Study for the strategy for a non-toxic environment of the 7th EAP

Sub-study c: Protection of children and vulnerable groups from harmful exposure to chemicals
Study for the strategy for a non-toxic environment of the 7th EAP

Sub-study c: Protection of children and vulnerable groups from harmful exposure to chemicals
This sub-study report has been prepared by Yoline Kuipers and Matteo Mascolo of Milieu Ltd.

The views expressed herein are those of the consultants alone and do not necessarily represent the official views of the European Commission.

Milieu Ltd (Belgium), Chaussée de Charleroi 112, B-1060 Brussels, tel.: +32 2 506 1000; e-mail: julia.lietzmann@milieu.be; web address: www.milieu.be.
# Sub-study c - Protection of children and vulnerable groups from harmful exposure to chemicals

## TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIST OF TABLES</td>
<td>7</td>
</tr>
<tr>
<td>LIST OF BOXES</td>
<td>7</td>
</tr>
<tr>
<td>ABBREVIATIONS USED</td>
<td>8</td>
</tr>
<tr>
<td>ABSTRACT</td>
<td>11</td>
</tr>
<tr>
<td>EXECUTIVE SUMMARY</td>
<td>12</td>
</tr>
<tr>
<td>1 INTRODUCTION</td>
<td>17</td>
</tr>
<tr>
<td>1.1 Who are the vulnerable groups in society?</td>
<td>18</td>
</tr>
<tr>
<td>1.2 How are vulnerable groups exposed to harmful chemicals?</td>
<td>19</td>
</tr>
<tr>
<td>1.2.1 Ingestion</td>
<td>19</td>
</tr>
<tr>
<td>1.2.2 Inhalation</td>
<td>19</td>
</tr>
<tr>
<td>1.2.3 Skin contact</td>
<td>21</td>
</tr>
<tr>
<td>1.2.4 Other routes of exposure</td>
<td>22</td>
</tr>
<tr>
<td>1.3 What are the main adverse health effects in vulnerable populations?</td>
<td>24</td>
</tr>
<tr>
<td>2 CHILDREN: FROM THE DEVELOPING FOETUS TO LATE ADOLESCENCE</td>
<td>28</td>
</tr>
<tr>
<td>2.1 Foetus</td>
<td>28</td>
</tr>
<tr>
<td>2.2 Children</td>
<td>32</td>
</tr>
<tr>
<td>2.2.1 Neonates and infants</td>
<td>35</td>
</tr>
<tr>
<td>2.2.2 Toddlers and school-aged children</td>
<td>37</td>
</tr>
<tr>
<td>2.3 Adolescence</td>
<td>38</td>
</tr>
<tr>
<td>3 REPRODUCTIVE HEALTH AND PREGNANT WOMEN</td>
<td>40</td>
</tr>
<tr>
<td>3.1 Reproductive health</td>
<td>42</td>
</tr>
<tr>
<td>3.2 Pregnancy</td>
<td>46</td>
</tr>
<tr>
<td>4 THE ELDERLY AND AN AGEING SOCIETY</td>
<td>48</td>
</tr>
<tr>
<td>5 OCCUPATIONAL GROUPS</td>
<td>50</td>
</tr>
<tr>
<td>6 OTHER VULNERABLE GROUPS</td>
<td>55</td>
</tr>
<tr>
<td>7 REGULATING AND ASSESSING CHEMICAL EXPOSURE OF VULNERABLE POPULATIONS</td>
<td>57</td>
</tr>
<tr>
<td>7.1 Legislative framework</td>
<td>57</td>
</tr>
<tr>
<td>7.1.1 Regulation of chemicals and the exposure of vulnerable groups</td>
<td>57</td>
</tr>
<tr>
<td>7.1.2 Chemical legislation containing reference to vulnerable groups</td>
<td>59</td>
</tr>
<tr>
<td>7.1.3 Chemical legislation that could contain references to vulnerable groups</td>
<td>65</td>
</tr>
<tr>
<td>7.2 Risk Assessment</td>
<td>67</td>
</tr>
<tr>
<td>7.3 Biomonitoring</td>
<td>70</td>
</tr>
<tr>
<td>8 GAPS AND DEFICITS</td>
<td>74</td>
</tr>
<tr>
<td>8.1 Regulatory issues</td>
<td>74</td>
</tr>
<tr>
<td>8.2 Insufficient assessment methodologies and criteria</td>
<td>74</td>
</tr>
<tr>
<td>8.3 Research gaps</td>
<td>75</td>
</tr>
<tr>
<td>8.4 Information and awareness gaps</td>
<td>75</td>
</tr>
</tbody>
</table>
8.5 Available tools to respond to gaps and deficits IDENTIFIED .......................... 77

9 CONCLUSIONS ........................................................................................................... 84

10 REFERENCES ............................................................................................................. 85

   Literature and webpages ................................................................................................. 85
   Acts & official documents from international and European institutions .................. 116
   Legislation relevant to chemicals and vulnerable groups ........................................... 118
   Other legislation considered ........................................................................................ 121

