG	Raphanus
1RUBG	Rubus	1PARG	Petroselinum	1SECG	Secale
1SECG	Secale	1PHSG	Phaseolus	1SOLG	Solanum
1SOLG	Solanum	1PIAG	Pistacia	1SORG	Sorghum
1TRZG	Triticum	1PIBG	Pisum	1SPQG	Spinacia
1TTLG	Triticosecale	1PRNG	Prunus	1TRZG	Triticum
1VACG	Vaccinium	1PYUG	Pyrus	1TTLG	Triticosecale
1VITG	Vitis	1RAPG	Raphanus	1VICG	Vicia
1VLLG	Valerianella	1SECG	Secale	1VITG	Vitis
1ZEAG	Zea	1SOLG	Solanum	1ZEAG	Zea
TOTAL	**47**	1SORG	Sorghum	**TOTAL**	**47**
		1SPQG	Spinacia		
		1TRZG	Triticum		
		1TTLG	Triticosecale		
		1VICG	Vicia		
		1VITG	Vitis		
		1VLLG	Valerianella		
		1ZEAG	Zea		
		TOTAL	**55**		

ANNEX 13

SECTORIAL COMPETITIVENESS: EU AGRICULTURE

Contents

This Annex complements Annex 12 and contains data on the sales of pesticides compiled under Regulation (EC) No 1185/2009 of the European Parliament and of the Council of 25 November 2009 concerning statistics on pesticides. The article 3.4 of this regulation states that the Commission (Eurostat) must aggregate the data before publication, taking due account of the protection of confidential data at the level of individual Member States. The confidential data can be used by the Commission (Eurostat) exclusively for statistical purposes. Therefore, this data cannot be published in this impact assessment report.

This Annex focuses on the assessment of potential impacts, which build on the results of the screening study explained in Annexes 3 to 5. The results of the screening do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation. The methods and results presented in this Annex are to be interpreted as an estimation of the potential impacts.

Annexes 8 to 15 describe the impacts expected when implementing the criteria to identify EDs (Options 1 to 4) under the current regulatory framework (Option A). In addition, it was assessed whether these expected impacts would remain the same or not under consideration of different regulatory implementations (Options B and C, only applicable to the PPP Regulation). The analyses of the impacts described in these Annexes translate into the "performance" of the options, which is one of the input parameters to the MCAs (Annex 6 and 7).

The MCAs results are not concluding on any preferred option for setting scientific criteria to identify endocrine disruptors, but aim at providing additional information to decision makers with regards to the potential impacts expected when implementing the criteria, after those would have been selected on the basis of science (two MCAs were performed: Options 1 to 4 under the current regulatory context, and Options A compared to Options B and C).

At a preliminary stage of the impact assessment it was anticipated that Option C should be discarded, nevertheless it was maintained for the analysis of the impacts for methodological reasons (see Section 4.2.3 of the main report and Annexes 6 and 7). Option C only applies to the PPP Regulation.

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PART 14/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annex 14 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

{COM(2016) 350 final}
{SWD(2016) 212 final}

ANNEX 14

SECTORIAL COMPETITIVENESS: PPP, BP AND RELATED INDUSTRIES

Contents

This Annex focuses on the assessment of potential impacts, which build on the results of the screening study explained in Annexes 3 to 5. The results of the screening do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation. The methods and results presented in this Annex are to be interpreted as an estimation of the potential impacts.

Annexes 8 to 15 describe the impacts expected when implementing the criteria to identify EDs (Options 1 to 4) under the current regulatory framework (Option A). In addition, it was assessed whether these expected impacts would remain the same or not under consideration of different regulatory implementations (Options B and C, only applicable to the PPP Regulation). The analyses of the impacts described in these Annexes translate into the "performance" of the options, which is one of the input parameters to the MCAs (Annex 6 and 7).

The MCAs results are not concluding on any preferred option for setting scientific criteria to identify endocrine disruptors, but aim at providing additional information to decision makers with regards to the potential impacts expected when implementing the criteria, after those would have been selected on the basis of science (two MCAs were performed: Options 1 to 4 under the current regulatory context, and Options A compared to Options B and C).

At a preliminary stage of the impact assessment it was anticipated that Option C should be discarded, nevertheless it was maintained for the analysis of the impacts for methodological reasons (see Section 4.2.3 of the main report and Annexes 6 and 7). Option C only applies to the PPP Regulation.

1. IMPORTANCE OF SECTORIAL COMPETITIVENESS

Boosting jobs, growth and investment in the EU is one of the ten priorities of the Juncker Commission, as clearly illustrated in the title of the agenda presented by the President in July 2014 before the European Parliament "*An Agenda for Jobs, Growth, Fairness and Democratic Change*"[1]. This priority also features prominently in the Commission Work Programme[2] for the year 2016. One way legislation in the food and public health sectors, and therefore setting criteria to identify endocrine disruptors (EDs), contributes to this priority is by promoting and protecting health and food safety and adding to a well-functioning single market.

Since the global economic and financial crisis, the EU has been suffering from low levels of investment. Besides, more than six million people lost their job during the crisis and several EU economies are still far away from sustainable growth.[1] One of the key objectives of the Juncker Commission is therefore to put Europe on the path of economic recovery.

The chemical speciality sectors developing and manufacturing plant protection products (PPP) and biocidal products (BP) can help achieving this objective as they can be potential sources of job creation and innovation. This applies also to many – downstream - sectors which rely on the availability of effective and high quality PPP and BP (food and feed industry; agricultural sector, manufacturers of application equipment; healthcare facilities, textile industry, paints and coatings industry, maritime industry etc.). More broadly, the health and food sectors represent about 17% of the EU's GDP and 10% of the EU's workforce. It is important that these sectors are supported by a solid framework based on scientific facts and a high level of protection that supports growth, investment, innovation and competitiveness, which enables them to achieve their economic potential and long-term sustainability.

1.1. Public consultation

The impact of setting criteria for EDs on innovation and competitiveness was pointed out many times in the public consultation, mainly related to the chemical industry and sectors relying on PPP and BP (for example, farming, food industry, paints and coatings industries). The information provided reflected diverging views on how stricter rules may impact innovation and competitiveness.

It was indicated that the positive effects from stricter regulations on innovation should not be underestimated. The setting of criteria for EDs is considered to strengthen businesses seeking to develop better, safer and sustainable alternatives ensuring that the EU industry has its share of the growing market for safer products and move to a more sustainable production. Several companies stated that they avoid the use of suspected EDs in their consumer products. A downstream user indicated that setting ED criteria would facilitate the internal and supply chain management once this group of chemicals is officially identified as such. ED criteria

[1] Jean-Claude Juncker, Opening Statement in the European Parliament Plenary Session. A New Start for Europe: My Agenda for Jobs, Growth, Fairness and Democratic Change. Political Guidelines for the next European Commission. Strasbourg, 15 July 2014. Retrieved on: https://ec.europa.eu/priorities/sites/beta-political/files/juncker-political-guidelines_en.pdf

[2] Commission Work Programme 2016; No time for business as usual. Retrieved on: http://ec.europa.eu/atwork/pdf/cwp_2016_en.pdf

would also enable the companies to take a long-term perspective on developing products without EDs, instead of facing increased costs by developing new ones at a later stage.

Other respondents considered the setting of ED criteria a significant barrier for innovation as it is adding uncertainty, costs and complexity to the regulatory process. In particular Option 3 (WHO definition + categories) was considered to imply the collection of a significant body of evidence involving considerable cost over time. For small start-up companies, often responsible for technology development, the associated costs and risks are expected to increase, and thus this source of innovation is assumed to be far less common. Many respondents considered the ED issue as adding another level of complexity and uncertainty to the chemical industry in the EU that already struggles to cope with existing legislation. Those respondents indicated that downstream industry continuously assesses trade-offs between performance, health, safety, environmental impacts and economic consequences.

One specific issue raised was the specific requirements of the in-vitro diagnostic manufacturers. It was stressed that the use of EDs are an essential requirement in the positive controls or in biologically active reagents. Furthermore, many respondents stressed that the lack of tools to control pests and diseases is not only a crucial factor for the cultivation of crops, it would compromise also the competitiveness of the entire agri-food chain and supporting industries.

2. SECTORS AFFECTED

2.1. Introduction

The PPP and BP supply chain can be divided into:

- Producers of raw materials (producers of active substances)
- Producers of processed active substances (formulators of PPP and BP)
- Downstream users (industrial end-users, professional end-users, distributors and manufacturers of application equipment)
- Consumers

Legislation on PPP and BP not only influences the companies that manufacture active substances or process active substances (formulators of PPP and BP), but also the downstream users of these products (for example, producers of goods in which or during the production process PPP or BP have been used, for example paints and textiles; farmers; food industry).

The BP (USD 2,6 billion in 2016[3]) and PPP (EUR 8 billion in 2010[4]) markets are relatively small markets compared to the EU markets for human medicines (EUR 228,1 billion, 2011,EFPIA[5]) and the chemical industry (EUR111 billion, value added, Eurostat[6]; sales EUR

[3] Based on the assumption that EU has a 27% share of world market for BP (USD 9,4 billion) as indicated by Markets and Markets. 2016. Biocides Market by Type – Global Trends and Forecasts to 2020. Retrieved from: http://www.marketsandmarkets.com/PressReleases/biocides.asp

[4] ECPA. 2016. Industry Statistics – ECPA Total. Retrieved on: http://www.ecpa.eu/information-page/industry-statistics-ecpa-total

[5] European Federation of Pharmaceutical Industries and Associations (efpia). Industry & Economy. Retrieved on: http://www.efpia.eu/topics/industry-economy

527 billion, EC) (see Figure 1). The market for veterinary medicines is of a similar magnitude as the markets for PPP and BP (veterinary medicines EUR 5 billion (2015, IFAH-Europe[7]).

The chemical industry producing and developing PPP and BP could be considered as specialty chemicals sector (see Table 1). The High Level Group on the Competitiveness of the European Chemical Industry concluded that the European chemicals industry is facing strong competition from emerging countries notably in Asia, the Middle East and Russia[8] (see Table 2)

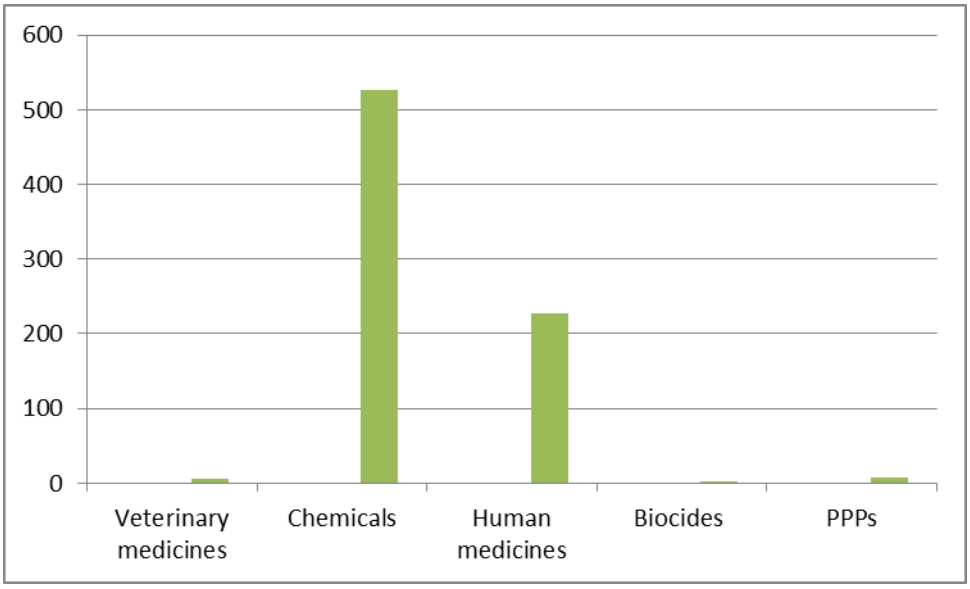

Figure 1. Market values of different chemical sectors (in millions EUR)[6]

Table 1. Weight of speciality chemicals in chemical industry (excluding pharmaceuticals)[9]

Chemical sub-sector	Weight (%)		Weight (%)
Petrochemicals	26,6		
Basic inorganics	13,7		
Polymers	21,5		
Speciality chemicals	26,5		
		Dyes and pigments	9,5
		Crop protection	7,0
		Paints and inks	29,4
		Auxiliaries for industry	54,1
Consumer chemicals	11,7		

[6] Eurostat archive. Manufacture of chemicals and chemical product statistics. Retrieved on: http://ec.europa.eu/eurostat/statistics-explained/index.php/Archive:Manufacture_of_chemicals_and_chemical_products_statistics_-_NACE_Rev._2
[7] IFAH Europe. About the industry. Retrieved on: http://www.ifaheurope.org/about/about-the-industry.html
[8] CEFIC Final Report of the High Level Group on Competitiveness of the European Chemicals Industry. Retrieved from:.http://www.cefic.org/Documents/PolicyCentre/HLG-Chemical-Final-report-2009.pdf
[9] The European Chemical Industry Council (CEFIC). Facts and figures 2016. Retrieved on: http://www.cefic.org/Facts-and-Figures/

Table 2. Chemical sales, exports and imports in the world (in billion Euro)[9]

	2013	Share
EU28	527	16,7%
Rest of Europe	103	3,3%
NAFTA	528	16,7%
Latin America	144	4,6%
Rest of Asia	408	12,9%
China	1047	33,2%
Japan	152	4,8%
South Korea	132	4,2%
India	72	2,3%
Rest of the World	44	1,4%
World	3156	100,0%

2.2. PPP and BP industries

The companies that manufacture active substances or formulate PPP or BP and place these on the market are directly affected by the setting of ED criteria. In

Table 3, key data are provided on these industries. In the following subparagraphs the particularities of the PPP and BP industries (active substance manufacturers and product formulators) are described in more detail. Downstream users are discussed in the next section 2.3.

Table 3. Key data of the PPP and BP market

	PPP	BP
Market value	Global market USD 34 billion; market value in Europe USD 8 billion in 2010[10;11] USD 59 billion forecast for world market in 2016[12] (Freedonia group) Pesticide sales by product category (USD million): fungicides 9.910, herbicides 17.321, insecticides 9.982, others 1.100[11]	Global market: EUR 3 billion in 2000[13], USD 7,2 billion in 2010, USD 9,4 billion forecast for world market in 2016[14] USD 10 billion in 2012[15] USD 7,9 billion in 2014[16] European market: EUR 890 million in 2000[17]
New product introductions	1980-1990 four agrochemical active ingredient introductions per year, now 1.2 per year[18]	
Share of global R&D focussed on European markets	33% in the 1980s, 7.7% 2012[18]	
Jobs	26,223 in 2010 (5,431 in R&D, 11,236 in production/logistics, 6,541 sales/marketing, 3,016 administration)[10]	

[10] ECPA. 2016. Industry Statistics – ECPA Total. Retrived from http://www.ecpa.eu/information-page/industry-statistics-ecpa-total

[11] Library briefing of the European Parliament 29/03/2012. Pesticide legislation in the EU. Towards sustainable use of plant protection products. Retrieved from: http://www.europarl.europa.eu/RegData/bibliotheque/briefing/2012/120291/LDM_BRI(2012)120291_REV1_EN.pdf

[12] Freedonia. 2016.World Agricultural Pesticides. Found on: http://www.freedoniagroup.com/industry-study/2902/world-agricultural-pesticides.htm

[13] Commission Staff Working Document SEC(2009)773. Impact Assessment for a proposal for a Regulation concerning the placing on the market and use of BP: http://ec.europa.eu/smart-regulation/impact/ia_carried_out/cia_2009_en.htm#env.

[14] Markets and markets. 2016. Biocides Market by Type – Global Trends and Forecasts to 2020. Retrieved from: http://www.marketsandmarkets.com/PressReleases/biocides.asp

[15] BusinessWire. Research and Markets: Global Biocides Market 2013 Report. Retrieved from: http://www.businesswire.com/news/home/20130709005713/en/Research-Markets-Global-Biocides-Market-2013-Report

[16] Grand View Research. Biocides Market Analysis by product, by application and segment forecasts to 2022. Retrieved from: http://www.grandviewresearch.com/industry-analysis/biocides-industry

[17] Commission Staff Working Document SEC(2009)773, Impact Assessment for a proposal for a Regulation concerning the placing on the market and use of BP: http://ec.europa.eu/smart-regulation/impact/ia_carried_out/cia_2009_en.htm#env.

[18] Phillips McDougall. 2013.R&D trends for chemical crop protection products and the position of the European market. A consultancy study undertaken for ECPA. Retrived from: http://www.ecpa.eu/files/attachments/R_and_D_study_2013_v1.8_webVersion_Final.pdf

	PPP	BP
Pre-market approval/authorisation system	In EU: 482 approved substances, 792 non-approved and 37 substances for which approval is pending[19].	In EU: 159 approved active substance-product type combinations, 548 under review and 22 non-approved[20]
Total costs for discovery, development and registration	USD 152 million in 1995, USD 184 million in 2010, USD 256 milllion (25 million registration, 146 million development and 94 million research in 2005-8)[21]	EUR 0.2-2.0 million for a biocidal product; the time for gaining return in investment: biocidal products 3-10 years, active substances 2-15 years[22]
Product development time (of a new product)- time lag between discovery and commercialization	9,8 years in 2005-8[6]	5-15 years for an active substance, biocidal product 1-3 years[22]
Direct costs for approval/authorisation	The fee for the substance evaluation of one product type (PT) varies considerably from one Member State to another,	EUR 0,2-0,7 million;[23] active substance EUR 3-10 million;[24] biocidal product EUR 0,15-1 million[25]. The fee for the substance evaluation of one product type (PT) varies considerably from one Member State to another, ranging from less than EUR 150.000 to above EUR 200.000[26]
Industry consolidation	The number of companies involved in the research and development of new agrochemical active ingredients worldwide	

[19] European Commission. EU pesticides database (state of play February 2016). Retrieved from: http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.selection&language=EN

[20] European Chemical Agency (ECHA) database on Biocidal Active Substances. Found on: http://echa.europa.eu/web/guest/information-on-chemicals/biocidal-active-substances

[21] Philips McDougal. 2010. The cost of new agrochemical product discovery, development and registration in 1995, 2000 and 2005-8. A consultancy study for Crop Life America and the European Crop Protection Agency.

[22] Ecorys. 2016. Background study for the assessment of the appropriateness and impact of the existing fee model for the Biocidal Products Regulation and its possible revision. Draft Final Report

[23] Costs consist of preparing dossier for a biocidal product, Letter of Access for the use of BPR fees: impact on the active substance and product authorisation fee; The future of biocidal products, Aise. Biocides 2015, 18th Annual Conference, Vienna, November 2015.

[24] Costs to develop and submit an approval dossier for an active substance (including fees), not including R&D costs for developing a new substance. Cefic-EBPF information for the socio-economic analysis part of the impact assessment on criteria to identify endocrine disruptors (2016).

[25] Costs to develop and submit an authorisation dossier for a biocidal product or a family (including fees). Cefic-EBPF information for the socio-economic analysis part of the impact assessment on criteria to identify endocrine disruptors (2016).

[26] 58th meeting of representatives of Members States Competent Authorities for the implementation of Regulation 528/2012 concerning the making available on the market and use of biocidal products. Report on the fees payable to Members States Competent Authorities pursuant to Article 80(2) of the Biocidal Product Regulation. Retrieved from: https://circabc.europa.eu/sd/a/896cf317-7b62-4604-a736-c18e02fc3ead/CA-Nov14-Doc.7.2%20-%20Report%20on%20fees.doc

	PPP	BP
	has halved, from 34 companies in 1995 to 17 in 2012. [18]	
Patents		Most of the patents associated with the active substances on the market have expired[27]

2.3. PPP industry

Between 2003 and 2011 Europe was the leading regional agrochemical market worldwide; in 2012 it was overtaken by Asia.

Competitive pressure has fuelled consolidations as companies seek economies of scale to cover the global market and to generate funds for research and development. This has resulted in the situation that a small number of companies dominate the industry.

Generic pesticide products (companies making off-patent products) increased their share of the market. In 1996 generics had a market share of the world market of about 20%. This increased gradually to about 30% in 2008[28]. It appears that a product being off-patent does not automatically mean that the main producer loses the share of the market.

In the EU a new PPP has to displace in general existing products to generate revenue as markets in EU are saturated for major crops. A new PPP must therefore be superior to be successful.

In the EU the number of PPP available for minor uses is decreasing[29]. Many PPP are not anymore available on the EU market because they either do not comply any more with regulatory standards or the regulatory costs do not allow them to be considered a profitable product. The review programme of existing active substances carried out between 1993 and 2009 led to the withdrawal of approximately 70% of the active substances that were on the market before 1993.[29] It is clear that the withdrawn substances were not all substituted by new active substances: before 1993 almost 1000 active substances had been approved and currently 482 approved active substances are included in the EU PPP database. Also a substantial decrease in the number of efficacious PPP authorisations for minor crops in the period 1990-2010 was found, supporting the view that innovation is targeted at major crops.

The value of the manufacturing of PPP in Europe was EUR 9,9 billion in 2014 (see Table 4), an increase in value of 50% compared to 1995.

Table 4. The value of the manufacture of PPP in the EU (EUROSTAT-PRODCOM data).

Year	1995	1998	2002	2006	2010	2012	2013	2014
Value (in EUR millions)	6675	6879	6333	5441	6326	7533	7116	9990

[27] Most of the biocidal active substances on the market are on the market for decades. Cefic-EBPF information for the socio-economic analysis part of the impact assessment on criteria to identify endocrine disruptors (2016).

[28] Phillips McDougall (2010). Trends in crop protection R&D, Bratislava, Slovakia. Retrieved from: http://www.ecpa.eu/files/gavin/presentation_Matthew_Phillips.pdf.

[29] Report from the Commission on the establishment of a European fund for minor uses in the field of plant protection products: http://ec.europa.eu/food/plant/pesticides/legislation/docs/com_2014_82_en.pdf.

2.4. BP industry

BP is a wide category of products including amongst others disinfectants, pest control products, wood preservatives and antifouling products. They are widely employed in water treatment, wood preservation, paints, food and beverage production, and as disinfectants to kill or inhibit hazardous organisms. Professional use is prevalent for all preservatives, some pest control products, antifouling products and embalming and taxidermist products. Non-professional use (consumers) prevails for some pest control products (rodenticides, insecticides, repellents and attractants) and some disinfectants. The BP Regulation sets out a two-tiered system of approving active substances at EU level and authorising BP (containing one or more active substances) at EU or national level, following a similar approach as the PPP Regulation.

No detailed, consolidated data is available on the BP market in the EU. By the use of several information sources an indication of the size and the structure of this market is provided. The value of the global market is about USD 8 billion (

Table 3). In 2000 North America was representing about 43% and Europe 27% of the world market.

In the EU the market is dominated by three companies that held 25% of the market in 2000[30]. Also the global BP market share is concentrated with top three participants accounting for over 45% of total demand in 2014. Companies require significant amount of investment at the start up stage due to stringent regulations regarding testing and labelling of these products. This discourages entry of new players[31].

In the EU the BP market is fragmented on Member State (MS) level as there is a difference on the number of BP allowed on the national markets.

[30] Commission Staff Working Document SEC(2009)773, Impact Assessment for a proposal for a Regulation concerning the placing on the market and use of BP. Retrieved from: http://ec.europa.eu/smart-regulation/impact/ia_carried_out/cia_2009_en.htm#env.

[31] Grand View Research. Biocides Market Analysis by product, by application and segment forecasts to 2022. Retrieved from: http://www.grandviewresearch.com/industry-analysis/biocides-industry

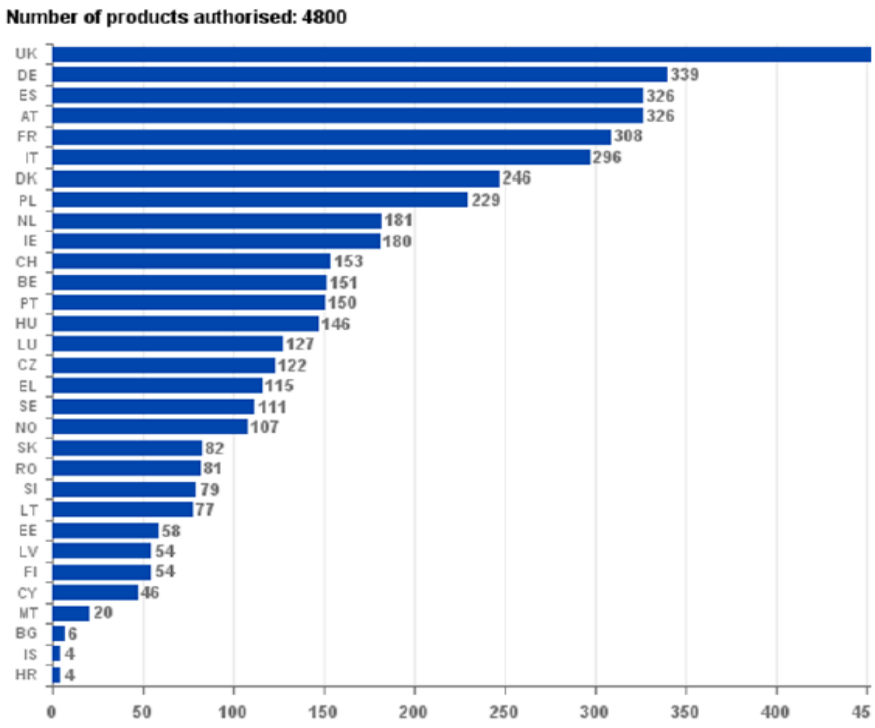

Figure 2. Number of BP authorisations per MS by 15th of January 2016[32].

The BP market is further fragmented because approvals for active substances are provided for product types (the BP Regulation defines 22 product types, (see Figure 2). For example, an active substance approved for use in a disinfectant for the product type veterinary hygiene cannot be used for disinfecting sites in healthcare facilities.

[32] ECHA-report on product authorisations to the 15th meeting of the co-ordination group of competent authorities for BP.

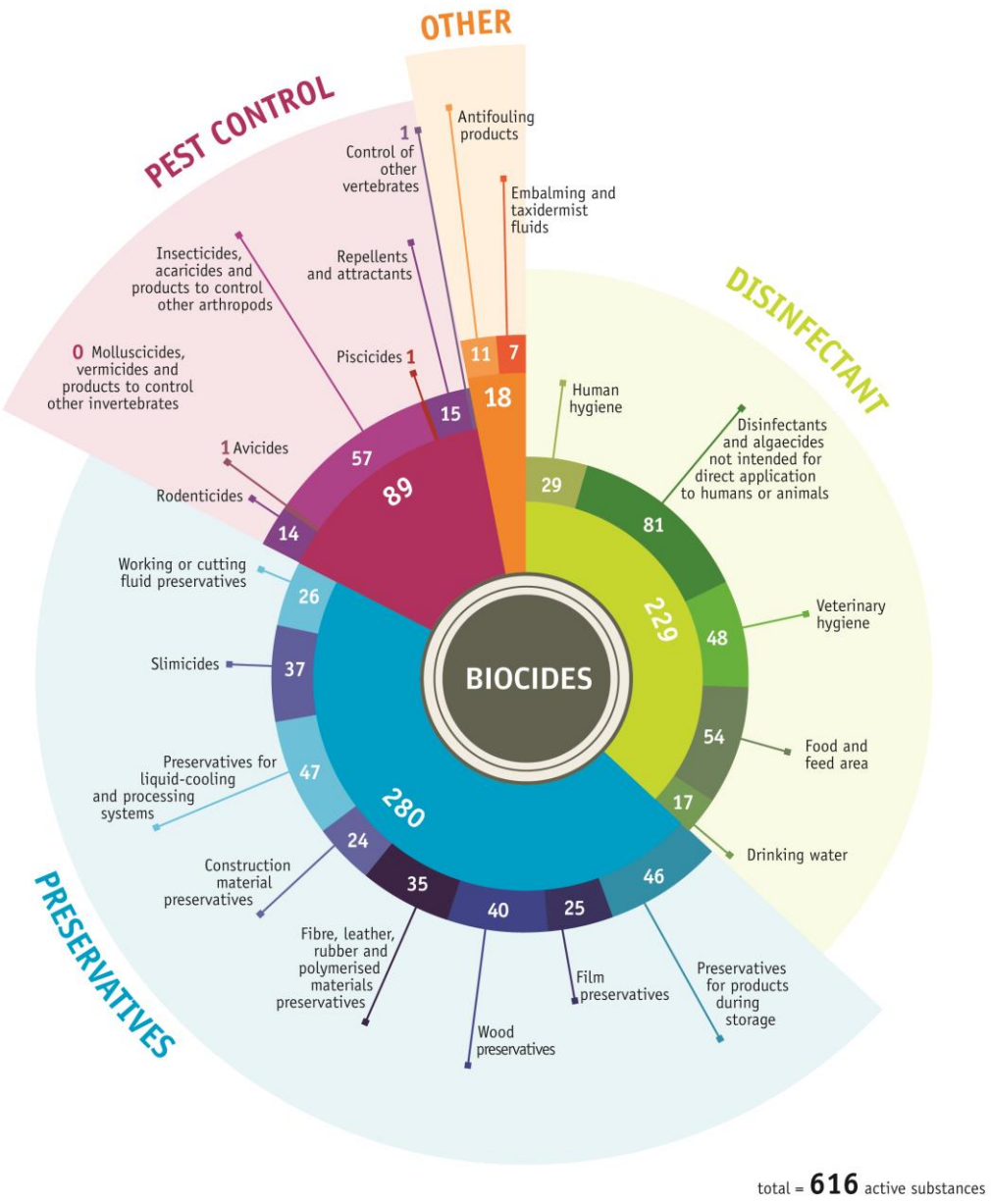

Figure 3. BP market structure, number of approved active substances per product type.

2.5. Related and downstream industry

The use of PPP plays an important role in the EU agricultural production. Farmers use PPP (mainly herbicides, fungicides, insecticides) to ensure less weed and pest damage to crops and a consistent yield. PPP have played a major role in increasing farm productivity[33]. The agricultural sector is characterised by small enterprises (farms), and is described in more details in the Annexes 12 and 13. In addition to agriculture, other professional users and

[33] Headley, J.C. 1968. Productivity of agricultural pesticides. Journal of Farm Economics 50: 13-23.

consumers use PPP for non-agricultural purposes, for example weed control in public areas and private gardens.

A related industry are manufacturers of pesticide application equipment (agricultural, horticultural and forest machinery). Most PPP are applied by professionals using sprayers of different type (boom sprayers, orchard sprayers) which may be also specialised machines built on demand for specific crop situations. Accessory parts to these machines are often specialised, as for instance drift reducing nozzles which reduce impact to the environment. This market has a window of opportunity to innovate, as shown by e.g. innovations which lead to more precise application of PPP, avoiding unnecessary exposure of the environment and/or operators to PPP.

The BP downstream market consists of major industrial sectors relying on the use of BP (see Table 5), either because they manufacture goods in which BP are incorporated (for example paints and detergents in which BP are used to preserve the products) or because BP are required in the manufacturing process (for example, use of biocidal disinfectants to ensure microbial safety of food).

Downstream users of BP may be indirectly affected by changes in prices of products, the disappearance of certain products and the need to switch to alternatives or other suppliers of the product. An important feature of the BP market is the diversity of end-users reflected in the product types that are acting independently of each other (for example, companies providing professional disinfection services to the food industry and others providing professional application of antifouling paints in shipyards). This implies that the BP market consists of multifaceted submarkets, which partly are relatively small and include many small and medium-sized enterprises (SMEs).

Table 5. Examples of sectors relying on BP in manufacturing process or manufacture treated articles[34].

INDUSTRY MANUFACTURING SECTOR	VALUE ADDED (EMPLOYEES) EUROSTAT DATA	PRODUCT TYPES MAINLY USED IN THE MANUFACTURING SECTOR
Food/feed	EUR150 billion VA (4.8 million)	3; 4; 6; 11; 12; 14; 18
Motor vehicles	EUR141 billion VA (2.2 million)	2; 6; 9; 11; 13
Paper	EUR 41 billion VA (646 million)	2; 6; 7; 9; 11; 12; 18
Household and professional cleaning and hygiene	~ EUR 15 billion (VA)	1; 2: 4; 6; 11; 12; 18; 19
Paints & coatings	~ EUR 10 billion (VA)	2; 6; 7; 8; 10; 11; 12; 21

In some industries the proportion of goods in which BP are being used can be close to 100% (for example aqueous based paints, detergents). Other industries in which BP are often used in the manufacturing process produce end-products which do not contain BP, or if they do so only at very low, unavoidable levels (for example use of disinfectants in food industry). The most relevant product types for these industries are the product types 2 (disinfectants), 6 (preservatives for product during storage), 7 (film preservatives) and 9 (fibre, leather, rubber and polymerized materials preservatives) (see Table 6).

According to research companies three developments are expected to have a positive impact on demand for BP over the next years:

1. Rising demand from industrial applications, particularly in paints and coatings and water treatment;
2. Rising need to control microbial growth in food and drinks, along with increasing use of preservatives in ready-to-eat food; and
3. Increasing use in personal care products such as liquid soap, shower gel, cream and shampoo for inhibiting growth of fungus and bacteria, and to improve shelf life.[16]

The best growth opportunities for the BP are in the Asia-Pacific and Eastern Europe region, whereas the mature North American and West European markets are expected to register a modest growth.[15] The availability of approved active substances is critical for companies to develop BP[35]. The prices for BP vary and appear to be linked to the type of good in which it is being used or the aim of the use of biocide.

[34] Cefic-EBPF information for the socio-economic analysis part of the impact assessment on criteria to identify endocrine disruptors (2016).

[35] BPR fees: impact on the future of BP. Aise. Biocides 2015, 18th Annual Conference, Vienna, November 2015.

3. IMPACT ON SINGLE MARKET

Both the PPP and BP Regulations work in a two-step process: approval of active substances at EU level and authorisation of products at national level. Also both regulations provide the possibility, notwithstanding a substance is identified as an ED, to authorise it with restrictions for a fixed time period (see also Annex 8). However, these approvals and authorisations will be MS specific (see Table 6).

Table 6. Conditions for approval of substances identified as ED and conditions of authorisation at MS level for products containing such substances.

	Plant Protection Product Regulation (EC) 1107/2009 (PPPR, 2009)	**Biocides Product Regulation (EU) 528/2012 (BPR, 2012).**
Procedure for approval	Commission Implementing Regulation (Article 13) Examination procedure by standing Committee (Article 79(3) of PPP Regulation in combination with Article 13 of Regulation 182/2011)	Commission Implementing Regulation (Article 9) Examination procedure by Standing Committee (Article 82(3))
Cases in which approval is allowed	- Annex II, section 3.6.5: […] the exposure of humans to that active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with point (b) of Article 18(1) of Regulation (EC) No 396/2005. - Annex II, section 3.8.2: […] the exposure of non-target organisms to that active substance in a plant protection product under realistic proposed conditions of use is negligible. Article 4(7): An active substance is necessary to control a serious danger to plant health which cannot be contained by other available means including non-chemical methods MS may authorise PPP containing active substances approved in accordance with this paragraph only when it is necessary to control that serious danger to plant health in their territory.	- Article 5(2):At least one of the following conditions is met: -The risk to humans, animals or the environment from exposure to the active substance in a biocidal product, under realistic worst case conditions of use, is negligible, in particular where the product is used in closed systems or under other conditions which aim at excluding contact with humans and release into the environment; -It is shown by evidence that the active substance is essential to prevent or control a serious danger to human health, animal health or the environment; -Not approving the active substance would have a disproportionate negative impact on society when compared with the risk to human health, animal health or the environment arising from the use of the substance. When deciding whether an active substance may be approved, the availability of suitable and sufficient alternative substances or technologies shall be a key consideration.

	Plant Protection Product Regulation (EC) 1107/2009 (PPPR, 2009)	**Biocides Product Regulation (EU) 528/2012 (BPR, 2012).**
Risk-mitigation measures	Article 4(7): The use of the substance approved in accordance with Article 4(7) is subject to risk mitigation measures to ensure that exposure of humans and environment is minimised	- Article 5(2): The use of a BP containing active substances approved in accordance with this paragraph shall be subject to appropriate risk-mitigation measures to ensure that exposure of humans, animals and the environment to those active substances is minimised. - Article 5(2):The use of the BP with the active substance concerned shall be restricted to MS in which at least one of the conditions set out in this paragraph is set. - Article 19(4): Not for use by general public
Approval period	- In case of derogations under Annex II, sections 3.6.5 - 3.8.2, approval (and renewal) for maximum 7 years as candidate for substitution (Article 24 read in combination with section 4, 7th indent, of Annex II) - Five years for the substance approved in accordance with Article 4(7)	Approval five years as candidate for substitution (Article 4(1))
Other conditions	For candidates of substitution MS shall carry out a comparative risk assessment before authorising a PPP use. In case of the derogation under Article 4(7), MS shall draw up a phasing out plan concerning the control of the serious danger by other means, including non-chemical methods, and shall without delay transmit that plan to the Commission (Article 4(7))	For candidates of substitution MS shall carry out a comparative risk assessment before authorising a BP use.

The co-legislators introduced these provisions to ensure that the applied derogation will occur only where it is necessary and subject to specific conditions. However, it will create new complexity in the EU market as regards the specific conditions linked to the derogations that will apply in each MS and the interpretation and the enforcement of those conditions. Therefore the availability of PPP and BP to related and downstream users (farmers, professional users, health care sector and food chain producers, industry, etc.) may differ between MS, creating different competitive situations also to the related and downstream industry.