LIST OF TABLES

Table 1: Examples of health effects of chemicals on different organ systems .......... 24
Table 2: Commonly identified environmental chemical exposures and birth defects in the developing foetus ................................................................. 31
Table 3: Behavioural factors by age group that can affect children’s exposure to chemicals ........................................................................................................ 32
Table 4: Characteristics, exposure and vulnerability to environmental health hazards by developmental stage ................................................................. 33
Table 5: Overview of EDCs, their pathways of exposures, mechanisms of action and observed health impacts in relation to female reproductive health .......... 44
Table 6: Overview of relevant EU and international chemicals legislation and their provisions concerning vulnerable groups ........................................ 60
Table 7: Overview of gaps in legislation and the responses identified ....................... 78
Table 8: Overview of gaps in risk assessment methodologies and criteria and the responses identified ................................................................................. 79
Table 9: Overview of gaps in research and evidence and the responses identified ...... 81
Table 10: Overview of gaps in awareness raising and information distribution and the responses identified .............................................................. 82

LIST OF BOXES

Box 1: Problem definition of sub-study c ....................................................................... 17
Box 2: The thalidomide crisis ......................................................................................... 22
Box 3: The Minamata disaster ....................................................................................... 22
Box 4: DES case ............................................................................................................ 43
Box 5: WHO Definition of ‘vulnerable groups’ in relation to chemical exposure ........ 58
Box 6: EU legislation definition of ‘vulnerable groups’ in relation to chemical exposure ........................................................................................................... 58
Box 7: Examples of relevant HBM programmes ......................................................... 72
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD</td>
<td>Attention Deficit Hyperactivity Disorder</td>
</tr>
<tr>
<td>ANSM</td>
<td>French National Agency for Medicines and Health Products Safety</td>
</tr>
<tr>
<td>ATSDR</td>
<td>Agency for Toxic Substances and Disease Registry</td>
</tr>
<tr>
<td>BBP</td>
<td>Benzyl butyl phthalate</td>
</tr>
<tr>
<td>BBzP</td>
<td>Butyl benzyl phthalate</td>
</tr>
<tr>
<td>BM</td>
<td>Biomarkers</td>
</tr>
<tr>
<td>BPA</td>
<td>Bisphenol A</td>
</tr>
<tr>
<td>CEHAP</td>
<td>UK Children’s Environment and Health Action Plan</td>
</tr>
<tr>
<td>CHMS</td>
<td>Canadian Health Measures Survey</td>
</tr>
<tr>
<td>CLP</td>
<td>Classification, Labelling and Packaging</td>
</tr>
<tr>
<td>CNS</td>
<td>Central Nervous System</td>
</tr>
<tr>
<td>CO</td>
<td>Carbon monoxide</td>
</tr>
<tr>
<td>CONTAMED</td>
<td>Contaminant mixtures and human reproductive health – novel strategies for health impact and risk assessment of endocrine disruptors</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>COPHES</td>
<td>Consortium to Perform Human Biomonitoring on a European Scale</td>
</tr>
<tr>
<td>CRCE</td>
<td>Centre for Radiation, Chemical and Environmental Hazards (UK)</td>
</tr>
<tr>
<td>CZ-HBM</td>
<td>Human Biomonitoring Project (Czech Republic)</td>
</tr>
<tr>
<td>DBP</td>
<td>Dibutyl phthalate</td>
</tr>
<tr>
<td>DDE</td>
<td>Dichlorodiphenyldichloroethylene</td>
</tr>
<tr>
<td>DDT</td>
<td>Dichlorodiphenyltrichloroethane</td>
</tr>
<tr>
<td>DEER</td>
<td>Developmental effects of environment on reproductive health</td>
</tr>
<tr>
<td>DEHP</td>
<td>Di 2-ethylhexyl phthalate</td>
</tr>
<tr>
<td>DEMOCOPHES</td>
<td>Demonstration of a study to Coordinate and Perform Human biomonitoring on a European Scale</td>
</tr>
<tr>
<td>DES</td>
<td>Diethylstilbestrol</td>
</tr>
<tr>
<td>DiDP</td>
<td>Diisodecyl phthalate</td>
</tr>
<tr>
<td>DinP</td>
<td>Diisononyl phthalate</td>
</tr>
<tr>
<td>DiNP</td>
<td>di-n-hexyl phthalate</td>
</tr>
<tr>
<td>DNP</td>
<td>Dinitrophenol</td>
</tr>
<tr>
<td>EAP</td>
<td>Environment Action Programme</td>
</tr>
<tr>
<td>EC</td>
<td>European Commission</td>
</tr>
<tr>
<td>ECHA</td>
<td>European Chemicals Agency</td>
</tr>
<tr>
<td>ED</td>
<td>Endocrine-disrupting</td>
</tr>
<tr>
<td>EDC</td>
<td>Endocrine-disrupting chemical</td>
</tr>
<tr>
<td>EEA</td>
<td>European Environment Agency</td>
</tr>
</tbody>
</table>
EEC  European Economic Community
EHC  Environmental Health Criteria
ENNS  French National Survey on Nutrition and Health
EPA  Danish Environmental Protection Agency
EU  European Union
EU-OSHA  European Agency for Safety and Health at Work
FACET  Flavourings, Additives, and food Contact materials Exposure Tool
FLEHS  Flemish Environment and Health Study
GerES  German Environmental Survey
HBM  Human biomonitoring
HELIX  Human Early-Life Exposome - novel tools for integrating early-life environmental exposures and child health across Europe
HERMOSA  Health and Environmental Research in Make-up Of Salinas Adolescents project
HPA  Health Protection Agency (UK)
ILO  International Labour Organisation
IPCS  International Programme on Chemical Safety
IQ  Intelligence Quotient
JRC  Joint Research Centre
KorSEP  Korea National Survey for Environmental Pollutants in the Human Body
MoBa  Norwegian Mother and Child Cohort Study
MOCEH  Mothers and Children's Environmental Health study (South Korea)
NECTAR  Network for Environment Chemical Toxicants Affecting Reproduction
NEWGENERIS  Newborns and genotoxic exposure risks project
NHANES  National Health and Nutrition Examination Survey (US)
NIOSH  National Institute for Occupational Safety and Health (US)
NO₂  Nitrogen dioxide
NTE  Non-toxic environment
O₃  Ozone
OECD  Organisation for Economic Co-operation and Development
OEL  Occupational exposure limits
OSH  Occupational Safety and Health
PAH  Polycyclic aromatic hydrocarbon
PBB  Polychlorinated biphenyl
PBDE  Polybrominated diphenyl ethers
PCB  Polychlorinated biphenyl
PCE  Perchloroethylene
PCOS  Polycystic ovary syndrome
PCT          Polycyclohexylenedimethylene terephthalate  
PFAS         Per- and polyfluoroalkyl substances  
PFOS         Perfluorooctane sulfonate  
PHIME        Public Health Impact of long-term, low-level Mixed Element Exposure in Susceptible Population Strata  
PM$_{2.5}$   Particulate matter (diameter of 2.5 µm or less)  
PM$_{10}$    Particulate matter (diameter of 10 µm or less)  
POF          Premature Ovarian Failure  
POP          Persistent organic pollutant  
PROBE        Programme for Biomonitoring the Italian Population Exposure  
PVC          Polyvinyl chloride  
REACH        Registration, Evaluation, Authorisation and Restriction of Chemicals  
RFR          Replacement flame retardants  
RIVM         Dutch National Institute for Public Health and the Environment  
ROS          Reactive oxygen species  
SERM         Selective oestrogen receptor modulator  
SMEs         Small and medium-sized enterprises  
SO$_2$       Sulphur dioxide  
TBBPA        Tetrabromobisphenol A  
TCE          Trichloroethylene  
TTR          Transthyretin  
UNEP         United Nations Environment Programme  
UK           United Kingdom  
US           United States  
VOC          Volatile organic compound  
US EPA       United States Environmental Protection Agency  
WHO          World Health Organization
ABSTRACT

This sub-study report focuses on the population groups that are particularly vulnerable to the negative effects of exposure to chemicals, and how these groups can be (better) protected. The study describes the main vulnerable groups in society, showing how these groups can be exposed to harmful chemicals and setting out the main adverse health effects that may arise from chemical exposure. Examples of groups with higher susceptibility are children (from the developing foetus to adolescence), pregnant women and the elderly, as well as certain occupational groups and people with lower socioeconomic status. The analysis of the EU legislative framework relevant to the scope of the sub-study shows that provisions referring to vulnerable groups are often lacking or inconsistent between similar types of legislation. In particular, where relevant, EU legislation should include provisions defining any vulnerable population groups where special protection should be ensured. This would include specific windows of vulnerability, which would be particularly useful for the protection of children. In addition, certain EU legislation, such as the Drinking Water Directive and Food Contact Materials Framework Regulation, are not updated with the most relevant scientific evidence and lack specific measures which can strengthen the protection of vulnerable groups. This study also highlights how current risk assessments typically focus on single substances and do not consider the risks to children and other vulnerable groups from combined exposure to toxic chemicals. Therefore, as humans are usually exposed to numerous chemicals simultaneously, a regulatory approach for cumulative risk assessment needs to be developed.

While a wealth of information and evidence on the impacts of chemicals on specific vulnerable populations has been collected in recent decades, significant knowledge gaps remain. Some areas of considerable concern include the lack of knowledge on non-intentionally added substances, nanomaterials, as well as on the potentially harmful effects of certain neurotoxic chemicals on brain development. During sensitive early life stages, exposure to EDCs and neurotoxins - such as lead, arsenic, mercury, PCBs, pesticides, and solvents - can cause lifelong damages, and further research on the impact of chemicals on the brain is therefore of paramount importance. The potential effects of new substances such as nanomaterials also need to be further investigated, as does the ‘early exposure – late effect’ pattern, particularly in relation to chemicals with endocrine-disrupting properties. Finally, the study shows the need to develop communication strategies among the general public and specific vulnerable groups on how to reduce exposure from certain toxic compounds (i.e. household dust) and classes of chemicals (EDCs and neurotoxicants), as well as on how to avoid certain harmful behaviors (i.e. hand to mouth). Improving labelling and packaging of consumer products would also help to increase knowledge on the potential harmful effects of exposure to certain ingredients or compounds.
EXECUTIVE SUMMARY

Certain groups of the population – such as children, pregnant women, the elderly, and workers – are particularly vulnerable to the risks stemming from chemical exposure, and, as such, have a higher probability of developing adverse health effects throughout their life. This increased vulnerability depends on a variety of reasons, spanning from specific behaviours, increased sensitivity to chemicals, specific biophysical characteristics, health status, constant exposure to highly hazardous chemicals, reduced ability to protect from exposure, and social factors (e.g. where a person lives or works or spends the majority of his/her time). In light of their higher vulnerability, these categories of the population need special protection from the hazardous effects that chemical exposure can cause on their health.