With respect to the impact of the different options on this criterion, the more substances are identified as ED, the more likely that substances would be taken out of the market or approved only under restricted conditions, leading consequently to higher negative impacts on the single market. Because both the PPP and BP Regulations are recent, no relevant experience exist with the derogations for active substances, being for substances with ED properties or other kind of properties which are subjected to similar derogations (e.g.

cancerogenic). Therefore, it is not possible to extrapolate form existing data or experiences. Thus, the best indicator for assessing the impact is the number of substances identified. Option 4 would rate better than Options 2 and Option 3 Category I, and these better than Option 1 (performance of the options is 4 > 2/3 > 1). With respect to regulatory decision making options, Option C would rate better than B, and this better than A as it is expected that less MS specific derogations would occur when less substances are identified as EDs, leading to the following performance of the options C > B > A.

4. IMPACT ON INNOVATION AND RESEARCH

Under the current PPP and BP Regulations, substances identified as ED will be either withdrawn or approved under strict conditions for a fixed period of time.

Before analysing the impacts on the different sectors it is important to refer to the general discussion about the impact of stricter rules on innovation. Many companies and industry organizations consider stricter rules as having a negative impact on innovation and competitiveness as it diverts personnel and resources away from R&D and production activities. On the other hand, it is argued that regulation can have a positive effect on innovation and growth, for example, requirements could promote innovation by encouraging the replacement of hazardous chemicals with newer, more sustainable alternatives[36]. Both views were expressed by respondents in the public consultation. For the EU rules that apply for the registration of chemicals (REACH) it was found that the rules led to an increase of R&D. However, it is important to underline that the scope and the approach of REACH differs substantially of the PPP Regulation and the BP Regulation (for example, no pre-market approval system applies), so that extrapolation is subject to uncertainties[37].

Competitiveness and innovation in companies in the supply chain is driven by a wide range of factors (energy prices, labour costs and productivity, infrastructure, taxation, regulatory environment etc.). It is stressed that setting criteria for EDs is just one issue that may affect the innovative capacity or competitiveness of EU companies. Information is lacking in order to compare the size of the impact of setting EDs in relation to those other factors impacting innovation. Also should be considered that in general, not linked to the setting of criteria for EDs, a decrease takes place of the number of active substances and BP and PPP available on the market in the EU.

[36] World Wildlife Fund (WWF). 2003. Innovation in the Chemicals Sector and the New European Chemicals Regulation, a WWF chemicals and health campaign report. Retrieved from: http://www.wwf.org.uk/filelibrary/pdf/innovationreport.pdf

[37] Monitoring the impacts of Reach on Innovation, Competitiveness and SMEs (CSES)-2015. In the report on the monitoring of the impacts of REACH on innovation it was concluded that the implementation of the REACH Regulation has led to an increase in R&D activity for some 26% of companies surveyed. The report pointed out that there are different views as regards the extent to which that has led to innovation, as opposed to regulatory compliance. The same report analysed the response of companies that had experienced withdrawals of substances; 62,2% of those companies indicated that they carried out research to identify an alternative substance, and over a third said that they changed their manufacturing process to avoid the need to use the substance withdrawn.

4.1. PPP industry and downstream users

The process of developing new PPP and obtaining an authorisation to place these on the EU market is lengthy and costly. Researchers have found positive relationships between R&D spending and the rates of technological innovation and it was shown that pesticide research expenditures relate positively to new pesticide registrations[38].

In PPP the driver of new product development for the EU-15 markets is improved solutions for existing problems, particularly where pest, weed or disease resistance has become an issue. The industry focusses for R&D on major crops. In Europe the focus for new product development are cereals. The next major crop is maize, however, R&D in this area has been reduced because of the shift of this market to biotech solutions of genetically modified races. The third major crop in Europe is oilseed rape.

Higher development and regulatory costs discourage some types of innovation because a product must generate greater revenue in order to be profitable: analysing historical data a 10% increase in the anticipated cost resulted into a 15% decline in innovation for PPP.[38] Therefore an increase in regulatory costs may affect R&D spending and thus also influence innovation. It may also result in some uses of PPP becoming unprofitable because of the regulatory costs to maintain a product on the market, or deter firms from initiating research for minor crop market uses. This is confirmed by the fact that regulatory costs encouraged firms to register PPP only for major crop market usages[39]: a 10% increase in regulatory costs caused an 8% increase in the proportion of PPP for major crops.

The number of new active substances in development worldwide is falling. In 2000 there were 70 new active substances in the development pipeline. In 2012 there were only 28. This is primarily due to fewer companies being involved, it is scientifically more challenging to find new active substances, a greater share of R&D investment being spent on defending products as they come off patent, and a greater focus by these companies on plant breeding. Companies with sufficient resources are maintaining research departments and development expertise in house. However, even the largest companies recognise that research is being carried out outside the company. Partnering, in-licensing, collaborations with universities and research institutions are all part of the innovation mix. There are a number of small, often start-up companies involved in technology development. The majority of these small companies do not have the financial capability of bearing the cost of bringing a new active substance from discovery through the market development. As a result the major way for products developed by these companies to get to market is for the product or the company, to be acquired by one of the major industries in the sector.

The share of crop protection R&D investments attributable to products being developed for the European market has fallen from 33.3% in the 1980s to 7.7% in the 2005-14 period.[18] The number of companies involved in the research and development of new agrochemical active

[38] Ollinger, M. 1995. Innovation and regulation in the pesticide industry. CES 95-14.
[39] Gianess. L.P. and Puffer, C.A. 1992. Registration of minor pesticides: some observations and implications. In: Inputs Situation and Outlook Report, U.S. Dept. Agri. Econ. Res. Serv.: 52-60.

ingredients worldwide has halved, from 35 companies in 1995 to 18 in 2012, of which the number of European companies also halved from 8 in 1995 to 4 in 2012 (Japan 11, USA 3)[40].

For PPP it can be concluded that the withdrawal of active substances in the EU will probably not trigger substantial innovation for replacing these by other substances on the EU market. The main reason for this is that the 18 companies involved in research and development of PPP are multinationals that focus their innovation on growth markets outside the EU or on one major crop in the EU. Moreover, less new potential active substances are in the pipeline. This provides companies with lesser opportunities to develop new PPP for crops in the EU.

Regulatory action on PPP may promote innovation in non-chemical methods like plant breeding for resistance. The rewards for resistance research can be great, for example USD 9.3 million on developing resistance in wheat, alfalfa and corn against some pests resulted in saving to farmers at several hundred million dollars annually[41].

Innovation in application technology of PPP may be also triggered by regulatory action on pesticides demanding less exposure of the environment and operators. Better technology may improve targeting of application of PPP and minimising human and environmental risks during application. Besides evidence on the development of safer application technology like e.g. sprayers classified as spray-drift-reducing-technology (SDRT), band field crop sprayers, shielded band field crop sprayers, sensor field crops sprayers, automatic boom height control, weed wipers, GPS controlled machinery, or drift reducing nozzles, no overview data are available. Non-approval of substances, with no or very limited possibility of restricted approval, is expected to discourage innovations in application technology.

An overview of the impact of setting ED criteria on the different types of companies is provided in Table 7. The term "input" is used to indicate the availability of resources, products or services required to make a product or deliver a service. The term "demand" indicates the market demand for the product made or service delivered by this type of companies. The analysis is on group/sector level, so not on individual company level.

[40] If otherwise stated the data in this section are based on Phillips McDougall. 2013. R&D trends for chemical crop protection products and the position of the European market. A consultancy study undertaken for ECPA. Retrieved from: http://www.ecpa.eu/files/attachments/R_and_D_study_2013_v1.8_webVersion_Final.pdf

[41] Pesticide innovation and the economic effects of implementing the Delaney Clause (1987). Retrieved from: http://www.ncbi.nlm.nih.gov/books/NBK218035/

Table 7. Impact of setting ED criteria for companies active on the PPP-market.

Pesticides Market										
Description of the EU-market					**Potential impact of ED criteria**					
Type of business		Input	Demand/sales	Number of products or services	Number of firms	Input	Demand/sales	Innovation on EU market	Number of products or services	Competitiveness
Manufacturers and developers of active substances	Multinationals	Not relevant	World		→	Not relevant	→	→	↘	→
Formulators of PPP	Multinationals and SMEs	Europe	Europe		→	↘	→	→ or ↗	↘ → ↗	↘ or →
Downstream users PPP										
Manufacturers of application technology	Many SMEs	Europe	Europe	>>>> many	→	→	→ or ↘	→ or ↘	→ or ↘	→
Professional end-user	Many SMEs	Europe	Europe	>>>> many	→	→ ↘	→	→	→ or ↘	→
Consumer		World	Not relevant	Not relevant	Not relevant		→	Not relevant	Not relevant	Not relevant

4.2. BP industry and downstream users

During the last 15 years less than 10 new biocidal active substances have been developed.[34] In a recent survey conducted by the International Association for Soaps, Detergents and Maintenance products (AISE) and the European Chemical Industry Council (CEFIC), the following main obstacles for innovation had been reported: (1) The costs for authorisation of a product are considered too high to justify R&D efforts, (2) Regulatory compliance is taking a lot a companies' resources, and as a consequence no resources remain for innovation, (3) The timelines for authorisation are too long and the process involves much uncertainty, and (4) The number of active substances is decreasing which directly impacts the possibilities for innovation in BP.[34]

It is expected that the withdrawal of active substances in the EU will probably not trigger innovation for replacing it by another substance. The main reason for this is that the companies involved in research and development of biocidal active substances are multinationals that will probably focus their innovation on growth markets outside the EU or will not refocus their R&D in Europe because of the disappearance of one specific substance. Formulators of BP have the focus on Europe. Those companies, of which many SMEs, may try to develop new products in order to respond the market demand of effective BP. However, this type of innovation may have to compete with the additional compliance costs linked to the approval process of identified EDs under the derogations as included in the BP and pesticides legislation. For companies these derogations will trigger additional costs and personal resources.

As mentioned before, many major industrial sectors are relying on the use of BP, either because they manufacture goods containing BP or because BP are required in the manufacturing process. These sectors may be impacted by the disappearance of active substances on the EU market and the associated BP. It is difficult to judge whether this will lead to additional innovation at downstream users level as it depends on many factors. Firstly, it can be expected that the many different types of downstream users will respond differently. The market is segmented and a highly diverse group of enterprises and downstream users participate in market activities. In view of this complexity, a disadvantage for one company might be an advantage for another and vice versa. Secondly, it can be questioned whether non-EU suppliers are prepared to invest in compliance with the BP Regulation. It may be challenging for EU importers to get the information from non-EU companies about the composition of substances, articles or mixtures that are bought. This will imply the need for increased investments in supply chains, especially in countries outside the EU, in order to have an adequate information flow in the supply chain for ensuring compliance with the BP Regulation. This means that it will be generally more difficult to switch to other suppliers in the short term. Consequently, this reduces flexibility in the supply chain choice for those EU based companies and may reduce their competitiveness.[34] However, some EU companies may benefit from this situation as companies may decide, or have to, switch from non-EU to EU BP Regulation-compliant suppliers. In the context of the information flow in the supply chain, it is important to stress that companies, from 1 March 2017, have to comply with the regulatory requirement that in treated articles only biocidal active substances can be used that

are approved or under review in the EU. So, downstream users will have also to invest in the information flow in supply chains in order to comply with this regulatory requirement.

Thirdly, it will depend on the substance in question and the type of supply chain. For example, for key substances in the supply chain, and high value added substances, probably quicker increased R&D will occur as key substances have a shorter return of investment (this return of investment varies from 2 up to 15 years, see Table 3). It is important to note that replacing a chemical in an article or mixture can imply that companies need to significantly change their technologies or processes. It can also affect their business model or supply chain as they need to establish new relations with suppliers. The screening of biocidal substances on ED properties is not representative for the biocidal active substances on the market (see Annex 5 on results of the screening study). This implies it is not possible to determine what type of biocidal substances would be in particular impacts and whether key substances will be affected by the setting of ED criteria. It is important to underline that the BP Regulation provides the possibility to approve an active substance if it is shown that it is essential to prevent or control a serious danger to human health, animal health or the environment (for example, key disinfectants) or not approving the active substance would have a disproportionate impact on society when compared with the risk (see also Table 7 for further details). No experiences exist with the application of this possibility in the legislation, so it is unclear under which circumstances MS would agree to apply these possibilities.

The same impacts are expected on domestic and foreign companies for products placed on the EU market as the same ED criteria will apply. It is noted that companies may use for exports a withdrawn substance in the EU for manufacturing a mixture or an article (if the substance is allowed in the country of destination). However, a company conforming to two standards must manage substances sourcing, production and logistics separately for two standards, and this is expected to created additional costs.

For downstream users it is expected that the setting of criteria will not affect the level of innovation or additional R&D or may lead to an increase. However, this activity is driven by the need to comply with the legislation. As indicated at the section on the results of the public consultation there are different views whether this will lead to an increase in competitiveness in terms of having more and/or higher quality products. The companies may gain competitive advantages by producing safer products and benefitting from a green and innovative image[42]. This positive marketing effect is less obvious if products are meant to be used by commercial actors or for complex articles.[37]

An overview of the impact of setting ED criteria on the different types of companies is provided in Table 8. The term "input" is used to indicate the products or services required to make a product or deliver a service. The term "demand" indicates the market demand for the product made or service delivered by this type of companies. The analysis is on group/sector level, so not on individual company level.

[42] Nidumolu, R., Prahalad, C.K., and Rangaswami, M.R. 2009. Why sustainability if now the key driver of innovation. Harvard Business Review. September issue 2009. Retrived from: https://hbr.org/2009/09/why-sustainability-is-now-the-key-driver-of-innovation

Table 8. Impact of setting ED criteria for companies active on the BP market.

Biocides Market										
Description of the EU-market					**Potential impact of ED criteria**					
Type of business		Input	Demand/sales	Number of products or services	Number of firms	Input	Demand/sales	Innovation on EU market	Number of products or services	Competitiveness
Manufacturers and developers of active substances	Multinationals	Not relevant	World		→	Not relevant	→	→	↘	→
Formulators of BPs	Many SMEs	Europe	Europe		→	↘	→	→ or ↗	↘ → ↗	↘ or →
Downstream users of BPs										
Industrial end-user	Multinationals and SMEs	World	World and Europe	>>>> infinite	→	↘ or →	→	→ or ↗	↘ → ↗	→
Professional end-user	Many SMEs	Europe	Europe	>>>> infinite	→	↘ or →	→	→	↘ → ↗	→
Consumer		World	Not relevant	Not relevant	Not relevant		→	Not relevant	Not relevant	Not relevant

4.3. Summary and performance of the options

Competitiveness and innovation in companies in the supply chain is driven by a wide range of factors (energy prices, labour costs and productivity, infrastructure, taxation, regulatory environment etc.).It is emphasised that setting criteria for EDs is just one issue that may affect the innovative capacity or competitiveness of EU companies in the PPP and BP supply chain. Moreover, the information is lacking in order to determine the size of the impact of setting criteria for EDs compared to other factors affecting innovation.

The criteria for EDs may lead to additional costs and increase the time-to-market for PPP and BP as more tests and data may be required in order to fulfil the regulatory requirements. It is expected that the ED criteria would imply that some active substances incorporated in PPP or BP will be withdrawn of the market or approved under strict conditions (see Annex 5). The withdrawal of active substances contained in PPP and BP in the EU will probably not trigger substantial innovation for replacing these by other substances. The main reason for this is that the multinational companies involved in R&D would probably not refocus their R&D. Moreover, the higher development and regulatory costs (for obtaining approval for an active substance and maintaining it on the market), will consume part of the investments available for R&D for new active substances and products.

For downstream users and formulators of PPP and BP it is very difficult to judge whether the proposal will lead to additional innovation because of the many factors involved. For downstream users it is expected that that the setting of criteria does not affect the level or may lead to an increase in innovation. However, this innovation will be driven by the need to comply with legislation. Different views exist whether this increase in innovation will lead to an increase in competitiveness in terms of having more and/or higher quality products.

Taking into account the impacts on the different and many actors involved in the supply chain ,and the lack of information on the supply chain, overall ranking of the four options for innovation and research can be only done assuming that the option having the less number of chemicals identified, will be performing the best. As a consequence, the options would perform 4>2/3>1. With respect to the options related to regulatory decision making, Option C would have less impacts than Option B and A, respectively (C>B>A), because they would respectively lead to the non-approval of less substances.

5. IMPACT ON SMES (EXCLUDING FARMERS)

The agricultural sector is constituted by SMEs, impacts on this sector are discussed in Annexes 12 and 13.

Small and medium-sized enterprises (SMEs) operate in the supply chain of PPP (importers, distributors). No specific data are available on these SMEs. SMEs are important for the BP market as more than 60% of the companies are SMEs (see Figure 4).

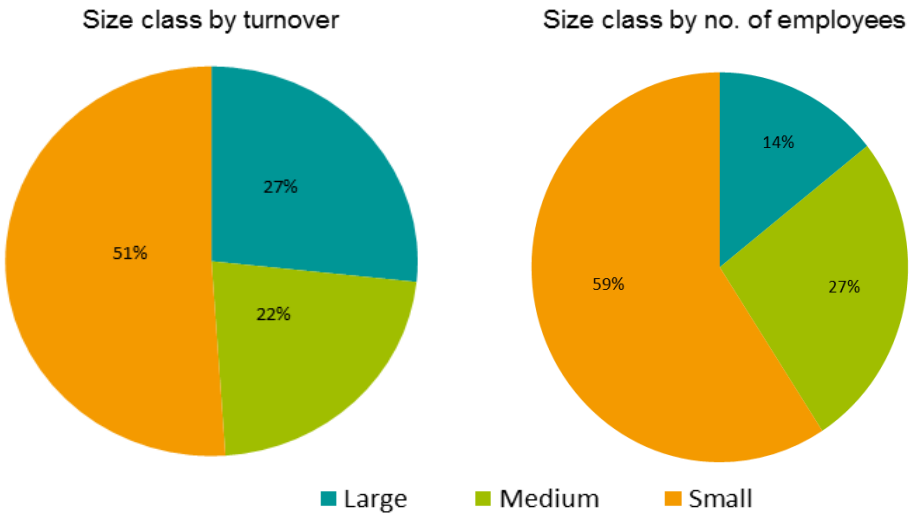

Figure 4. The percentage of SMEs in the EU biocides market[43].

Several economists assert that high cost research, as that required for PPP and BP, favour larger firms because of their greater financial capacity[44]. Larger firms are also better able to take advantage of their research because they have more market outlets[45]. Contrarily, SMEs have more difficult access to capital and their cost of capital is often higher than for larger businesses. Finally, to comply with detailed legislation does not match with the success factors of an innovative SME: an informal organisational structure with high flexibility, and less overhead and bureaucracy[46]. Therefore, SMEs, due to their specificities, can be affected by the ED criteria options assessed in this report more than their bigger competitors. In addition, under both the PPP and BP Regulations SMEs have to comply to the same rules as larger companies.

In general SMEs have products based on less active substances in their portfolio than larger companies, making them more vulnerable to the withdrawal of substances linked to the setting of ED criteria. However, the PPP and BP Regulation provide both the possibility, notwithstanding a chemical is identified as an ED, to approve the substance with restrictions for a fixed time period (see Table 7). A company would have to support this with additional data (for example for the comparative assessment whether suitable alternative substances and technologies are available). In order to prepare the additional data SME probably have to outsource it because of the limited personal resources and expertise in a SME. It is clear that applicants would need to invest and would be uncertain about the status of the substance for some time as the provided evidence for using the specific derogations has to be evaluated and the conditions for approval need

[43] Ecorys, Background study for the assessment of the appropriateness and impact of the existing fee model for the Biocidal Products Regulation and its possible revision. Draft Final Report (2016).
[44] Schumpeter, J.A. 1961. Theory of economic development, New York, Oxford University Press.
[45] Teece, D.J., 1982. Towards an economic theory of the multiproduct firm. Journal of Economic Behavior and Organisation 3: 39-63.
[46] European Commission. 2012. Interim Evaluation, Impact of the REACH regulation on the innovativeness of the EU chemical industry, Annexes, 2012 (Ares (2015)3396029).

discussion. In case of an approval, it would be for a shorter time than the normal period, so it will be re-assessed earlier increasing the cost to maintain the active substance on the market. These additional costs and demand on expertise and personal resources will constitute a, comparatively, higher burden to SMEs than for larger companies.

It is clear that the criteria will trigger additional costs and resources. In general it can be concluded that an increase in costs and a further demand in personal resources would favour bigger companies and negatively affect the market position of SMEs as bigger companies have greater financial capacity and can better spread risks. Moreover, SMEs are considered to be relatively more vulnerable than larger companies to the withdrawal of an substances because their portfolio consist of less substances. The options result to different levels of additional costs and resources and are expected to be related to the number of substances identified as ED. In general it can be concluded that the ranking of the options for SMEs can be done in the same way as innovation and competitiveness, but that the size of the impacts on SMEs will be expected to be larger. The impacts can lead to a reduction of SMEs, even a further concentration in the PPP and BP-sector, and less competition. Summarising the options would perform 4>2/3>1. With respect to the options related to regulatory decision making, Option C would have less impacts than Option B and A, respectively (C>B>A), because they would respectively lead to the non-approval of less substances.

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PART 15/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annex 15 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

{COM(2016) 350 final}
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ANNEX 15

FOOD SUPPLY AND INTERNATIONAL TRADE

Contents

This Annex focuses on the assessment of potential impacts, which build on the results of the screening study explained in Annexes 3 to 5. The results of the screening do not constitute evaluations of individual substances to be carried out under the respective chemical legislations [Regulation (EC) No 1107/2009 on plant protection products and Regulation (EU) No 528/2012 on biocidal products] and in no way prejudge future decisions on active substances to be taken pursuant to these two Regulations. It would thus be erroneous to consider that the substances listed in Annex 5 are considered as endocrine disruptors within the meaning of the EU legislation. The methods and results presented in this Annex are to be interpreted as an estimation of the potential impacts.

Annexes 8 to 15 describe the impacts expected when implementing the criteria to identify EDs (Options 1 to 4) under the current regulatory framework (Option A). In addition, it was assessed whether these expected impacts would remain the same or not under consideration of different regulatory implementations (Options B and C, only applicable to the PPP Regulation). The analyses of the impacts described in these Annexes translate into the "performance" of the options, which is one of the input parameters to the MCAs (Annex 6 and 7).

The MCAs results are not concluding on any preferred option for setting scientific criteria to identify endocrine disruptors, but aim at providing additional information to decision makers with regards to the potential impacts expected when implementing the criteria, after those would have been selected on the basis of science (two MCAs were performed: Options 1 to 4 under the current regulatory context, and Options A compared to Options B and C).

At a preliminary stage of the impact assessment it was anticipated that Option C should be discarded, nevertheless it was maintained for the analysis of the impacts for methodological reasons (see Section 4.2.3 of the main report and Annexes 6 and 7). Option C only applies to the PPP Regulation.

1. INTRODUCTION

Trade is essential to economic growth and job creation in the European Union (EU) and covers exports and increasingly also imports. Two-thirds of EU imports are raw materials, intermediary goods and components needed for companies' production processes. The share of foreign imports in the EU's exports has increased by more than half since 1995, to reach 13%.[1]

Food, feed, and treated articles are the three commodity groups used to analyse the impacts of the different options in this impact assessment (IA), and were the basis for MCA-criteria. With these three groups, many products imported to the EU are covered. These three groups are essential for food security, as well as for wellbeing and health. The three categories are also important to a range of trading partners. While feed are mainly imported from the Americas, and food mainly imported from the Americas, Africa and Oceania, treated articles, and especially textiles are heavily concentrated in Asia. The commodities falling under the different groups considered in this IA are briefly described below:

- **Food**; fresh, frozen and dried crops. Processed food and products are, with the exception of wine, not considered in this analysis because the residue monitoring is linked to a higher complexity including several ingredients and origins in one product, as well as processing factors.
- **Feed**; fresh and dried crops. Milled products, such as soya meal, are considered to be impacted to the same extent as the unprocessed products.
- **Treated articles**; a substance, mixture or article which has been treated with, or intentionally incorporates, one or more biocidal products[2]. The article can be a solid object, for instance a bathroom mat that gets an additional value by the treatment of an antibacterial substance.

In 2014, the EU imported agricultural commodities to a value of EUR 105 billion. Agriculture accounts for 6% of total imports from third countries to the EU both in terms of value and volume. Imported crops, especially from tropical countries, constitute a major part of the European diet. Coffee, tea, and bananas are three commodities most Europeans would consider essential to their diet but where Europe would not be able to meet demand without imports. The main trading partners for agricultural commodities, including animals and fish are United States, Brazil, Norway[3] and China.

[1] Import into the EU. DG Trade. http://ec.europa.eu/trade/import-and-export-rules/import-into-eu/
[2] See Article 3(1)((l) of BP Regulation (EU) 528/2012.
[3] Norway is the largest exporter of animal products to the EU-28, supplying 22 % of the total in 2013. 98 % of the animal products imported from Norway fell under the fish chapter, and represented EUR 4.5 billion. Source: Extra-EU trade in agricultural goods. Retrieved from: http://ec.europa.eu/eurostat/statistics-explained/index.php/Extra-EU_trade_in_agricultural_goods

Table 1. EU trade in 2014 with countries outside the EU-28.

EU TRADE IN 2014 WITH COUNTRIES OUTSIDE THE EU-28[4]		
Commodity	**Value in billion EUR**	**Quantity y in thousand tonnes**
Agriculture and food imports	106	99,088
as share of total	6%	6%
TOTAL IMPORTS	1,689	1,635,311

This Annex is outlined as follows. In the next section, the consequences of endocrine disruptor (ED) criteria on food security and international trade are lined out. Then the various data and information sources that have been used in the analysis of the case studies are listed, followed by the definition of each indicator /MCA criterion. In the methodology, it is explained how the IA was carried out, followed by the results and analysis for food, feed, and treated articles respectively. Last, the impacts on third countries' economies are assessed and discussed with case studies for bananas, wine, rapeseed, and citrus fruits.

2. CONSEQUENCES OF ED CRITERIA ON FOOD SECURITY AND INTERNATIONAL TRADE

The bottom line of EU regulation is that countries exporting to EU should meet the safety standards of the EU when producing food to be exported to the EU.

Regarding food and feed (agricultural commodities and processed products), when an active substance used as a PPP is non-approved for use within the EU, it will in extension have an impact on third countries and crops imported to the EU. The impact is due to the lowering of Maximum Residue Levels (MRL) to the limit of determination (LOD), as a consequence of implementation of point 3.6.5 of Annex II of Regulation (EC) No 1107/2009 and in compliance with Regulation (EC) No 396/2005.

What it means in practice for a MRL to be lowered to LOD is that in most cases it cannot be used in the production process of the crop to either fight pests or control diseases. Producers would therefore have to find substitutes or seek alternative practices to grow their crops if they still aim at exporting their products to the EU.

The main problems with losing part of the pesticide portfolio are:

i. increased risk of crop losses due to pests and diseases where there is no effective plant protection product available;
ii. increased risk of pests developing resistance to plant protection products due to reduced number of alternatives;
iii. increased risk of occurrence of mycotoxins in food and feed. These problems are more extensively discussed in Annex 12 on impacts of agriculture and Annex 10 on Human Health (Transmissible diseases and food safety).

[4] All import data and tables in this annex are extracted from Eurostat considering imports to EU-28 during Jan-Dec 2014, from countries outside the EU. Intra-EU trade is not assessed or analysed.

The consequences for trade and food security in the EU may be:

- smaller quantities of crops and products on the EU market, consequently sold to higher prices;
- food products of inferior quality compared to the quality of fruits and vegetables available on the market today;
- less feed available for animal production within the EU – resulting in feed of less quality and consequently this impacts the entire value chain of animal production.

Regarding treated articles, the BP Regulation foresees that a treated article shall not be placed on the EU market unless all active substances contained in the biocidal products that it was treated with or incorporates are approved. This is expecting to have consequences also on products produced outside the EU and imported.

In the **public consultation** in 2015 (see Annex 2), six public authorities and six governments from non-EU countries gave their comments. One of the main issues authorities from non-EU countries stressed was the potential impact on trade[5]. Countries and crops that may be affected are e.g. wine from Chile, bananas from Latin America, imports for feed such as soybeans, as well as citrus fruit from South Africa, just to name a few.

Further, the topic of ED criteria has raised **increasing attention in the WTO TBT and SPS Committees** during the last years. The issue was raised by the US for the first time in October 2013 and in March 2014 respectively. Since then it has been discussed, in one form or another, at every TBT and SPS Committee meeting. Overall, it is clear that the pressure on the EU is mounting as demonstrated by the growing number of WTO Members taking the floor to express concerns or to question the EU's ongoing work on defining the criteria to identify EDs. Please refer to Annex 8 for more details.

3. EVIDENCE AVAILABLE AND DATA USED

The results of the screening study, identifying which active substances of PPP and BP would be identified under each of the four options, are considered as a basis for the analysis. This information is then combined with the datasets and information sources described below in order to execute the analysis of the impact on trade. Therefore, the analysis underlying this Annex is considered as set of case studies which is based on the identity of substances identified under each option, and the MRLs which would be consequently lowered for a number of imported crops. For BPs, textiles have been selected as case study in order to illustrate potential impacts.

[5]Report on Public consultation on defining criteria for identifying endocrine disruptors in the context of the implementation of the PPP Regulation and BP Regulation. Retrieved from: http://ec.europa.eu/health/endocrine_disruptors/docs/2015_public_consultation_report_en.pdf

EU Pesticide Database

The EU Pesticide Database[6] has been used to obtain both the MRLs as well as information on active substances. MRL levels are extracted on an active substance and crop basis. A MRL marked with an asterisk (*) in the database signals that this is the LOD for that crop and active substance. For each active substance there is also a lot of other information listed in the database such as pesticide characteristics, and which sub-group of pesticide an active substance belong to (e.g. herbicide, fungicide, or insecticide).

Eurostat international trade data

The trade data is from Eurostat, COMEXT databases.[7,8] Imported goods are classified according to the Combined Nomenclature[9] (CN) and have to be declared stating under which subheading of the nomenclature they fall. For this IA it was necessary to use up to 6-digits of the CN Code, therefore, to match the trade data with the data on MRLs and crops, both the "EU trade since 1995 by HS6" as well as "EU trade since 1988 by HS2-HS4" were used depending on how refined the crop groups were for trade.

Report and list on candidates for substitution

The results of the screening were filtered for other "cut off" criteria:

1. none of the substances identified as ED were classified or to be classified as M1 nor persistent in the environment (see Annex 5).
2. substances which are classified or to be classified as C1, or R1[10] were flagged and not considered for the impacts on trade in this IA.

In this way, substances which are already having regulatory consequences under Regulation (EC) No 1107/2009 under consideration of other "cut off" criteria are not double counted.

For active substances used in BP, it was analysed whether the identified substances as potential ED in the screening would fall under any of the exclusion criteria[11] and for which product types the identified substances were approved.

[6] EU Pesticide Database (2016). Retrieved from: http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=homepage&language=EN
[7] Eurostat (2015a) EU trade since 1995 by HS6 (DS-016893)
[8] Eurostat (2015b) EU trade since 1988 by HS2-HS4 (DS-016894)
[9] Explanatory notes to the combined nomenclature of the European Union. (2015/C 076/01) Publication made in accordance with Article 9(1) of Council Regulation (EEC) No 2658/87 of 23 July 1987 on the tariff and statistical nomenclature and on the Common Customs Tariff. Retrieved from: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:C:2015:076:FULL&from=EN
[10] C1 is a known or presumed human carcinogen, and R1 is a known or presumed human reproductive toxicant, according to Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures.
[11] Article 5 of the BP Regulation (EU) 528/2012.

The 2013 European Union report on pesticide residues in food

The European Food Safety Authority (EFSA) report "The 2013 European Union report on pesticide residues in food"[12] was used to get an overview of the current state of MRL compliance with legal limits for imports as well as actual consumer exposure to pesticides for European consumers. The report was used to screen if there were any relevant substances or crops that could be used as case studies, however, none were identified and the selection of case studies was done based on the value of imports and how important the crop or product is for third countries.

4. METHODOLOGY

The purpose of the analysis is to describe potential impacts on trade and to rank the options of each aspect in the multi criteria analysis, in which the following criteria have been defined to assess how the options perform:

i. Potential impact on imports of agricultural commodities for food related to the lowering of the MRL level to the default value for substances identified as ED. No import tolerances are applied. The analysis considered different regions, e.g. Africa, Asia, US, Latin America, and particular goods; wine, cereal, depending on volume or trade impact.
ii. Potential impact on imports of agricultural commodities for feed related to the lowering of the MRL level to the default value for substances identified as ED. The analysis will focus on the main agricultural commodities imported as feed, e.g. soya.
iii. Potential impact on imports of treated articles (biocides). The supply chains for the manufacturing of articles are very complex. It is very difficult to estimate the impacts of a non-approval of a certain biocidal substance of the market (see also Annex 14). Textiles have been used as case study to evaluate of potential impacts.

General Assumptions

The LOD is the lowest amount or concentration of analyte in a sample that can be reliably quantified with an acceptable level of precision and accuracy, and this level can differ between substances. If an active substance has a MRL higher than the LOD for a certain crop in the MRL-database, it was assumed that the substance is needed and consequently used in practice. This assumption is made because it is costly to seek approval for an import tolerance and if it is not used on a specific crop there would be no need to seek approval for it.

However, a recent paper[13] analysing the impact of MRLs on trade came to the conclusion that the impacts from lowering MRLs are ambiguous. The authors note that the net impact of MRLs is positive on high-income OECD members' imports of plant products, which

[12] European Food Safety Authority (2015). *The 2013 European Union report on pesticide residues in food*. EFSA Journal 2015;13(3):4038, 169 pp. doi:10.2903/j.efsa.2015.4038

[13] Xiong, B., and Beghin, J., 2014. Disentangling demand-enhancing and trade-cost effects of maximum residue regulations. Economic Inquiry. Vol. 52, No. 3, 1190–1203. doi:10.1111/ecin.12082

invalidates the conventional wisdom that stringent food safety will impede trade. However, the impact on least developed countries is more severe due to their lack of financial and technological resources to comply with the MRLs adopted in the high-income OECD countries. The results in this IA are expected to follow the same line with developing countries being more severely impacted than developed countries. However, the effect will be the same over all options and would not contribute to the ranking of the options for the multi-criteria analysis.

There are multiple ways producers and third countries can react to the lowering of MRLs in EU. Expected responses could be; some producers will continue growing the same crop but try to swap to alternative approved substances that fight against the same pests; other producers may continue with their old practice but their produce may be exported to another part of the world or sold domestically; and others will discontinue with the crop they used to export to the EU and instead grow crops that is possible to produce with pesticides that are approved within the EU. This assessment will not delve deeper into the possible responses for each crop and country, instead, the focus is on the total value and volume of crops imported to the EU, and the share of crops in relation to the third country's total exports to the EU. Quantifying the precise welfare loss and socio-economic costs is not attempted and beyond the scope of this IA. However, the negative effects on trade are recognised.

The assessment will rank for PPP the four options against each other based on the number of MRLs lowered for the most valuable crops imported to the EU. It is assumed there will be no import tolerances.

For BP it is assumed that the non-approval of active substances or the approval under strict conditions would probably not initiate replacement of these substances (see Annex 14). Therefore less approved BP substances are expected to be available for treated articles. The impact on trade can be assessed by assuming that the option having the least number of chemicals identified performing relatively the best.

Data extraction and organisation

A database was built in order to identify the number of MRLs lowered for each imported crop under the different options. The first step was to combine trade data retrieved from Eurostat with the MRL Pesticide database for each active substance. The data extraction from both Eurostat and the Pesticide database was done in December 2015. The matching was done by identifying which crop or crop group in the trade data best corresponded with the crops in the MRL database. In most cases the matching was straightforward; however, some crops were divided into several categories (such as dried/fresh/frozen) in the trade data while this distinction was not made for the MRLs. In those cases the values of imports were added together for all subcategories of the crop, (e.g., this was the case for apples, CN Code 080810 and 081330). Another issue when matching the two datasets was not only that the trade data was further refined in some cases, in other cases the trade data was coarser in comparison with the crop specific data on MRLs. For trade, several crops were grouped together in the

same category (e.g., cauliflower and head broccoli, CN Code 07041000). In those instances care was taken to e.g., avoid double counting for sums.