Chemicals can enter the human body in various ways and can cause different kinds of health effects. A chemical can produce a health effect directly at the site of contact (local) or elsewhere in the body (systemic) and the effect can be either immediate or delayed. Organ systems that can be affected by exposure to hazardous chemicals include the nervous system, the reproductive system, the endocrine system, the thyroid system and the immune system. Recent reports have also suggested that when chemical substances are combined, they might cause adverse effects to human health even if they are harmless individually. These chemicals, even at low dose levels, can give rise to subtle but long-term health effects such as reduced fertility, lower birth weights and neurodevelopmental diseases. Pathways of exposure to chemicals in products involve indoor air as well as household dust. Another area of concern is that of environmentally induced epigenetic changes, which may have far-reaching consequences, particularly for foetuses and young children.

The human foetus is considered to be particularly vulnerable to chemical exposure because of its rapid cell reproduction rates, sensitive developmental periods of different organ systems, greater surface areas in skin, lungs, and intestinal mucosa per unit of body weight (so that more toxins are absorbed per unit of body weight), immature liver and kidney enzyme systems to metabolise, conjugate, and eliminate toxicants, and an undeveloped blood-brain barrier that allows transport into the brain. While the placenta was initially believed to protect the foetus from harmful chemicals, evidence now demonstrates that the placenta does not block the passage of many environmental toxicants from maternal to foetal circulatory systems. Over 200 foreign chemicals have been detected in umbilical cord blood, including pesticides, ingredients in consumer products, food packaging, and chemical by-products from burning coal and flame retardants.

The developing human brain is particularly vulnerable to chemical exposures, with major windows of developmental vulnerability occurring in utero, during infancy and early childhood. During these sensitive life stages, exposure to neurotoxins such as lead, arsenic, mercury, PCBs, pesticides, and solvents – of which more than 200 have been identified, with many more suspected to exist - can cause functional deficits and life-long adverse health effects at low levels of exposure that would have little or no adverse effect in an adult. Early-life epigenetic changes are also known to affect subsequent gene expression in the brain.

In addition to impacts on the cognitive development of the foetus, prenatal exposure to environmental toxicants has also been linked to negative reproductive effects, severe congenital malformations, premature birth and growth retardation. Studies also show links to early puberty in girls, feminisation of male children, and decreased fertility in both men and women later in life, as well as breast and testicular cancer. There is a growing body of evidence to suggest that in utero exposure to harmful chemicals can impact the metabolic system and influence the onset of adult diseases such as atherosclerotic cardiovascular disease, hypertension, type 2 diabetes, stroke and cancer.

After birth, children remain uniquely vulnerable and can be exposed to harmful chemicals in a number of ways. Firstly, research has shown that a large number of chemicals, such as polychlorinated biphenyls, dioxins, dibenzofurans, polybrominated diphenyl ethers, and heavy metals, are transferred
to the infant through human breastmilk. Some of the highest levels of contaminants are found among women in agricultural areas and those in remote areas whose diet is heavily based on the marine food chain that accumulates heavy burdens of persistent organic pollutants. Another source of exposure for neonates are nurseries and hospital settings, where they can be exposed to chemicals such as polyvinyl chloride (PVC), di 2-ethylhexyl phthalate (DEHP), Bisphenol A (BPA), and parabens, which have been shown to impact fertility in later life, as well as causing neurological defects, obesity, and cancer. Health implications can also evolve due to environmental chemicals found in water, food, and body care and consumer products.

As children grow up, they begin exploring, touching and testing, which exposes them to chemicals through various pathways. Given their specific exploring and hand-to-mouth behaviour, together with their inability to read warning labels, the main danger for toddlers is the ingestion of toxic chemicals that may cause permanent damage to their health. Toddlers also spend a large part of their time at home, making them particularly vulnerable to indoor pollution and exposure to household dust, which has been shown to contain chemicals linked to reproductive toxicity, endocrine disruption, and cognitive and behavioural impairment. Such chemicals can cause diseases such as cancer, asthma, immune dysfunction and various chronic illnesses. Recent studies in the U.S. have shown that, indoors, phthalates and phenols are found at the highest levels, phthalates and replacement flame retardants (RFRs) have the highest estimated intakes, and phthalates and PFASs are associated with the most hazardous traits in terms of human health.

In addition to indoor air pollution, when children start to move around, they are more likely to go outside, where their exposure to outdoor air pollution is a special concern in light of their breathing in higher volumes of air relative to their body weight, together with their continuing tissue growth and organ development. Air pollution, particularly traffic-related pollution, is associated with infant mortality and the development of asthma and atopy, as well as acute bronchitis. Air pollutants may also adversely affect infant lung development, cause coughing, and aggravate asthma. A growing body of evidence suggests that air pollution can affect mental and cognitive health in children, even at low levels of pollution, resulting in mental illnesses (including autism) or impacting their overall learning and development.

Puberty and adolescence are also periods of increased risk of exposure to chemicals. During this time, endocrine, neurological, and other systems undergo development and growth, making the developing tissues and organs particularly sensitive to the effects of carcinogenic and endocrine-disrupting chemicals. Changes in behaviour, such as the use of toxic substances such as tobacco and alcohol, may expose them to greater risks. Adolescents are more likely to increase their use of personal care products containing toxic chemicals such as parabens and phenols. Studies show that when teenage girls stop using personal care products, even briefly, the levels of hormone-disrupting chemicals drop significantly. Another area of concern is the impact of endocrine-disrupting chemicals (EDCs) on the reproductive health of adolescent girls. Most information on the effects of endocrine disruption on female reproductive health comes from molecular, cellular and animal studies, which have shown that exposure to EDCs during both prenatal and adult life can play a role in the pathogenesis of several female reproductive disorders.