To be able to refine the analysis of the impacts on trade, characteristics about the substances were collected from various sources and then added to the database. E.g., what type of pesticide an active substance is, if the substance is a Candidate for Substitution, the chemical class, if the substance would also fall under the cut-off criteria (classified as C1 or R1) in Reg 1107/2009 and hence non-approved regardless the criteria for EDs. The data sources and matching process is depicted in Figure 1. Flow chart describing the steps in which the data was organised

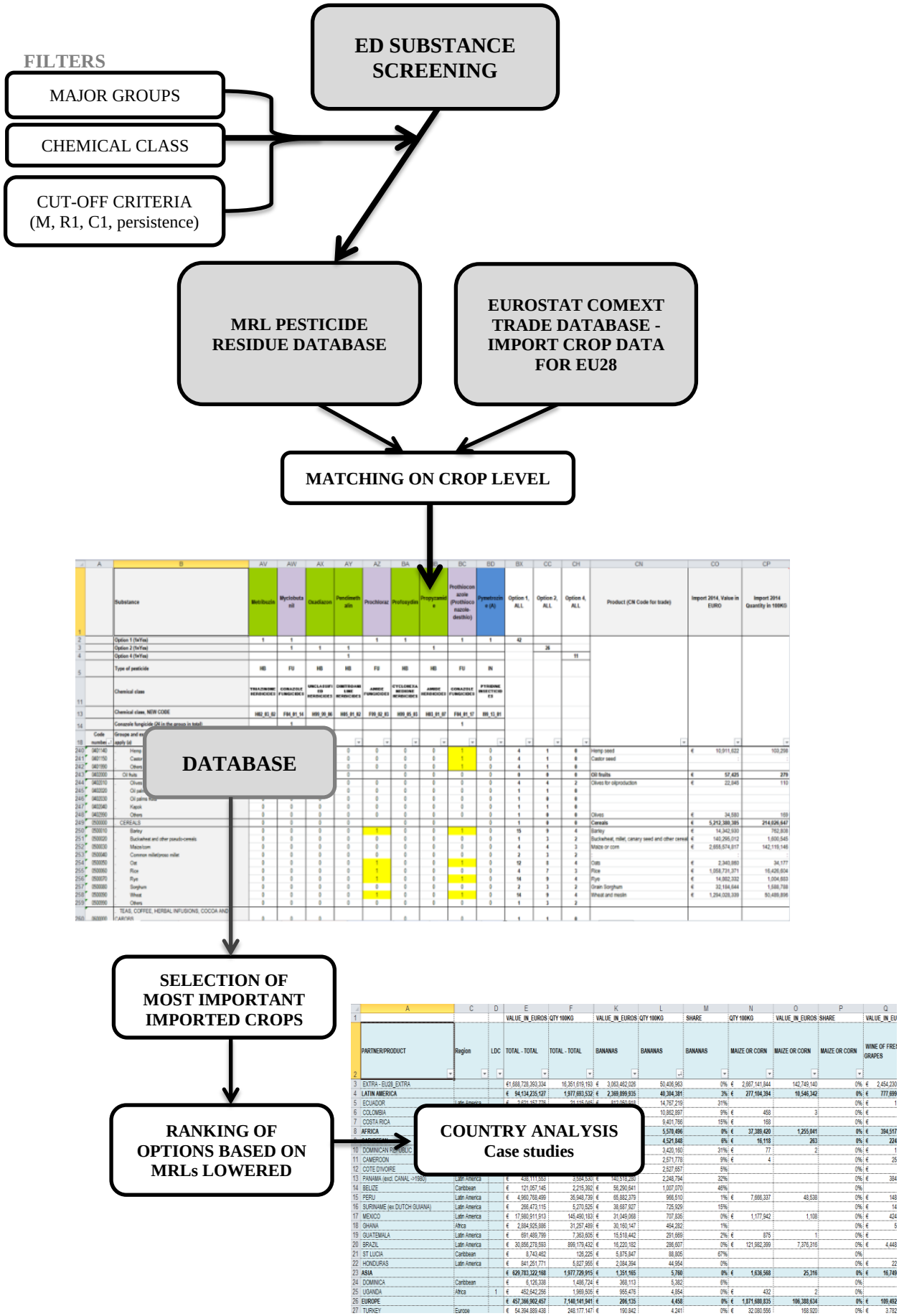

Figure 1. Flow chart describing the steps in which the data was organised. Data extracted in December 2015.

Analysis of the evidence

To determine how the options rank against each other and their respective impact on trade of food and feed the following rationale was followed for PPP.

- The more MRLs that are lowered for a certain crop, the greater the negative impact. I.e. 10 MRLs are lowered for Bananas under Option 1, 8 MRLs under Option 2 and 3 Category I, and 3 MRLs under Option 4. Thus, Option 4 performs better than Option 2 and 3, which in turn performs better than Option 1.
- The higher value and volume of imports that is expected to be affected, the worse the option performs.
- The higher the number of active substances from the same group of pesticides affected, the worse the option performs, i.e. if 80% of all the fungicides within a subgroup of fungicides are potentially affected, then the impacts are expected to be more severe since there are fewer substitutes available for a specific pest.

The first step in the **analysis for food** was to prioritise the analysis for the most imported commodities in terms of value. Trade is often measured in terms of volume not value, however, in this IA the value of crops was found to be a more relevant unit of comparison rather than volume because such diverse crops as wheat and bananas had to be compared against e.g., spices and nuts. The cut off for the above prioritisation was set at EUR 1 billion for the year 2014.[14] The most imported commodities are in descending order; coffee, nuts, cocoa beans, bananas, maize, wine, citrus fruit, wheat, table grapes, rape seed, and rice.

All commodities except for nuts and citrus fruit are measured individually. For nuts and citrus fruit, the decision to analyse them together is because the active substances that are affected are the same under the four options. Both nuts and citrus are two important crop groups for the European diet. Wine is included in the analysis although it is a product rather than a crop. The reasoning behind is that MRLs are differentiated and set specifically for wine grapes, however the imported product are not wine-grapes but wine, where the corresponding MRL corrected by a processing factor apply. Wine is also an important commodity for the EU as well as an important traded product internationally. Soyabeans are used both as food for humans and feed for animals, with the bulk of imports being used as animal feed. In this IA, soyabeans are assessed in the chapter for feed rather than food.

The second step of the analysis was to see which crops would be most affected in terms of the number of MRLs lowered, irrespective of value of the imports. This gives the absolute number of MRLs affected per crop for each option. Then it can be assessed which group of pesticides will be impacted the most. The four options were then ranked from best performing to worst in terms of the number of MRLs that would be lowered. The greater the number of MRLs affected, the greater the impact on trade, see Section 5.

The **analysis of feed** focusses on the four most important feed products; soyabeans, maize, rapeseed, and cottonseed. The ranking of the four options have been done in the same way as

[14] The cut off EUR 1 billion was chosen in order to include the most valuable food crops imported to the EU in the analysis.

for food with the option having the least number of MRLs lowered performing the best. The main source of information on the value of the feed market and potential impact on feed is taken from the report *Statistics on agricultural markets 2014* by DG AGRI.

To complement the quantitative analysis, a more qualitative analysis of the most valued imported crops is carried out and presented as **case studies**. EU import data was used to see which continents, regions and countries were most affected. Since EU has a developmental policy objective it is relevant to see if Least Developed Countries, as well as EU main trading partners were affected in particular. It is of importance to identify countries with a heavy dependence on exports of a certain crop. Two examples are Belize and St Lucia whose main exporting goods to the EU are bananas, that make up 46% and 67% of their total exports to the EU respectively.

Assessing the impact on third countries, the focus was not only on the total value and volume but also the share of the value of the affected crops of a country's total exports to the EU. Only data on EU imports and not on third country exports to the whole world have been used. This is because the impact of ED regulation is concerning EU only and may have no impact on crops grown for other markets.

Treated articles, i.e. articles treated with biocides are widely marketed often expressed in terms as anti-mold, anti-bacterial or anti-odour. Articles can be anything from kitchen ware, bathroom accessories, cleaning supplies, to toys and child care articles as well as a wide range of clothing such as sportswear, underwear, shoe insoles, hats, gloves, socks, mattresses, mattress covers, pillows, bedding, towels, rugs, furniture and curtains.[15] One issue assessing the impacts on treated articles is the lack of data on imports. Today there is no distinction between regular and treated articles with special features such as anti-mould. This makes it difficult to quantitatively assess the impacts in terms of value and volume. In 2009 it was noted that non-EU producers represent a non-negligible share of the EU market with treated materials which is estimated at EUR 22.2 billion per year; for example, imports amount to 10-20% of the EU market for treated wood and 25 to 40% of the EU market for wool carpets[16]. However, by applying an assumption on the share of treated articles among all imports there are rough estimates on the value of affected products. However, one category that is listed with a unique CN code are disinfectants – which are essential to health care. In 2014, the EU imported 22,000 tonnes of disinfectants to a value of EUR 65 million.

With the non-approval of a biocidal active substance, it can be assumed that manufacturers and importers have to make a considerable effort to adapt to the new requirements. They need to be aware of the obligations to use biocides in articles and gather detailed knowledge about the articles they place on the EU market. As a consequence, the following main impacts are expected:

[15] Chemicals in textiles – Risks to human health and the environment. Report from a government assignment. Swedish Chemicals Agency. Stockholm 2014.

[16] Commission Staff Working Document SEC(2009)773, accompanying document to the Proposal for a Regulation of the European Parliament and of the Council concerning the placing on the market and use of biocidal products - Impact Assessment. Retrieved from: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52009SC0773&from=EN

- more information exchange in the supply chain is required to make sure suppliers and exporters are aware of EU rules on treated articles;
- implementing control measures will require considerable efforts from manufacturers, importers and authorities alike.

For the purpose of this IA, textiles were used as a case study because their majority, approximately 80% of the textile articles consumed in the EU, are imported from a non-EU country.[15] Biocidal products are used in the textile industry for three main purposes:

1. to improve the storage stability of aqueous raw materials and auxiliaries by preventing microbial material destruction;
2. to preserve fibrous material from microbial deterioration (to prevent rot and mildew);
3. to protect keratin-containing textiles from damage caused by insect pests[17].

In 2014, the EU imported apparel to a value of EUR 73 billion (4.6 million tonnes), and textiles (excl. apparel) to a value of EUR 26 billion (6.8 million tonnes).[15] In total, imported textile are as important in terms of value as the whole agricultural sector imports combined. It therefore constitutes a relevant case study as some textiles are treated with biocides that may fall under one or several of the four options in the screening of EDs.

5. RESULTS OF THE ANALYSIS

MCA-criterion i) volume of imports of food potentially affected by lowering the MRLs

In **Table 2** are the most valuable imported food crops to the EU. These eleven crops are imported to a value of close to EUR 30 billion, which is roughly 30% of all agricultural imports to the EU. The options are ranked in accordance with the number of MRLs that may be lowered under the four options, with the best performing option being the one with the least MRLs being lowered.

Option 4 consistently performs the best for all crops and consequently will have the least disruptive impact on trade and imports of the four options.

Looking beyond the best performing option it is clear that all Options 1, 2 and 3 Category I will have a significant negative impact on trade and food supply in Europe. However, it is not clear which option has the most negative impact on trade, rather it depend on the crop. E.g. citrus fruits will be more heavily impacted by Option 2 and Option 3 Category I with 11 substances potentially removed from the pesticide portfolio, while wheat is more impacted by option 1 compared to 2 and 3. Citrus fruits and wheat are comparable in terms of value of imports; however, it is not obvious which crop is more important to the EU as a whole in terms of food, health, jobs and growth. Therefore, for the purpose of MCA, the performance is considered equal between Option 1 and 2/3 Category I.

These top imported crops to the EU are used as proxy for the full list of crops that will be affected by lowered MRLs. The same pattern re-appears across the entire list. Option 4

[17] Lacasse, K.,Baumann, W. 2004. Textile chemicals, environmental data and facts. Springer, ISBN 978-3-642-62346-2. DOI 10.1007/978-3-642-18898-5

consistently has the least impact on the crops and trade while it varies depending on the crop if Option 1, Option 2 or Option 3 Category I will affect the most MRLs.

Table 2. Most valuable imported food crops in 2014 and how they rank

FOOD - MOST VALUABLE IMPORTED CROPS 2014 AND HOW THEY RANK							
Product	**Value in million EUR**	**Qty in thousand tonnes**	**Performance**	**Number of MRLs**			
				Opt. 1	**Opt. 2**	**Opt. 3 Cat I**	**Opt. 4**
Coffee	€7,854	2,887	**4>2/3>1**	3	2	2	0
Nuts	€4,373	791	**4>1>2/3**	3	5	5	2
Cocoa beans	€3,167	1,384	**4>1/2/3**	1	1	1	0
Bananas	€3,063	5,041	**4>2/3>1**	10	8	8	3
Maize	€2,656	14,212	**4>1/2/3**	4	4	4	3
Wine	€2,454	1,389	**4>1>2/3**	12	15	15	7
Citrus fruits	€1,485	1,914	**4>1>2/3**	7	11	11	5
Wheat	€1,294	5,049	**4>2/3>1**	14	9	9	4
Table grapes	€1,225	598	**4>1>2/3**	11	13	13	7
Rape seed	€1,170	3,072	**4>2/3>1**	12	9	9	4
Rice	€1,059	1,643	**4>1>2/3**	4	7	7	3
TOTAL	**€29,800**						

A weighted ranking was done to get a better perspective of the difference between the options in terms of value and number of MRLs affected. This was done by multiplying the total import value with the number of MRLs potentially lowered. Thus, the most valuable crops get a high weight but it is also important how many active substances might disappear from the market. The ranking varies slightly between the options with cereals and oilseed more impacted under Option 1 and citrus fruit under Option 2 and 3 Category I (see Table 3).

Table 3. Weighted ranking – most affected crops in terms of value and MRL

WEIGHTED RANKING - MOST AFFECTED CROPS IN TERMS OF VALUE AND MRLS			
Option 1	**Option 2**	**Option 3 Cat I**	**Option 4**
Bananas	Wine	Wine	Wine
Wine	Bananas	Bananas	Bananas
Coffee	Nuts	Nuts	Nuts
Wheat	Citrus fruits	Citrus fruits	Table grapes
Rape seed	Table grapes	Table grapes	Maize
Table grapes	Coffee	Coffee	Citrus fruits
Nuts	Wheat	Wheat	Wheat
Maize	Maize	Maize	Rape seed
Citrus fruits	Rape seed	Rape seed	Rice
Rice	Rice	Rice	Coffee
Cocoa beans	Cocoa beans	Cocoa beans	Cocoa beans

The main ranking is based on the most valuable imported crops to the EU; however, Table 4 lists the most impacted crops with regards to the number of MRLs that may be lowered. Tomatoes is the most impacted food crops in absolute terms with 17 MRLs lowered under

Option 1.This represents 12 % of the total number of MRLs for tomatoes. Another crop highly impacted by Option 1 is barley with 15 MRLs lowered which is 13% of the MRLs set. Crops with high expected impacts under Option 2/3 Cat I are wine and pears with 15 MRLs lowered. This represents 11% and 12% of the MRLs set respectively. Peaches is affected equally by option 1, 2 and 3 Cat I with 14 MRLs lowered, this represents 13% of the MRLs set for peaches.

Table 4. Most affected crops based on the number of MRLs lowered.

MOST AFFECTED CROPS BASED ON THE NUMBER OF MRLS LOWERED							
MRL	**Option 1**	**MRL**	**Option 2**	**MRL**	**Option 3 Cat I**	**MRL**	**Option 4**
17	Tomatoes	15	Wine	15	Wine	8	Tomatoes
15	Barley	15	Pears	15	Pears	7	Wine
14	Peaches	14	Tomatoes	14	Tomatoes	7	Pears
14	Wheat	14	Peaches	14	Peaches	7	Table grapes
14	Rye	14	Apples	14	Apples	7	Strawberries
13	Capsicum	14	Apricots	14	Apricots	7	Capsicum
13	Melons	14	Cherries	14	Cherries	7	Cucumbers
12	Wine	14	Plums and sloes	14	Plums and sloes	7	Gherkins
12	Cucumbers	13	Table grapes	13	Table grapes		
12	Apples	13	Pumpkins	13	Pumpkins		
12	Courgettes	13	Quinces	13	Quinces		
12	Rape seed	13	Medlars/Loquats	13	Medlars/Loquats		
12	Oats	13	Strawberries	13	Strawberries		

MCA-criterion ii) volume of imports of feed potentially affected by lowering the MRLs

Four imported commodities that is mainly used for feed are listed in Table 5; soyabean, maize, rapeseed and cottonseed. They represent the bulk of EU feed imports and crucial to the animal husbandry sector. Roughly five million EU farmers raise animals for food production with a value of about EUR 130 billion. Every year, they need approximately 450 million[18] tons of feed, most of which are roughages grown and used on the farm of origin. The balance includes cereals grown and used on the farm as well as feed purchased by livestock producers to supplement their own feed resources[19] (such as maize, soyabean, rapeseed, and cottonseed). The EU is a major importer and dependent on imports of agricultural commodities for feed use. It is therefore relevant to evaluate the impact of ED criteria on feed imports and in extension the entire livestock sector in the EU.

The four options are ranked in accordance with the number of MRLs that will be lowered with the best performing option being the one with the least MRLs being lowered. In the next

[18] European Commission, DG SANTE. Accessed on: http://ec.europa.eu/food/food/animalnutrition/index_en.htm

[19] Feed & food Statistical Yearbook 2014. European Feed Manufacturers Federation (FEFAC).

paragraphs, feed products and the importance of imported feed to EU is explained, followed by a discussion of the performance of the options.

In the event of an interruption of soy product exports to the EU, the EU meat markets, poultry and pork in particular, would be affected due to the more costly and limited feed alternatives.[20] The increase in feed costs could weaken the competitiveness of the EU livestock sector and reduce the EU shares in domestic and world markets. A trade disruption would amplify the current EU protein deficit for the livestock sector and the need for alternative sources. These alternatives may come from increased production of oilseeds, such as rapeseed and sunflower seeds, or protein crops, such as field peas, field beans and sweet lupines.[20] Given the low level of EU competitiveness, the European Commission estimates that an increase in oilseed and protein seed acreage could replace at most 10–20% of EU imports of soyabeans and soyabean meal[21], but in that case farmers would need to be able to protect their crops with plant protection products and may face similar situations with respect to the residue levels as the imported commodities.

The EU production of soyabean, rape and sunflower seeds, as well as pulses and other legume crops, compensates to a limited extent the EU dependence on soyabean and soymeal imports. However, for now these products cannot, on their own, meet the EU protein needs for feed.[22] The low self-sufficiency (of e.g. soya) exposes the EU to possible trade distortions, sustainability problems, scarcity and price volatility of soyabean on the global market.[23]

Table 5. Feed imports 2014 and how the options perform.

FEED IMPORTS[24] 2014 AND HOW THE OPTIONS PERFORM							
Product	**Value in million EUR**	**Quantity in thousand tonnes**	**Performance**	**Number of MRLs**			
				Opt 1	**Opt 2**	**Opt3 Cat I**	**Opt 4**
Soyabeans[25]	€5,264	13,079	**4>2/3>1**	7	4	4	0
Maize	€2,656	14,212	**4>1/2/3**	4	4	4	3
Rape seed	€1,170	3,072	**4>2/3>1**	12	9	9	4
Cotton seed	€19	69	**4>2/3>1**	10	5	5	2
TOTAL	**€9,109**						

[20] Henseler, M., Piot-Lepetit, I., Ferrari, E., Gonzalez Mellado, A., Banse, M., Grethe, H., Parisi, C., Hélaine, S. 2013. On the asynchronous approvals of GM crops: Potential market impacts of a trade disruption of EU soy imports. Food Policy 41: 166-176

[21] DG AGRI of the EC. 2007. Economic Impact of Unapproved GMOs on EU Feed Imports and Livestock Production. European Commission, DG AGRI Report.

[22] EIP-AGRI Focus Group Protein Crops: final report. http://ec.europa.eu/eip/agriculture/en/content/eip-agri-focus-group-protein-crops-final-report.