Environmental chemicals not only harm people’s ability to reproduce, but can also negatively affect pregnancy. As explained above, many chemicals absorbed or ingested by pregnant women can cross the placenta to the foetus and can cause an array of adverse health effects. However, women are also particularly vulnerable during pregnancy as physiological changes such as weight gain and increases in blood and plasma volume occur, which can alter concentrations of chemicals and result in a greater absorption of toxic substances. Studies have shown that BPA and high levels of flame-retarding chemicals (polybrominated diphenyl ethers) can alter pregnant women’s thyroid hormones, which are essential for normal foetal growth and brain development.

As a part of the ageing process, people experience a gradual deterioration in body function and their
capacity to respond to chemical exposure, including the metabolism and elimination of chemical substances. This development, as well as people’s life-long, chronic exposure to environmental chemicals which have been accumulating within the body, and the high prevalence of various age-related diseases, make that elderly susceptible to the harmful effects of environmental chemicals. Research shows that chemicals, such as solvents and lead, can contribute to cognitive impairment and have adverse effects on immune and respiratory function. They can also increase blood pressure and insulin levels, possibly resulting in cardiovascular effects or the onset of metabolic syndromes, including diabetes mellitus.

Another area of concern is the potential for drug-toxicant interactions, as the elderly, in general, use more medication than the rest of the population. This includes polypharmacy (the use of more medications than may be medically necessary), as well as pharmaceutical-to-environmental chemical reactions. Pharmaceuticals in drinking water present an additional environmental challenge as they may, even at very low concentrations, impact the health of elderly adults whose metabolic capability is already compromised and who are taking a variety of pharmaceutical medications. Finally, the elderly, like young children, typically spend a significant portion of each day indoors at home or in care facilities, which makes them more susceptible to indoor air pollution.

In addition to the different life phases, particular vulnerability to chemical exposure can arise from living and working environments or overall socioeconomic situation. Types of work that carry a higher risk include agriculture, construction and painting, cleaning and maintenance services, and hairdressers and beauty salons. For example, a growing number of studies have identified cleaners as a group at risk for adverse health effects to the skin (e.g. dermatitis) and the respiratory tract (e.g. asthma). The emission of volatile organic compounds (VOCs) and particulates which can be easily inhaled have been associated with asthma. Hairsprays, permanent waves, acrylic nail application and numerous other salon products have been linked to higher incidences of cancers, neurological diseases such as dementia and depression, immune diseases, birth defects, reproductive disorders, skin diseases, asthma and other breathing problems. The waste management and recycling industry is another particular sector of concern; large numbers of substances are emitted during work activities that could give rise to a significant burden of ill health. Few studies have examined the potential impacts on the health of people working in this sector, but the most significant issues appear to be presence of dust, bioaerosol and hazardous metals.

Evidence exists that people from lower socioeconomic groups are at higher risk of adverse health outcomes after chemical exposure compared to wealthier social groups. Factors such as living environment, level of education, ethnicity, type of employment and lifestyle can have a significant effect on the burden of environmental toxicants, their accumulation in the body and the prevalence of diseases and health problems. Recent studies have shown that food habits and lifestyle can have a profound impact on the types and level of intake of harmful chemicals by disadvantaged communities.

The EU is equipped with a comprehensive regulatory framework to protect human health and the environment from the risks associated with chemical exposure. Since 2006, the EU has achieved substantial progress in the area of chemicals management by adopting its flagship regulation on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). Its chemicals regulatory framework is, however, fragmented as far as the protection of vulnerable groups from chemical hazards is concerned. In certain key acts, references to vulnerable groups are lacking, despite the subject of the legislation being directly relevant. While a reference alone would not provide protection, it would nonetheless be useful for such legislation to describe the particular vulnerable groups requiring special protection and to clarify how such protection might be provided. For example, in certain cases, protection might mean requiring a greater margin of safety in risk assessment and management measures, while in other cases protection might involve restrictions on chemicals such as not allowing use of endocrine disrupting chemicals in products aimed at young populations.
Chemicals regulation depends on a hazard identification and a risk assessment procedure to estimate the extent of the exposure and on that basis the probability of harm as well as its possible severity. On the basis of such assessments, measures can be set in place to manage the known risks so that they are at levels considered acceptable (safe) to humans and the environment. But controlling the risk of harm is a moving target, given that quantities of chemicals and subsequent exposures are likely to increase dramatically. Moreover, risk assessments, usually carried out by a chemical’s proponents (e.g., the producer), often underestimate the risk of harm. Additional scientific research into the possible hazards posed by chemicals almost always leads to increased (and seldom to lessened) concern over risks to human health and the environment.

Moreover, recent studies have pinpointed the detrimental effects caused by combined exposure to certain chemicals on the foetus, which can ultimately lead to persistent pathological diseases later in life. As such, these studies stressed that risk assessment based on single substances alone is not to sufficient to interpret the effects that combined exposure may cause on human health and thus urged policymakers to develop a cumulative risk assessment which could take into account all chemicals, spanning from pesticides, to industrial chemicals, and environmental contaminants (e.g. food, cosmetics, dust, and other sources).