[23] Visser, C.L.M., Schreuder, R., and Stoddard, F. (2014) The EU's dependency on soya bean import for the animal feed industry and potential for EU produced alternatives. Oilseeds & fats Crops and Lipids (OCL) 21(4). DOI: 10.1051/ocl/2014021

[24] EUR 9 billion is the total value of soyabeans, maize, rapeseed and cotton seed considering beans and seeds only, not milled products. This figure should therefore be considered as a lower bound value of the imports for feed. Note that feed imports are generally not estimated in value but in volume.

[25] Note that this figure is for soyabean imports only which constitute less than half of the total share of soya feed, the rest (roughly 18 million t) are imported as soyameal. In total, the EU imports on a yearly basis on average 36.1 million tonnes of soyabean equivalent.

Soy

Soyabeans are one of the most important feedstuffs for the EU due to their high protein content and is used by livestock producers in the EU to achieve a balanced diet, particularly for pigs and poultry. The EU has a self-sufficiency rate of only 3% for its soyabean and soyameal needs.[26;27] Since the overall import volumes of soyabeans and soyabean meal are much higher than EU domestic production, they are crucial for the EU animal sector. Few alternatives exist to replace these protein rich crop imports in the short term.[28]

Around two thirds of soyabeans used in the EU feed industry are imported, mostly from Argentina, Brazil and the US.[20] In the last three years, the EU has imported on average 36.1 million tonnes of soyabean equivalent[29] on a yearly basis. On average, 12.7 million tonnes of soyabeans are imported into the EU for crushing into soyabean oil and meal; and 18.5 million tonnes of soyameal (i.e. 23.4 million tonnes of soyabean equivalent) are directly imported into the EU. Commodity imports are concentrated in a few EU ports, from where they are traded to other Member States. The total value of soybean and soymeal imports to the EU mounted to EUR 10.6 billion in 2014-2015.

Between 0.43 and 0.56 million hectares of soyabean crops have been cultivated in the EU in the last three years, producing between 0.96 and 1.85 million tonnes of soyabeans. In the EU, soyabeans are mainly produced in Italy (around half of the EU production), Romania, France, Hungary and Austria.[20]

Maize

The EU has imported, in the last three years, between 8 and 14 million tonnes of maize per year. In addition, the EU has also imported between 0.2 and 0.7 million tonnes of Corn Gluten Feed CGF which is a by-product of the starch industry used as an animal feedstuff.

More than 9 million hectares of maize crop are cultivated in the EU per year producing between 60 and 78 million tonnes of maize. The EU self-sufficient rate on maize depends on the year, fluctuating between 82% and 102% in recent years.[30]

[26] The Self-Sufficiency Ratio (SSR) expresses the magnitude of EU production in relation to domestic use, i.e. SSR = production / (production+ imports - exports ± changes of stock).

[27] Statistics on agricultural markets 2014, DG AGRI. http://ec.europa.eu/agriculture/markets-and-prices/market-statistics/index_en.htm

[28] DG AGRI of the EC. 2007. Economic Impact of Unapproved GMOs on EU Feed Imports and Livestock Production. European Commission, DG AGRI Report.

[29] Soyabeans are crushed to extract oil. The remaining by-product is soymeal, which is used for feed. One tonne of soyabean grains produces 0.20 tonne of oil and 0.79 tonne of meal. Data on soyabeans and soymeal have to be expressed into the same equivalent unit to allow adding them up. In order to compare EU imports of soyabeans and soymeal versus EU production of soyabean crops, data have been expressed in soyabean equivalent (SOE). A conversion factor of 0.79 has been applied.

[30] Statistics on agricultural markets 2014, DG AGRI. Retrieved from: http://ec.europa.eu/agriculture/markets-and-prices/market-statistics/index_en.htm

Rapeseed

The EU imports, on average, 3.5 million tonnes of rapeseeds per year, and between 0.2 and 0.47 million tonnes of rapeseed meal. In total, on average, the EU imports 4.2 million tonnes of rapeseed equivalent. More than 6 million hectares of oilseed rape are cultivated in the EU on a yearly basis, producing between 19 and 21 million tonnes of rapeseed. The EU self-sufficiency rate on rapeseed reaches about 85%.[30] For more information on rapeseed, see case study III in this annex.

Cottonseed

On average, the EU imported 0.054 million tonnes of cottonseeds and 0.009 million tonnes of cottonseed meal in recent years. In total this equals 0.76 million tonnes of cottonseed equivalent.[31] The EU cultivates around 0.3 million hectares of cotton, producing around 0.5 million tonnes of cottonseed per year. There is no data on EU self-sufficiency of cottonseed.

Performance of the options for feed

Option 4 consistently performs the best for all the four feed products and consequently will have the least negative impact on trade and imports. Option 1 is the worst performing option with the most MRLs potentially affected. Therefore, compared with the impact on food, it is possible to draw the conclusion that Option 1 is performing worse than Option 2 and Option 3 Category I. The ranking for feed is 4>2/3>1.

Both the number of MRLs and which chemical class they belong to differ between the four options. The main impacted major group are fungicides, and this is a general conclusion not just for soyabeans, maize, rapeseed and cottonseed but for all crops. Among the four feed crops evaluated, rapeseed has an even more pronounced impact on fungicides than the others.

MCA-criterion iii) volume of imports of goods which may be affected as a consequence of implementing the Biocidal Products Regulation in relation to treated articles

Biocides are used to control harmful organisms from causing health and environmental risks, or damaging products. The EU legislation relating to biocides is aimed at improving the functioning of the internal market and to ensure a high level of protection of human and animal health as well as of the environment. The EU biocides rules apply to articles placed on the market, either produced within the EU or imported.

The term treated article means any substance, mixture or article which has been treated with, or intentionally incorporates, one or more biocidal products.[32] A treated article may only be placed on the market if the active substances contained have been approved in the EU, or are included in the corresponding review programme of active substances.

[31] The conversion factor applied between cottonseed and cottonseed meal is 0.45.
[32] Article 3(1)(l) of BP Regulation

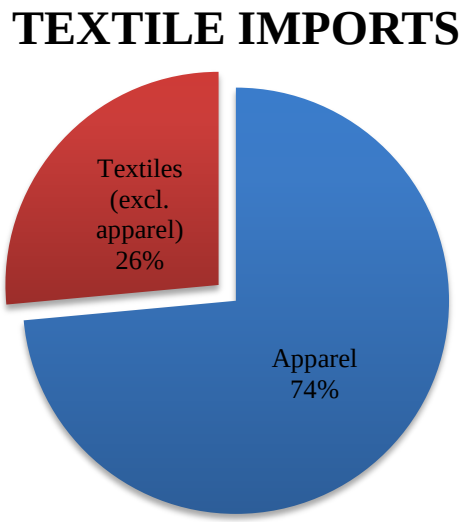

Figure 2. Textile imports to the EU divided into textiles and apparel.

The analysis of this IA focuses on textiles, since their majority, approximately 80%, of the textile articles consumed in the EU are imported from a non-EU country.[33]

If a biocide is non-approved in the EU, it means it cannot be used on or incorporated in any article imported to the EU as well. It applies to all goods falling in the scope of the definition of treated article, not only those goods with a claim to be a biocidal treated article. However, unless a specific claim that the product is treated with a biocide is made, it is difficult to find out if an article has been treated or not.34

There are two ways in which textile could be designated as a treated article in statistics:

1) to prevent growth of mould during storage and transport;
2) to create special functions of clothes or garments, such as anti-odour in tops and sportswear. Treated textile materials are for instance pure or blended cotton, wool, polypropylene, acrylics, polyamide and polyester.33

Not all textiles imported to the EU are treated articles. Currently, there is no reliable data on the share of treated articles with respect to all imported textiles. This is because treated articles do not have a separate CN Code for trade and imports. With the Biocides Products Regulation, applying from 1 September 2013,[35] data will be collected to get a better overview of the volumes and values of treated articles. Due to the current lack of data, the assumption is made that 5% of all imported textiles could be considered a treated article. This is a based on

[33] Chemicals in textiles – Risks to human health and the environment. Report from a government assignment. KEMI Swedish Chemicals Agency. Stockholm 2014. Retrieved from: https://www.kemi.se/files/8040fb7a4f2547b7bad522c399c0b649/report6-14-chemicals-in-textiles.pdf

[34] KEMI PM 2/12 Biocide treated articles - an Internet survey (2012). Retrieved from: https://www.kemi.se/global/pm/2012/pm-2-12-biocide-treated-articles.pdf

[35] The transitional measure for treated articles will apply until 1 March 2017.

the estimate of 25% for wool carpets and taking into account the relatively low percentage of chemicals used for treatment of textiles.[16;36] This is a conservative estimate; however, considering the total value and volume of textiles, the market value for treated textile articles would still be more than EUR 3.5 billion. So the potential impact from removing certain biocidal products from the EU market may affect EUR 3.5 billion worth of imports.

Table 6. Top EU-28 import of apparel in 2014.

TOP EU-28 IMPORT OF APPAREL 2014		
Partner	**Value billion EUR**	**Qty (tonnes)**
China	€28.35	2,035,743
Bangladesh	€11.04	928,687
Turkey	€9.19	412,632
India	€4.64	262,962
Cambodia	€2.23	146,927
Vietnam	€1.64	84,351
Morocco	€1.63	53,668
Tunisia	€1.47	50,141
Pakistan	€1.06	85,973

The main trading partners for textiles are Asian countries with China being the biggest exporter by far. In contrast with food and feed, the textile industry is heavily concentrated in Asia.

As with the downstream use of biocidal products in general (see annex on competitiveness and innovation), it is difficult to estimate the impact of the setting the criteria for EDs. For example, it will depend on the alternatives available for the biocidal active substance not any more allowed on the EU market. For textiles an EU Ecolabel[37] exist including restrictions on the use of biocides in textiles. This shows that alternatives for biocidal substances may be available. One outcome could be higher prices of treated articles in an initial phase before a substitute is found. In 2015 the EU Ecolabel was awarded to 2501 textile products (in total of 44711 EU Ecolabel products on the market). One impact of withdrawing a biocidal substance from the market could be higher prices of treated articles as a limited number of companies would be able to supply treated articles of the same quality. Another possible impact may be the removal of certain treated articles from the EU market, either indefinitely or temporary.

6. PERFORMANCE OF THE OPTIONS

From the analysis of the evidence illustrated in previous sections of this annex (based on the screening study results, MRL and trade data), it can be concluded, that for all MCA-criteria

[36] See Windler, L., Height, M., and Nowack, B. 2013. Comparative evaluation of antimicrobials for textile applications. Environment International 53: 62-73. http://dx.doi.org/10.1016/j.envint.2012.12.010

[37] EU Ecolabel Textile Products User Manual. Retrieved from: http://ec.europa.eu/environment/ecolabel/documents/User_manual_textile.pdf

considered (import of food, import of feed, and import of treated articles) the ranking of the Options 1 to 4 would be 4 > 1/2/3.

Less substance would be affected for PPP in Option B (introducing elements of risk assessment) compared to Option A (basically based on hazard). Option C introduces in addition socio-economic elements, which are however not applicable for MRL setting (food and feed) which is the driver for trade impacts. Thus, Option C and B could be considered to be ranked equally. The ranking of the Options A to C would be, as a consequence, C /B > A for both import of food and feed indicators. For treated articles the options A, B and C were not evaluated as these options are only relevant for PPP.

7. CASE STUDIES - IMPACT ON THIRD COUNTRIES

The EUs main trading partners are the United States (US), China, and Japan. The EU is also committed to support Least Developed Countries (LDC)[38] and special attention is given to these countries when assessing any potential negative impact that new criteria for EDs may have. The EU market is the world's most open market toward developing countries. If fuels are excluded, the EU imports more from Least Developing Countries than the US, Canada, Japan and China together.[39]

The EU is the fifth largest export market for US agricultural products, while the US is the largest export market for EU agricultural products. US agricultural producers rely on a variety of plant protection products to control pests and plant diseases, improve quality and yield, and limit human disease outbreaks associated with rodent and insect populations. Without the availability of viable pest mitigation alternatives, the elimination of important pesticides could significantly limit the quantity and quality of US agricultural goods intended for export to the EU.[40]

Emerging and developing countries face the stringent European legislative requirements on safe food production, which restricts opportunities for exports. Developing or transition countries accounted for more than 88% of all EU food and feed rejections between 2002 and 2008. As roughly 70% of the imports of agricultural produce originate from developing

[38] **Least Developed Countries:** Afghanistan, Angola, Bangladesh, Benin, Bhutan, Burkina Faso, Burundi, Cambodia, Central African Republic, Chad, Comoros, Congo Dem Rep., Djibouti, Equatorial Guinea, Eritrea, Ethiopia, Guinea, Guinea-Bissau, Haiti, Kiribati, Lao PDR, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mozambique, Myanmar, Nepal, Niger, Rwanda, Sao Tome and Principe, Senegal, Sierra Leone, Solomon Islands, Somalia, South Sudan, Sudan, Tanzania, The Gambia, Timor-Leste, Togo, Tuvalu, Uganda, Vanuatu, Yemen, and Zambia. The World Bank IBRD-IDA, Least developed countries: UN classification. Retrieved from: http://data.worldbank.org/region/LDC

[39] EU position in world trade. http://ec.europa.eu/trade/policy/eu-position-in-world-trade/

[40] Comments of the US Government. European Commission's Public Consultation on Defining Criteria for Identifying Endocrine Disruptors (EDs) in the Context of the Implementation of the Plant Protection Product Regulation and Biocidal Products Regulation.

countries it can be expected that the rejections are mainly related to products from developing countries.[41]

In the EU, imports have to comply with several safety and quality standards – pesticide residues being one of them.[41] Another example is the obligation to treat or corporate in articles biocidal products containing only active substances approved in the EU. This might be quite challenging for some of the exporting countries. In addition, the economic consequences for complying with EU legislation by the exporting third countries are high. Several studies have demonstrated that investments in infrastructure, training and capacity building or workers and implementation of food safety management systems are demanding economical efforts from exporting countries.[41]

1.1. Case Study I - Bananas

Bananas[42] are one of the world's most important food crops in terms of gross value of production and the most commonly eaten fruit in the world.[43] It is a staple food and a key export commodity for many low-income countries.[44] Every year, more than 100 million tons of bananas are produced in around 130 countries.[45] The EU is the largest importer of dessert bananas in the world, followed by the United States. In 2014, 5 million tonnes of bananas were imported to the EU from Third Countries.

Most bananas are consumed domestically. However, around 20 % of the world production of bananas is traded internationally. The banana sector is a very dynamic industry. World production more than doubled since 1990, from around 47 million tonnes, to 107 million tonnes in 2013; bananas traded internationally show a similar growth, increasing from 9 million tonnes in 1990 to 20 in 2013.[45]

[41] Uttendaele, M. 2014. "Issues surrounding the European fresh produce trade: a global perspective". Global Safety of Fresh Produce: A Handbook of Best Practice, innovative commercial solutions and case studies. Ed. Hoorfar, J. Woodhead Publishing. Cambridge, UK.

[42] Bananas comprise a diverse group, including cooking types such as plantains and a wide range of dessert types.

[43] Banana is the eighth most important food crop in the world and the fourth most important food crop among developing countries according to the UN agency FAOSTAT.

[44] Jaime de Melo. 2015. "Bananas, the GATT, the WTO and US and EU domestic politics", Journal of Economic Studies, Vol. 42 Iss: 3, pp.377 - 399

[45] Anania, G., 2015. The role of trade policies, multinationals, shipping modes and product differentiation in global value chains for bananas. The case of Cameroon. International Conference of Agricultural Economists. Milan 29th May, 2015, published on the African Journal of Agricultural and Resource Economics 2015; 10(3): 174-191. Retrieved from: http://ageconsearch.umn.edu/bitstream/211666/2/1%20Anania.pdf

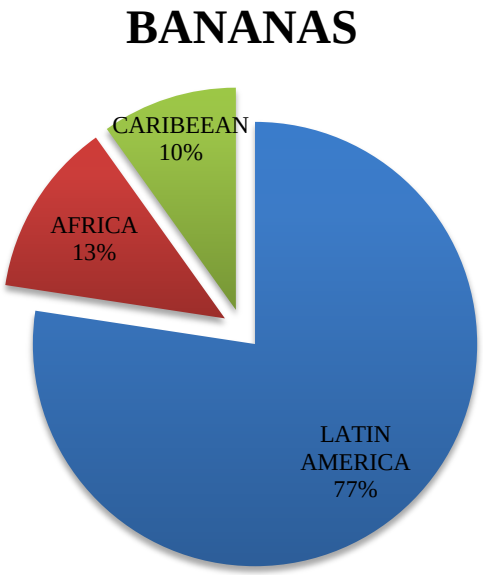

Figure 3. Banana imports to EU-28 based on region of production.

In 2013 the six main producers of bananas accounted for almost two thirds of global production; they were, in order of importance: India, China, the Philippines, Brazil, Ecuador, and Indonesia. The largest net exporters of bananas and their ranking do not coincide with those based on production, as India and China, the two largest producers, are marginal international traders and net importers. The largest net exporter in 2013 was Ecuador (27.7% of total world exports), followed by the Philippines (17.2%), Guatemala (16.3%), Costa Rica (9.8%) and Colombia (8.2%).[45] In 2013 the top five exporting countries alone accounted for 79% of the world market. Market concentration for imports is even higher than for exports.

The EU is supplied by three different groups of origins for bananas:

- Most Favoured Nation (MFN) countries, mainly Central and Southern America countries.
- Africa, Caribbean and Pacific (ACP) countries.
- EU own production.

In total, there are 61 MRLs set for bananas and depending on the option, more or less substances will be affected. Option 1 will have the greatest impact on bananas, since it will affect the most substances, 16% of all MRLs currently set. Option 4 will have the least impact on the production of bananas, with only 5% of total MRLs possibly affected. This is the general trend for all crops; however, the long term impact on availability, prices, welfare, and production techniques is not clear cut. In some cases there may be good crop protection alternatives available but in other cases not, and this has to be assessed on a region and pest level basis at the respective third countries.

Table 7. Banana imports and the share of potentially affected MRLs under the four options.

BANANAS - IMPORTS TO EU-28 AND POTENTIALLY AFFECTED MRLS							
Value in million EUR		Quantity in thousand tonnes	Total number of MRLs set	Share of MRLs			
				Opt 1	Opt 2	Opt3 Cat I	Opt 4
€	3,063	5,041	**61**	16%	13%	13%	5%

The removal of some pesticides could possibly benefit the health of workers in banana plantations and in sorting factories in third countries. Furthermore, the removal of some pesticides may also spur innovation or lead to a change in farming technique or crops. This type of legislation may promote an increase in the organic banana supply in the EU. Although organic bananas currently target higher income consumers,[45] an increase in supply may put downward pressure on prices.

Main impacts

- Latin America, Caribbean and African countries most affected
- Lower volumes imported sold to higher prices
- Some very small countries, such as St Lucia, are heavily dependent on their banana exports and will be impacted.
- May imply a shift towards other crops and affect farming practice.

Table 8. Banana imports to EU-28 in 2014 by main trading partner.

RANK	PARTNER/PRODUCT	VALUE IN EUR	QTY 100KG	SHARE OF EXPORTS TO THE EU
1	ECUADOR	€ 812,050,918	14,767,219	31%
2	COLOMBIA	€ 698,644,569	10,862,897	9%
3	COSTA RICA	€ 549,230,124	9,401,766	15%
4	DOMINICAN REPUBLIC	€ 239,456,233	3,420,160	31%
5	CAMEROON	€ 189,199,034	2,571,778	9%
6	COTE D'IVOIRE	€ 169,301,183	2,527,657	5%
7	PANAMA	€ 140,518,280	2,248,794	32%
8	BELIZE	€ 56,290,641	1,007,070	46%
9	PERU	€ 65,882,379	966,510	1%
10	SURINAME	€ 38,687,927	725,929	15%
11	MEXICO	€ 31,049,068	707,835	0%
12	GHANA	€ 30,160,147	464,282	1%
13	GUATEMALA	€ 15,518,442	291,669	2%
14	BRAZIL	€ 16,220,182	286,607	0%
15	ST LUCIA	€ 5,875,847	88,805	**67%**

Fair Trade and organic banana production constitutes the most important single factor explaining the rapid increase in recent years of volumes exported and market shares of some of the relatively smaller banana exporters, such as the Dominican Republic (today the largest

supplier of Fair Trade bananas), and Peru.[45] Other large exporters of Fair Trade bananas are Colombia and Ecuador.

Assuming a reduction in number of active substances will impact the quality of bananas due to the smaller range of pesticides available to fight certain pests, the EU may have to accept imports of lower quality. A potential scenario is also that if the quality of bananas decrease, more fruit will be sold domestically as they are seen unfit for exports.[45] The result would be a decrease in volumes of bananas exported to the EU, consequently sold to higher prices.

Another assumption is that new stringent criteria for ED will have the same impacts as new private standards. Thus, only prices will change due to costlier production processes, however, availability and quantity will not be significantly impacted.[4545]

Looking at the different chemical classes between the options, it is clear that fungicide is the most impacted major group.

1.2. Case Study II – Wine

The EU is the world's leading producer of wine; however, the EU is also a major importer of wine. Grapes used for wine are very susceptible to various pests and a whole range of pesticides are used on grapes. In total there are 137 MRLs set and grapes will be one of the crops most affected by the four different options, especially Option 1, 2 and 3 will impact the wine and grape industry considerably.

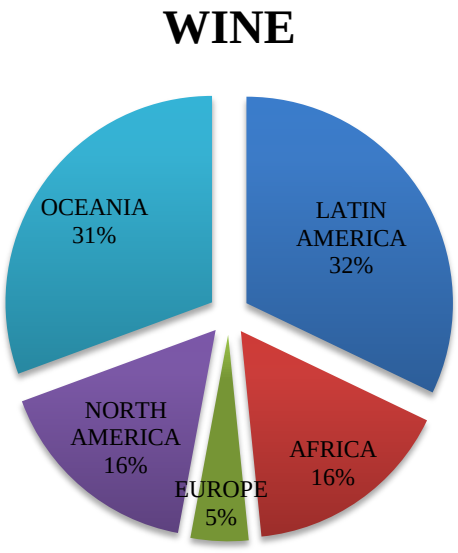

Figure 4. Wine imports to the EU-28 in 2014, based on region of production.

Looking at imports of wine and grapes, they are of considerable importance to the exporting countries as can be seen from the share of wine and grapes out of the total exports from the exporting country to the EU. For example Chile and New Zealand are highly dependent on EU as a trading partner for their wine sectors, and taking also the table grape exports into

account it is 10% of Chiles exports that will be impacted by changing regulation for plant protection products.

The volumes and values of the wine imports are quite significant with more than EUR 2 billion of imports from just the top five exporting countries. In total, close to EUR 2.5 billion of imported wine may be affected to a varying extent under the four options with relatively equal impact under Option 1, 2, and 3, while Option 4 would impact the least number of active substances.

Table 9. Wine imports to the EU-28 and the share of potentially affected MRLs under the options.

WINE - IMPORTS AND POTENTIALLY AFFECTED MRLs						
Value in million EUR	**Quantity in thousand tonnes**	**Total number of MRLs set**	**Share of MRLs**			
			Option 1	**Option 2**	**Option 3 Cat I**	**Option 4**
€2,454	1,389	**137**	9%	11%	11%	5%

Assessing which type of pesticide groups will be most impacted under the four options, the results are similar for wine as they are for bananas, with fungicides being the most impacted major group.

Main impacts

- The availability and price of wine in Europe unlikely to be affected by reduced imports, as countries within the EU are producing the bulk of wine in the world.
- Australia, Chile and South Africa will be affected the most as they are major wine producers, exporting a large share of their wine to the EU.
- May imply a shift towards other crops and affect farming practice.

Table 10. Wine imports to the EU-28 in 2014 by main trading partner

WINE				
RANK	**PARTNER/PRODUCT**	**VALUE IN EUR**	**QTY 100KG**	**SHARE OF EXPORTS TO THE EU**
1	AUSTRALIA	€ 427,793,357	3,301,999	5%
2	CHILE	€ 606,283,902	3,012,903	7%
3	SOUTH AFRICA	€ 385,725,654	3,003,289	2%
4	UNITED STATES	€ 396,734,529	2,269,743	0%
5	NEW ZEALAND	€ 313,459,969	675,184	9%
6	ARGENTINA	€ 164,813,730	613,082	2%
7	MACEDONIA	€ 31,441,151	529,274	1%
8	MOLDOVA	€ 23,103,104	211,636	2%
9	MOROCCO	€ 6,239,209	40,500	0%
10	KOSOVO	€ 2,021,519	35,633	2%

1.3. Case Study III - Rapeseed

Rapeseed is a member of the Brassica family and rapeseed oil is, after palm and soyabean oil, the most produced vegetable oil in the world.[46] Depending on the variety, rapeseed can be used in a wide range of purposes; from salad dressing, margarines and sauces to technical purposes, such as bio-degradable lubricating oil as an alternative to mineral oil based lubricants. Rapeseed can also be a substitute for diesel fuel, and the increasing demand for rapeseed oil over the last decade is due to its use in the biodiesel industry (non-food use).[47]

EU imports of rapeseed are dominated by Australia and Ukraine[48] which exported 1.5 and 1.2 million tonnes of rapeseed to the EU in 2014, representing approximately 50% and 40% of the import shares respectively. The EU has become the largest importer in recent years due to increasing needs related to the expansion of biofuels.[49]

The impacts under the various options are similar for rapeseed and other cereals. The impacts will be most severe under Option 1 with the highest number of pesticides affected. Fungicides are the most affected major group across all options, see Table 11.

Table 11. Rapeseed imports to EU-28 in 2014 and the share of potentially affected MRLs under the options.

RAPESEED - IMPORTS AND POTENTIALLY AFFECTED MRLS						
Value in million EUR	**Quantity in thousand tonnes**	**Total number of MRLs set**	**Share of MRLs**			
			Option 1	**Option 2**	**Option 3 Cat I**	**Option 4**
€1,170	3,072	**75**	16%	12%	12%	5%

An important feature of the rapeseed market is that the crop is not only used for foodstuffs but also as lubricants for machinery and as biofuels. The imports of rapeseed for industrial purposed may thus be affected via a lowering of the MRL, set considering consumption as food or feed. So far, there is not different treatment foreseen in the legislation for treating imports for food/feed or for industrial purposes differently.

Main impacts

- Ukraine and Australia most heavily impacted; the total imports from just these two countries reach more than EUR 1 billion, which is close to all imports of rapeseed to the EU.
- For all cereals and oilseeds, Option 1 will have the highest impact

[46] Gunstone, F. 2011. Vegetable Oils in Food Technology: Composition, Properties and Uses. 2nd Ed. Wiley Blackwell. ISBN 978-1-4443-3268-1

[47] National Edible Oil Distributor Association's website: http://www.neoda.org.uk/rapeseed-oil

[48] Canada dominates the world market for rapeseed but is a minor exporter to the EU in comparison with Australia and Ukraine.

[49] Carré, P., Pouzet, A. (2014) Rapeseed market, worldwide and in Europe. Oilseeds & fats Crops and Lipids (OCL) 21(1). DOI: 10.1051/ocl/2013054

Table 12. Rapeseed imports to EU-28 in 2014 by main trading partner

RAPESEED				
RANK	**PARTNER/PRODUCT**	**VALUE IN EUR**	**QTY 100KG**	**SHARE OF EXPORTS TO THE EU**
1	AUSTRALIA	€ 605,711,127	15,230,239	7%
2	UKRAINE	€ 444,461,896	12,699,294	3%
3	KAZAKHSTAN	€ 34,597,728	685,721	0%
4	CANADA	€ 25,763,121	644,898	0%
5	ARGENTINA	€ 24,583,262	589,363	0%

1.4. Case Study IV - Citrus fruit

During the summer months, the only source of citrus in the EU comes from the southern hemisphere. The major supplier of citrus fruit to the European market from June until October is South Africa (SA), followed by Egypt and Turkey.[50] Imports from South America, including Brazil, Argentina, Uruguay and Peru are also important. Fungicides are particularly important to the citrus industry because of the freight times overseas. It takes approximately three weeks for citrus fruit to reach a European port from SA and to avoid fungal diseases, pesticides need to be applied.

Table 13. Citrus fruit imports to EU-28 in 2014 and the share of potentially affected MRLs under the options.

CITRUS FRUIT - IMPORTS AND POTENTIALLY AFFECTED MRLS						
Value in million EUR	**Quantity in thousand tonnes**	**Total number of MRLs set for oranges**	**Share of MRLs**			
			Option 1	**Option 2**	**Option 3 Cat I**	**Option 4**
€1,485	1,914	**86**	8%	13%	13%	6%

The EU accounts for approximately 40% of SA citrus exports[50] and these exports are considered worth close to EUR 0.5 billion. The whole citrus growing industry in SA is considered to be worth around EUR 1 billion and in 2013 it employed around 100,000 people.[51] It can therefore be assumed an impact on the number of pesticides used on citrus may have a significant impact on the citrus industry in SA. The impact on citrus fruits will be most severe under Option 2 and Option 3.

A major concern for the SA citrus industry in recent years have been the occurrence of the fungal disease Citrus Black Spot (CBS), which resulted in a temporary ban of citrus imports from South Africa to EU during the winter season 2013/2014. However, in reality this had relative little impact on total imports because the temporary ban only came into effect when

[50] Source: USDA Citrus Semi-annual Report. Retrieved from: http://gain.fas.usda.gov/Recent%20GAIN%20Publications/Citrus%20Semi-annual_Pretoria_South%20Africa%20-%20Republic%20of_6-15-2015.pdf

[51] ENCA. 2013. Tight squeeze for SA citrus industry. Retrieved from: https://www.enca.com/south-africa/tight-squeeze-sa-citrus-industry

the citrus exporting season was almost over. Thus, it is difficult to draw any robust conclusions on the impacts on the South African economy due to decreased exports to the EU.

In order to control Citrus Black Spot, fungicides can be applied. In the latest Food and Veterinary Office (FVO) audit regarding citrus fruit exports from SA[52], one of the recommended active substances to use combat CBS is Mancozeb, a substance that falls under option 2, 3 and 4 for the ED criteria.

Table 14. Citrus imports to the EU-28 in 2014 by main trading partner

CITRUS FRUIT				
RANK	**PARTNER/PRODUCT**	**VALUE IN EUR**	**QTY 100KG**	**SHARE OF EXPORTS TO THE EU**
1	SOUTH AFRICA	€ 432,931,860	5,790,272	2%
2	TURKEY	€ 158,182,660	2,407,821	0%
3	EGYPT	€ 86,544,050	1,847,098	1%
4	MOROCCO	€ 123,476,193	1,679,824	1%
5	ARGENTINA	€ 178,520,047	1,621,450	2%
6	ISRAEL	€ 93,732,880	952,592	1%
7	BRAZIL	€ 90,596,818	936,324	0%
8	CHINA	€ 48,566,545	759,208	0%
9	URUGUAY	€ 54,749,977	756,342	5%
10	PERU	€ 53,274,718	582,315	1%

Main impacts

- South Africa will be most heavily impacted with imports to EU worth close to EUR 0.5 billion affected.
- Option 2 and 3 Category I will cause the greatest negative impact.
- The disappearance of certain pesticides may reduce the quality and availability of citrus fruit during the European summer.

[52] Final report of an audit carried out in South Africa from 24 February to 06 March 2015. In order to evaluate the system of official controls and the certification of citrus fruit for export to the European Union. Retrieved from: http://ec.europa.eu/food/fvo/audit_reports/details.cfm?rep_id=3483

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PART 16/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annex 16 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

{COM(2016) 350 final}
{SWD(2016) 212 final}

ANNEX 16
GLOSSARY AND BIBLIOGRAPHY

A	Androgenic pathway
AC50	Half maximal active concentration
ACTIVE SUBSTANCE (AS)	In the context of the PPP and BP Regulations, a substance or a micro-organism that has an action on or against harmful organisms[1,2]
ADVERSE EFFECT	A change in the morphology, physiology, growth, development, reproduction, or, life span of an organism, system, or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress, or an increase in susceptibility to other influences[3]
ADVERSE OUTCOME PATHWAY (AOP)	A linear sequence of events from the exposure of an individual to a chemical substance through to an understanding of the adverse (toxic) effect at the individual level (for human health) or population level (for ecotoxicological endpoints). Representation of existing knowledge concerning the linkage between the molecular initiating event and an adverse outcome at the individual or population levels[4]
ANDROGEN	Androgens are steroidhormones that help to develop sex organs in men. They also contribute to sexual function in men and women[5]
ANTISEPSIS	Preventing or stopping the growth of microorganisms
APICAL ENDPOINT	Traditional, directly measured whole-organism experimental results of exposure in *in vivo* tests, generally death, reproductive failure, or developmental dysfunction. Observable effects of exposure to a toxic chemical in a test animal. An observable outcome in a whole organism, such as a clinical sign or pathologic state, that is indicative of a disease state that can result from exposure to a toxicant[4] Results of an in vivo assay which describe a response by the organism as a whole, (e.g. fecundity or growth) which have

[1] Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products

[2] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC

[3] WHO/IPCS (World Health Organization/International Programme on Chemical Safety), 2009. Principles and Methods for the Risk Assessment of Chemicals in Food. Environmental Health Criteria 240. 689 pp. Available from: http://www.who.int/foodsafety/chem/principles/en/index1.html.

[4] Appendix I. OECD Collection of Working Definitions 2012. Retrieved from: http://www.oecd.org/chemicalsafety/testing/49963576.pdf

[5] EFSA Scientific Committee; Scientific Opinion on the hazard assessment of endocrine disruptors: Scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing effects mediated by these substances on human health and the environment. EFSA Journal 2013; 11(3):3132. [84 pp.] doi: 10.2903/j.efsa.2013.3132.

	possible implications for its biological fitness, rather than a response of the endocrine system alone (including physiological changes dependent on the endocrine system, such as Vitellogenin induction). Apical responses may or may not result from endocrine changes (e.g. fecundity may be affected both by some EDs and by some non-EDs)[5]
APICAL TEST	A test or assay aimed at detecting/measuring apical endpoints: generally in vivo testing describing a response by the organism as a whole (e.g. generally death, reproductive failure, or developmental dysfunction)
AUTOCHTHONOUS CASE	Case caused by a pathogen indigenous or endemic to a region
BENEFITS	The positive implications, direct and indirect, resulting from some action. This includes both financial and non-financial information[6]
BIOCIDAL PRODUCT (BP)	Biocidal products (BP) control unwanted organisms that are harmful to human or animal health, or that cause damage to human activities. BP include products such as insecticides, insect repellents, disinfectants, preservatives for materials and anti-fouling paints for the protection of ship hulls. BP are formulated products (e.g. liquid concentrates, wettable powder, granules) that contain at least one active substance that is responsible for the effect of the BP, which could be a chemical, a plant extract, a pheromone or a micro-organism (including viruses).
BP REGULATION	Biocidal Products Regulation
C1 (CARCINOGEN CATEGORY 1)	Known or presumed human carcinogen, according to Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures[7]
C2 (CARCINOGEN CATEGORY 2)	Suspected human carcinogen, according to Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures[7]
CAR	Competent Authority Report
CARCINOGEN	Substance or mixture of substances which induce cancer or increase its incidence. Substances which have induced benign and malignant tumours in well performed experimental studies on animals are considered also to be presumed or suspected human carcinogens unless there is strong evidence that the mechanism of tumour formation is not relevant for humans[7]
CLP	Classification, Labelling and Packaging
CMR	Carcinogenic, Mutagenic, Reprotoxic

[6] ECHA. Guidance on the preparation of socio-economic analysis as part of an application for authorisation. Helsinki: ECHA, 2011. Retrieved from: http://echa.europa.eu/documents/10162/13637/sea_authorisation_en.pdf

[7] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.