This report sets out some of the most important knowledge gaps on the protection of children and vulnerable groups, provides examples of policy measures and other activities in the field, and describes improvement opportunities in the short, medium and long term.

**Key Findings**

### The problem

- Children, pregnant women, workers, and the elderly are particularly vulnerable to risks arising from chemical exposure, and have higher probabilities of adverse health symptoms or diseases throughout their lives.

- The developing human brain is particularly vulnerable to chemical exposures, with major windows of developmental vulnerability occurring in utero, during infancy and early childhood. During these sensitive life stages, exposure to EDCs and neurotoxins such as lead, arsenic, mercury, PCBs, pesticides, and solvents can cause lifelong neurological damage.

- Chemicals can enter the body through ingestion, inhalation, skin contact, and injection. Everyday sources of exposure include consumer products, household dust and drinking water. Toddlers, who often play or crawl on floors and carpets, are especially vulnerable because of hand to mouth behaviour.

- Lack of attention to the vulnerabilities of specific populations has led to only sporadic protective measures in the relevant pieces of legislation.

### Gaps and inconsistencies

- Lack of provisions in EU legislation defining which vulnerable groups should be ensured special protection, especially for those pieces of legislation that are of particular relevance to the protection of certain groups in society from chemical exposure.

- Although the EU Toys Directive provides standards to protect children as a vulnerable group, other consumer products aimed at children such as clothing and bedding are not covered.

- Chemicals having developmental neurotoxic (DNT) properties should be further regulated in order to ensure an adequate level of protection for the foetus and children.
# Key Findings

- Certain EU legislation, e.g. the Drinking Water Directive and Food Contact Materials Framework Regulation, are not updated with the most relevant scientific evidence and lack specific measures which could strengthen the protection of vulnerable groups.

- EU risk assessments focus on single substances and do not protect children and other vulnerable groups from combined or cumulative exposures to toxic chemicals.

- Knowledge is lacking on the toxic effects that certain categories of chemicals (e.g. Non-intentionally added substances [NIASs] and nanomaterials) can have on vulnerable groups. More research is also needed on how chemicals interfere with brain development.
1 INTRODUCTION

Sub-study c focuses on those groups in the population that are particularly vulnerable to the negative effects arising from exposure to chemicals. Groups with higher susceptibility are children (from the developing foetus to adolescence), pregnant women and the elderly, as well as certain occupational groups and people with lower socioeconomic status.

More specifically, the sub-study aims to:

- Provide an overview of the current state in respect of issues of protection of children and vulnerable groups from harmful exposure to chemicals, highlighting current legislation and policy measures at the EU level, activities in international and regional organisations as well as Member States and other countries, and the activities of industry and civil society organisations.
- Identify and describe the most important health issues relating to children and vulnerable groups and the main causes of these issues (e.g. source of and/or route of chemical exposure) according to current knowledge. Where possible, the study describes or exemplifies the magnitude of the issues based on available studies.
- Provide a general analysis of current policy measures and other activities in terms of their impact on, and effectiveness at, improving the protection of children and vulnerable groups.
- Identify and describe the most important knowledge gaps on the protection of children and vulnerable groups, assessing if and how these hinder action.
- Identify and describe opportunities to close the gaps identified, from a short, medium and long-term perspective, including legislative and other policy measures, improvements to the knowledge base, and provision of support to research and development.

The study considers the following problem:

Box 1: Problem definition of sub-study c

<table>
<thead>
<tr>
<th>Problem Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>The increased use of chemicals stemming from economic development in various sectors exposes humans to a continuous cocktail of chemical substances present in sources such as food, water, medicines, air, cosmetics, health care and consumer products. Some of these chemicals can be harmful to human health, with immediate, acute effects or chronic effects, often resulting from long-term exposures. Chronic, low-level exposure to various chemicals may result in a number of adverse outcomes, including damage to the nervous and immune systems, impairment of reproductive development and function, cancer, and organ-specific damage.</td>
</tr>
<tr>
<td>Several groups in the population are particularly vulnerable to the risks arising from chemical exposure. This increased vulnerability depends on various factors, from specific behaviours, intrinsic biophysical characteristics and health status, as well as social factors, such as living or working environment. The developing foetus is considered to be one of the most vulnerable groups in the population for chemical exposure, largely because of its developmental mechanisms: at certain early stages of development, exposure to environmental toxicants can lead to irreversible damage. Also, after birth, children remain a group of particular concern, as they have some specific vulnerabilities to the toxic effects of chemicals. For example, they have greater exposures to toxic chemicals than adults in proportion to their bodyweight as they breathe in more air, consume more food and drink more water. Their behavioural tendencies (e.g. hand-to-mouth contact, crawling, chewing toys) also lends itself to contact with toxic chemicals unsafely used or stored.</td>
</tr>
<tr>
<td>Other vulnerable groups include: rural workers; industrial workers, who are often not properly equipped to work with large volumes of chemicals; pregnant women, who may expose themselves and the developing foetus to the effects of chemicals in their environments at crucial development periods; the elderly may be more susceptible to the toxic effects of some chemicals due to physiological changes; people with pre-existing medical conditions; illiterate people, who are unable to follow written instructions; and incompetently trained people, who tend to use chemicals unsafely.</td>
</tr>
<tr>
<td>A wealth of scientific literature exists, showing the hazardous health impacts of chemicals. However, research tends to focus on single compounds or the impacts of chemicals on specific health or organ systems. By contrast, knowledge of the effects of mixtures of chemicals, as well as environmentally induced epigenetic toxicity, is limited. Further investigation is also needed into the impacts of chemicals on vulnerable groups, particularly the foetus and its...</td>
</tr>
</tbody>
</table>
Problem Definition

Specific sensitive windows of development, adult onset effects resulting from early life exposures, and potential health impacts of new technologies, such as nanomaterials.

The EU’s 7th Environment Action Programme (EAP) recognises the need to ensure a high level of protection for vulnerable groups from chemical hazards. Numerous pieces of EU legislation incorporate measures to protect children and other vulnerable groups from toxic exposure. Yet, the overall EU chemical legal and policy framework is fragmented, with various opportunities identified to strengthen EU protection of vulnerable groups from harmful chemical exposure. Numerous gaps in relation to risk assessment methodologies, awareness raising and information distribution also need to be closed.

This sub-study aims to provide an analysis of the current state of the protection of vulnerable groups from harmful exposure to chemicals in terms of scientific evidence, policy measures and EU legislation. It highlights the current knowledge and regulatory gaps, as well as the opportunities to improve such protections in the framework of the EU strategy for a non-toxic environment.

The following chapter introduces the sub-study in general, describing the main vulnerable groups, outlining the ways in which these groups can be exposed to harmful chemicals and, finally, setting out the main adverse health effects that result from chemical exposure.

Subsequent chapters set out the legislative framework relevant to the scope of this sub-study, and describe in further detail the evidence, literature and information on vulnerable groups in relation to the negative effects arising from exposure to chemicals. They also provide an overview of current gaps and deficits, together with opportunities for improvement.

1.1 WHO ARE THE VULNERABLE GROUPS IN SOCIETY?

Vulnerability is the degree of susceptibility of a given population to cope with, resist or recover from the impact of harmful effects caused by exposure to hazardous events. In the framework of chemical exposure, certain groups in society may have an increased vulnerability because of their:

- Lower exposure thresholds for health effects;
- Constant exposure to highly hazardous chemicals;
- Reduced ability to protect from exposure;
- Particular health status;
- Specific behaviours.

The concept of vulnerability is deeply linked with that of risk, which is defined as the likelihood that a person will experience an adverse health effect if exposed to a hazard under specific conditions. Among the factors that might influence the degree of risk are: length of exposure to the chemical substance; route of the exposure (e.g., breathing in a vapour, skin contact); and severity of the effects stemming from the exposure.

When assessing risks, other factors which might lead to a greater vulnerability on the part of some populations should also be taken into account. For instance, individual factors, such as biophysical characteristics, can make certain individuals more vulnerable. Behavioural factors, such as certain activities, hobbies and occupational exposures, may increase the level of vulnerability. Social factors, such as where a person lives, works or spends the majority of the time, may also intensify the degree of vulnerability.

---

1 WHO, 2003
3 For a guide to terminology in the field of hazard and risk assessment in chemicals, see David J, 1992.
4 ANHE, official website.
Individual, behavioural and social factors can lead to an increased risk of chemical exposure, and, consequently, to a higher vulnerability across the population. Therefore, in this context, vulnerability can be defined as “a series of threshold factors that increase or amplify risk and lead to poorer health outcomes”\(^5\). This explains why the concept of vulnerability is linked to that of risk, as well as why certain categories of the population deserve special attention and protection from the risks of chemical exposure.

### 1.2 HOW ARE VULNERABLE GROUPS EXPOSED TO HARMFUL CHEMICALS?

Exposure is defined as the contact of an individual with a chemical substance for a given time. Exposure can be classified in terms of intensity, frequency, and duration\(^6\). A chemical can make contact with or enter the body and become hazardous to a person’s health through four major routes: ingestion, inhalation (breathing), skin contact and injection. As the first three routes of exposure are most relevant to the scope of the study, these are discussed below. Exposure through the placenta and breastfeeding, as well as workplace exposure are discussed separately. The route of exposure is an important consideration, as it often predicts the organ system or part of the body that will be affected directly or in later years.

#### 1.2.1 Ingestion

Chemicals can enter the human body through swallowing of contaminated mucus expelled from the lungs, or by eating or drinking contaminated food or drinks. Food and drink can be contaminated through contact with unwashed hands, gloves or clothing, or via contact with hazardous chemicals at the workplace. Nail-biting, smoking, as well as cosmetic products and medicines are also routes through which chemicals may be ingested\(^7\). Once ingested, chemicals travel down into the stomach. From there, the majority of chemicals end in the small intestine, where they eventually enter into the bloodstream. It is important to notice that some acids and caustics can damage the digestive system if ingested in high concentrations\(^8\).

Children and the elderly are more susceptible to the ingestion of chemicals products because of their behaviours and differences in some physiological parameters, as further explained in Chapters 2 and 4.

#### 1.2.2 Inhalation

Inhalation of contaminated air is one of the most common means of chemicals entering the body. Chemical vapours, gases and mists, if not trapped into the mucus, can reach the alveoli in the lungs, eventually enter into the bloodstream and ultimately circulate in the body. Certain solid particles in dusts, fumes and smoke which escape the filtering mechanisms of the nose may also be trapped by the mucus. However, the mucus can be either expelled through the mouth or ingested and travel down the stomach. In this latter case, the contaminating chemicals will enter the body via the same mechanisms explained in the ingestion section\(^9\).