CoRAP	Community Rolling Action Plan
COSTS	The negative implications, direct and indirect, resulting from some actions. Includes both financial and non-financial information[4]
COST BENEFIT ANALYSIS (CBA)	Analysis which quantifies, in monetary terms where possible, costs and benefits of a possible action, including items for which the market does not provide a satisfactory measure of economic value[4]
COST EFFECTIVENESS ANALYSIS (CEA)	Analysis widely used to determine the least cost means of achieving pre-set targets or goals (though it is not restricted to this use). CEA can be used to identify the least cost option among a set of alternative options that all achieve the targets. In more complicated cases, CEA can be used to identify combinations of measures that will achieve the specified target[4]
COST-OF-ILLNESS (COI)	Empirical approach to estimating the societal impact of disease and injury which combines 'direct costs' (medical care, travel costs, etc.) and 'indirect costs' (the value of lost production because of reduced working time) into an overall estimate of economic impact on society, often expressed as a percentage of current GDP[8]
CUT-OFF CRITERIA	The term "*cut-off criteria*" is not used in the legislation. It is used in common language to refer to *approval criteria* in Reg. 1107/2009[2] and *exclusion criteria* in Reg. 528/2012[1]. In Reg. 1107/2009, *approval criteria* are: - purely based on hazard considerations for certain classes of substances (*mutagens, PBT = persistent, bioaccumulative and toxic, vPvB= very persistent and very bioaccumulative, POP= persistent organic pollutants*); - based on a strong hazard component for other classes of substances (*carcinogens, toxic for reproduction, endocrine disruptors*). In Reg. 528/2012, *exclusion criteria* are: - purely based on hazard considerations for certain classes of substances (*mutagens, PBT = persistent, bioaccumulative and toxic, vPvB= very persistent and very bioaccumulative, carcinogens, toxic for reproduction, endocrine disruptors*) when used by consumers; - based on a strong hazard component for the same classes of substances when used by professional users.
DAR	Draft Assessment Report
DG	Directorate General
DISCOUNT RATE	Used to convert a future income (or expenditure) stream to its present value. It shows the annual percentage rate at which the present value of a future Euro, or other unit of account, is assumed

[8] WHO. 2009. WHO guide to identifying the economic consequences of disease and injury. Geneva.

	to decrease over time[4]
DISCOUNTING	A method used to convert future costs or benefits to present values using a discount rate[4]
DOSE-RESPONSE CURVE	Graphical presentation of a dose-response relationship[10]
DOSE-RESPONSE RELATIONSHIP	Relation between the exposure to an agent and the change developed in a population in reaction to it. Note: It may be expressed as the proportion of a population exposed to an agent that shows a specific reaction. It may also be used to signify the magnitude of an effect in one organism (or part of an organism); in that case, it is more specifically called "dose-effect relationship"[10]
DOWNSTREAM USER	Any natural or legal person established within the Community, other than the manufacturer or the importer, who uses a substance, either on its own or in a mixture, in the course of his industrial or professional activities. A distributor or a consumer is not a downstream user[4]
E	Estrogenic pathway
EASIS	Endocrine Active Substances Information System
EATS	Estrogen, Androgen, Thyroid and Steroidogenesis
ECONOMIC IMPACTS	Costs and benefits to manufacturers, importers, downstream users, distributors, consumers and society as a whole[4]
ECHA	European Chemicals Agency
EC50	Half maximal effective concentration
ED	Endocrine disruptor
EDSP	Endocrine Disruptor Screening Program
EFSA	European Food Safety Authority
ENDOCRINE / HORMONE SYSTEM	The endocrine system is the system in the body which produces hormones to provide an internal communication system between cells located in distant parts of the body.[9]
ENDPOINT	The measurement of a biological effect. The recorded observation coming from an in chemico method, an in vitro assay or an in vivo assay. A large number of endpoints are used in regulatory assessments of chemicals. These include lethality, carcinogenicity, immunological responses, organ effects, developmental and reproductive effects, etc. In QSAR analysis, it is important to develop models for individual toxic endpoints[4]
ENVIRONMENT	Waters (including ground, surface, transitional, coastal and marine), sediment, soil, air, land, fauna and flora, and any interrelationship between them, and any relationship with other living organisms

[9] Society of Endocrinology, UK. Retrieved from www.yourhormones.info

ESTROGEN	Estrogens are a group of steroid compounds that are the primary female sex hormones. They promote the development of female secondary sex characteristics and control aspects of regulating the menstrual cycle[5].
EU	European Union
EXPOSURE	Concentration, amount, or intensity of a particular agent that reaches an organism or population. It is usually expressed in as substance concentration, duration, frequency, and/or intensity[10]
FALSE POSITIVE	Test result that is incorrect because the test indicated a condition or finding that is not real[11]
FALSE NEGATIVE	Test result that is incorrect because the test failed to recognise an existing condition or finding[11]
FINANCIAL IMPACT	Costs and benefits incurred by identified actors in relevant supply chains. Financial costs will generally include taxes, subsidies, depreciation, capital charges and other transfer payments[4]
FOOD SAFETY	Activities to protect the food supply from microbial, chemical, allergenic and physical hazards that may occur during all stages of food production and handling[12]
FRICTION COST APPROACH	A refinement of the human capital approach that proposes to estimate the true level of foregone production by restricting itself to the short-term impact of illness at the level of the firm; it dies this by counting only the production lost while a replacement worker is found (i.e. it depends on the time that organisations require to restore initial production levels)[4]
FUNGICIDE	A substance used to kill fungi or eliminate/reduce unwanted effects of fungi
GENOTOXIC	agent (e.g. substance, radiation) or processes which alter the structure, information content, or segregation of DNA, including those which cause DNA damage by interfering with normal replication processes, or which in a non-physiological manner (temporarily) alter its replication. Genotoxicity test results are usually taken as indicators for mutagenic effects[7]
GENUS	Genus is part of the biological classification of organisms in biology and of the scientific binomial nomenclature: the genus name forms the first part of the binomial species name. For instance the crop "maize" has the scientific name *Zea mays*, being "*Zea*" the genus and "*mays*" the species name within the genus.
GD	Guidance Document
GOOD PLANT	A practice whereby the treatments with PPP applied to given plants

[10] Risk assessment terminology: http://iupac.org/publications/ci/2001/march/risk_assessment.html
[11] Definitions taken from www.dictionary.com
[12] Glossary of food safety related terms. Appendix A. Retrieved from: http://www1.agric.gov.ab.ca/$Department/deptdocs.nsf/all/afs12301/$FILE/appendix_a_glossary.pdf

PROTECTION PRACTICE (GPPP)	or plant products, in conformity with the conditions of their authorised uses, are selected, dosed and timed to ensure acceptable efficacy with the minimum quantity necessary, taking due account of local conditions and of the possibilities for cultural and biological control[2]
HAZARD	A biological, chemical or physical agent with the potential to cause an adverse health effect. Hazard is anything that can cause harm, whereas risk is the potential that a hazard will cause harm. In other words a hazard will not pose any risk unless exposure to that hazard is high enough so that it may cause harm. Risks associated with hazards can be zero, or at least greatly reduced, by reducing exposure. For instance, a knife – a hazardous object per se - would be banned completely if the decision is taken based on hazard, while it would be allowed for certain uses or restricted (e.g. not allowed for small children) if the decision is taken based on risk. Similarly, a substance (e.g. a drug or a pesticide active substance) is banned if the regulatory decision is based on its hazard, while it is allowed for certain uses, under certain (restricted) conditions and doses, if the decision is taken based on risk.
HAZARD ASSESSMENT	Process designed to determine factors contributing to the possible adverse effects of a substance to which a human population or an environmental compartment could be exposed. The process includes three steps: hazard identification, hazard characterisation, and hazard evaluation Note: Factors may include mechanisms of toxicity, dose-effect and dose-response relationships, variations in target susceptibility, etc.[10]
HAZARD CHARACTERISATION	The second step in the process of hazard assessment, consisting in the qualitative and, wherever possible, quantitative description of the nature of the hazard associated with a biological, chemical, or physical agent, based on one or more elements, such as mechanisms of action involved, biological extrapolation, dose-response and dose-effect relationships, and their respective uncertainties[10]
HAZARD IDENTIFICATION	The first stage in hazard assessment, consisting of the determination of substances of concern, the adverse effects they may have inherently on target systems under certain conditions of exposure, taking into account toxicity data Note: Definitions may vary in wording, depending on the context. Thus, here: [RISK ASSESSMENT] the first stage in risk assessment, consisting of the determination of particular hazards a given target system may be exposed to, including attendant toxicity data.[10]
HEALTH IMPACTS	Impacts on human health including morbidity and mortality effects.

	Covers health related welfare effects, lost production due to workers' sickness and health care costs[4]
HEALTHY LIFE YEARS (HLY)	Also called disability-free life expectancy (DFLE), is defined as the number of years that a person is expected to continue to live in a healthy condition[2]
HERBICIDE	A substance used to destroy or inhibit the growth of plants, especially weeds
HORMONE	Made by endocrine glands, hormones are chemical messengers that travel in the bloodstream to tissues or organs. They affect many processes, including growth, metabolism, sexual function, reproduction, and mood
HUMAN CAPITAL APPROACH	Measurement approach to estimate the value of production losses due to illness, disability or premature death, achieved by multiplying the total period of absence by the wage rate of the absent worker. This would be consistent with neo-classical theory where the firm employs labour to the point where the value of the marginal product of a worker is equated to the wage rate. The main limitation of the approach is that it (unrealistically) assumes the presence of full employment in the economy, and by focusing only on the productive capacity of individuals, ignores other benefits of improved health status[4]
IC50	Half maximal inhibitory concentration
IMPORT TOLERANCES	An MRL set for imported products to meet the needs of international trade where: - the use of the active substance in a PPP on a given product is not authorised in the Community for reasons other than public health reasons for the specific product and specific use; or - a different level is appropriate because the existing Community MRL was set for reasons other than public health reasons for the specific product and specific use[13]
INCIDENCE	The number of new cases of disease in a defined population over a specific time period[14]
INSECTICIDE	A substance used to kill insects or eliminate/reduce unwanted effects of insects
INTACT ORGANISM	Not in vitro systems, or castrated or ovariectomised test animals[5]
IN VITRO	In an artificial environment outside a living organism or body[14]
IN VIVO	Within a living organism or body[14]
IN VITRO ASSAY	Assay where whole live animals are not used. Systems used may include cell lines or subcellular preparations from untreated animals[5]

[13] Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC

[14] Centers for Disease Control and Prevention (CDC). Retrieved from: http://www.cdc.gov/

IN VIVO ASSAY	Assay where a whole live animal is treated. This may be a mammalian assay where individual animals are treated or a wildlife assay where a population of animals is treated[5]
IN SILICO METHODS	The expression in silico is used to mean „performed on computer or via computer simulation". The phrase was coined in 1989 as an analogy to the Latin phrases in vivo and in vitro which are commonly used in biology and refer to experiments done in living organisms and outside of living organisms, respectively[5]
JRC	Joint Research Centre
LIMIT OF DETERMINATION (LOD)	The lowest residue concentration which can be quantified and reported by routine monitoring with validated control methods[13]
M1 (MUTAGEN CATEGORY 1)	substances known to induce heritable mutations in the germ cells of humans, according to Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures [7]
M2 (MUTAGEN CATEGORY 2)	substances which cause concern for humans owing to the possibility that they may induce heritable mutations in the germ cells of humans, according to Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures.
MAXIMUM RESIDUE LEVEL (MRL)	The upper legal level of a concentration for a pesticide residue in or on food or feed set in accordance with Regulation (EC) No 396/2005, based on good agricultural practice and the lowest consumer exposure necessary to protect vulnerable consumers[13]
MECHANISM OF ACTION	Sequence of events leading from the absorption of an effective dose of a chemical to the production of a specific biological response in the target organ. Understanding a chemical's mechanism requires appreciation of the causality and temporal relationships between the steps leading to a particular toxic endpoint, as well as the steps that lead to an effective dose of the chemical at the relevant biological target(s). Mechanism of action for toxicity is the detailed molecular description of key events in the induction of cancer or other health endpoints. Mechanism of action represents a more detailed understanding and description of events than is meant by mode of action[4]
(ENDOCRINE) MODALITY	A modality is an axis, pathway, signalling process or hormonal mechanism within the endocrine system[5]
MODE OF ACTION (MOA)	A biologically plausible sequence of key events leading to an observed effect supported by robust experimental observations and mechanistic data. A mode of action describes key cytological and biochemical events – that is, those that are both measurable and necessary to the observed effect – in a logical framework[5]
MOLECULAR INITIATING EVENT	The initial point of chemical-biological interaction within the organism that starts the pathway. Direct interaction of a chemical with specific biomolecules.

	The molecular level, chemical-induced perturbation of a biological system. Chemical interaction at a molecular target leading to a particular adverse outcome[4]
MS	Member State
MULTI-CRITERIA ANALYSIS (MCA)	A computing technique which compares options and that involves assigning weights to criteria across the options will be compared, and then scoring options in terms of how well they perform against those weighted criteria. Weighted scores are then summed, and can then be used to rank options[4]
MUTATION	a permanent change in the amount or structure of the genetic material in a cell. The term 'mutation' applies both to heritable genetic changes that may be manifested at the phenotypic level and to the underlying DNA modifications when known (including specific base pair changes and chromosomal translocations) [7]
MUTAGEN	Agent (e.g. substance, radiation) giving rise to an increased occurrence of mutations in populations of cells and/or organisms.[7]
NOAEL	No Observed Adverse Effect Level
NON APICAL ENDPOINT	Alternative, suborganism-level, in vitro responses, biomarkers, QSARs, genomics. Intermediate event or step at a level of biological organisation below that of the apical endpoint[4]
OBESITY	The condition of severe overweight where a person has a body mass index (BMI) equal to or greater than 30[15]
OBESITY RATE	The proportion of the total population (or of a subgroup based on gender, age, etc.) with a BMI of 30 or above[2]
OECD	Organisation for Economic Co-operation and Development
PATHOGENIC ORGANISM	Organism causing or capable of causing disease[14]
PLANT PROTECTION PRODUCTS (PPP)	Plant protection products (PPP) protect crops as well as desirable or useful plants. They are used in agriculture, forestry, horticulture, industrial areas (e.g. railways), amenity areas and in gardens. PPP are formulated products (e.g. liquid concentrates, wettable powder, granules) that contain at least one active substance that is responsible for the effect of the PPP, which could be a chemical, a plant extract, a pheromone or a micro-organism (including viruses).
POTENCY	It's a measure of a substance's ability to produce an (adverse) effect. The higher the potency of a substance, the lower the dose sufficient to produce a certain adverse effect
PPP REGULATION	Plant Protection Products Regulation
PRESENT VALUE	The future value of an impact expressed in present terms by

[15] EUROSTAT: Health glossary, available on: http://ec.europa.eu/eurostat/statistics-explained/index.php/Category:Health_glossary

	means of discounting
PREVALENCE	The number of existing disease cases in a defined population during a specific period[14]
PRICE ELASTICITY	A measure of the responsiveness of demand to a change in price. If demand changes proportionally more than the price has changed, the good is "price elastic". An elasticity of 1 means that an 1% increase in price leads to a fall in demand of 1%. An elasticity of 0.5 means that a 1% change in the price leads to a fall in demand of 0.5%. If demand changes proportionally less than the price, it is "price inelastic"[4]
QUANTITATIVE STRUCTURE ACTIVITY RELATIONSHIP (QSAR)	(Q)SARs are methods for estimating properties of a chemical from its molecular structure and have the potential to provide information on hazards of chemicals, while reducing time, monetary cost and animal testing currently needed[5]
TOXIC FOR REPRODUCTION (OR REPRODUCTIVE TOXICANT)	Substance which induce reproductive toxicity or increase its incidence. Reproductive toxicity includes adverse effects on sexual function and fertility in adult males and females, as well as developmental toxicity in the offspring[7]
R1 (TOXIC FOR REPRODUCTION CATEGORY 1)	Known or presumed human reproductive toxicant, according to Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures[7]
R2 (TOXIC FOR REPRODUCTION CATEGORY 2)	Suspected human reproductive toxicant, according to Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures[7]
REACH	Registration, Evaluation, Authorisation and Restriction of CHemicals
RESIDUES	One or more substances present in or on plants or plant products, edible animal products, drinking water or elsewhere in the environment and resulting from the use of a PPP, including their metabolites, breakdown or reaction products[2]
RISK	A function of the probability of an adverse health effect and the severity of that effect, consequential to a hazard[10] Risk is the potential that a hazard will cause harm. Risks associated with hazards can be zero, or at least greatly reduced, by reducing exposure. For instance, a knife – a hazardous object per se - would be banned completely if the decision is taken based on hazard, while it would be allowed for certain uses or restricted (e.g. not allowed for small children) if the decision is taken based on risk. Similarly, a substance (e.g. a drug or a pesticide active substance) is banned if the regulatory decision is based on its hazard, while it is allowed for certain uses, under certain (restricted) conditions and doses, if the decision is taken based on risk.
RISK ASSESSMENT	A scientifically based process consisting of four steps: hazard identification, hazard characterisation, exposure assessment and risk characterisation[10], which calculates which and how bit the risk of adverse effects happening is after exposure to a certain hazard.

RISK MANAGEMENT	The process, distinct from risk assessment, of weighing policy alternatives in consultation with interested parties, considering risk assessment and other legitimate factors, and, if need be, selecting appropriate prevention and control options[10]
S	Steroidogenesis pathway
SCCS	Scientific Committee on Consumer Safety
SENSITIVITY ANALYSIS	A "what-if" type of analysis to determine the sensitivity of the outcomes of an analysis to changes in parameters. If a small change in a parameter results in relatively large changes in the outcomes, the outcomes are said to be sensitive to that parameter[4]
SIN	Substitute It Now
SOCIAL COSTS	Denotes the opportunity cost to society and includes also external costs or externalities[4]
STEROIDS	Any of various molecules—including hormones—that contain a particular arrangement of carbon rings. Some common steroids include sex steroids, corticosteroids, anabolic steroids, and cholesterol[16]
STOT-RE	Specific Target Organ Toxicity - Repeated Exposure
SUBSTANCES	Chemical elements and their compounds, as they occur naturally or by manufacture, including any impurity inevitably resulting from the manufacturing process[2]
SVHC	Substance of Very High Concern
SYSTEMATIC REVIEW	A systematic review is a method to review scientific literature. It attempts to identify, appraise and synthesize all the empirical evidence that meets pre-specified eligibility criteria to answer a given research question. Researchers conducting systematic reviews use explicit methods aimed at minimizing bias, in order to produce more reliable findings that can be used to inform decision making. (See Section 1.2 in the Cochrane Handbook for Systematic Reviews of Interventions.) http://www.cochranelibrary.com/about/about-cochrane-systematic-reviews.html
T	Thyroid pathway
TEDX	The Endocrine Disruptor eXchange
TOXCAST	Database of *in vitro* assay data from US Environmental Protection Agency (EPA)
TREATED ARTICLES	Any substance, mixture or article which has been treated with, or intentionally incorporates, one or more BP[1]
TYROID HORMONE	The thyroid gland makes T3 (triiodothyronine) and T4 (thyroxine), which together are considered thyroid hormone. T3 and T4 have identical effects on cells. Thyroid hormone affects heart rate, blood pressure, body temperature, and weight. T3 and T4 are stored as thyroglobulin, which can be converted back into T3 and T4[5]

[16] Endocrine society website. Retrieved from: https://www.endocrine.org/news-room/glossary

UNCERTAINTY	This is a state characterising a situation where related parameters are not known or fixed or certain. It stems from a lack of information, scientific knowledge or ignorance and is a characteristic of all predictive assessments[4]
VECTOR	A vector is an organism, often an invertebrate arthropod, that transmits diseases (it transmits a pathogen from reservoir to host).
VULNERABLE GROUPS	Persons or group of population to be expected to be at higher risk and therefore need specific consideration when assessing the potential health effects of BP or PPP. These include pregnant and nursing women, the unborn, infants and children, the elderly and, when subject to high exposure to BP or PPP over the long term, workers and residents[1]
WFD	Water Framework Directive
WHO	World Health Organization
WILLINGNESS TO PAY (WTP)	Technique to elicit the value that individuals place on an economic resource or change in welfare by observing how much a person is willing to pay in order to obtain it. In the case of market transactions, WTP is observed directly and amounts to the price that is paid, while the valuation of non-market services and goods (such as the value of human life or the value of pain/suffering) might require the use of indirect measures, such as revealed choices or stated preferences[3]
WEIGHT-OF-EVIDENCE (WOE)	A process in which all of the evidence considered relevant to a decision is evaluated and weighted[5]
WILDLIFE	Non-target species. This term does not cover wildlife intended to be controlled by the application of regulated products (i.e. target species)[5]
VALIDATED ASSAY	A test method for which validation studies have been completed to determine the relevance (including accuracy) and reliability for a specific purpose. It is important to note that a validated test method may not have sufficient performance in terms of accuracy and reliability to be found acceptable for the proposed purpose[5]

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