It is also worth noting that some of the solid particles mentioned above can cause permanent damage to the alveolar walls, which can eventually interfere with the lung's ability to transfer oxygen into the blood stream. Furthermore, certain organic chemicals, acids, or caustics, when inhaled in ample amounts, can critically damage the mouth, nose, trachea, bronchi and lungs\(^10\). With inhalation exposure, it is important to differentiate between indoor and outdoor pollutants.

---

\(^5\) ANHE, official website.
\(^7\) WHO, 2011a.
\(^8\) Canadian OSH website, 2016.
\(^9\) Canadian OSH website, 2016.
\(^10\) Canadian OSH website, 2016; see also para 1.2.1
Indoor air pollution

Indoor air pollution is responsible for two million deaths per year globally. People who are particularly susceptible to indoor air pollution include infants, children, pregnant women, elderly persons over 65 years of age, and those suffering from asthma, respiratory diseases, or cardiovascular diseases. For some pollutants (e.g. microbes), other health compromises (immunodeficiency) may render people more vulnerable. Genetic traits, nutritional status and lifestyle factors may also contribute. Furthermore, susceptibility of vulnerable groups to pollutants vary due to existing diseases and genetic factors.

In the framework of indoor pollution, a particular area of concern is indoor dust, which can harbour a cocktail of toxic chemicals linked to increased risk of a range of adverse health hazards, including endocrine disruption, cognitive and behavioural impairment, cancer, asthma, and immune dysfunction. A recently published study which conducted a comprehensive analysis of consumer product chemicals in U.S. indoor dust, concluded that a wide array of chemicals used in everyday products – including those associated with reproductive and developmental toxicity, endocrine disruption, cancer and other health effects - are present in indoor environments to which people are continuously exposed. As a consequence, toxic chemicals such as phthalates, phenols, flame retardants, and polyfluorinated alkyl substances (PFASs), which are responsible for various negative effects on human health, are extensively present in the general population and especially among vulnerable groups such as children and pregnant women. Children, who often play or crawl on the floor, are particularly vulnerable to inhaling or ingesting toxic chemicals in household dust.

Outdoor air pollution

Outdoor air pollution results from human activities, such as inefficient combustions of fuels for transport, home heating and cooking. In particular, combustion processes produce a mix of air pollutants, consisting of both primary emissions (e.g. diesel soot particles and lead), as well as the products of atmospheric transformation (e.g. ozone and sulphate particles). Outdoor pollutants vary according to density of traffic, degree of industrialisation, time and climate. According to the WHO, the six main outdoor pollutants are: ozone (O3), particulate matter (PM10 and PM2.5), lead, sulphur dioxide (SO2), carbon monoxide (CO) and nitrogen oxide (NO2).

Urban air pollution causes significant health problems throughout Europe, reducing the life expectancy of residents of more polluted areas by more than one year. Air pollution is a global health crisis that has long been linked to lung disease, heart disease and stroke. Children and the elderly are most vulnerable to the effects of outdoor pollution.

A recent study identified the abundant presence of magnetite nanoparticles in the human brain, which match the high-temperature magnetite nanospheres prolific in urban, airborne particulate matter. As many of the airborne magnetite pollution particles are <200 nm in diameter, they can enter the brain directly, with toxic effects, e.g. the production of reactive oxygen species (ROS), which has been

---

14 Balk S et al., 2004.
15 Mitro SD et al., 2016.
16 WHO, official webpage, Air pollution.
17 Mitro SD et al., 2016.
18 WHO, official webpage, Air pollution.
19 WHO, official webpage, Air pollution.
20 WHO, 2011b.
21 WHO, 2011b.
22 WHO/EURO, 2013.
23 Almeida SM et al., 2016.
24 Maher BA et al., 2016.
linked to neurodegenerative diseases such as Alzheimer’s disease. One study showed that magnetite was directly associated with the damage seen in Alzheimer’s brains\textsuperscript{25}.

Moreover, a 2015 large cohort study in Taiwan suggested that long-term exposure to O\textsubscript{3} and PM2.5 above the current U.S. EPA standards is associated with increased risk of Alzheimer’s disease\textsuperscript{26}. Other research showed a role for air pollution in damage of the central nervous system (CNS) among children and young adults, and its impact on the developing brain and the potential aetiology of Alzheimer’s disease and mood disorders\textsuperscript{27}. Air pollution has also been linked to cognitive decline in older men and women\textsuperscript{8,29}.

Children’s exposure to air pollution is a special concern because they breathe higher volumes of air relative to their body weight and their tissue and organs are growing\textsuperscript{30}. In addition, children spend more time outside, where the concentrations of pollution from traffic, power plants, and other combustion sources are generally higher. Scientific evidence has suggested that air pollution, particularly traffic-related pollution, is associated with infant mortality and the development of asthma and atopy, as well as acute bronchitis\textsuperscript{31}.

A recent study has linked outdoor air pollution to increased mental illness in children, even at low levels of pollution\textsuperscript{32}. New research found that relatively small increases in air pollution were associated with a significant increase in treated psychiatric problems. While this is the first study that establishes a link of this kind, it must be noted that the latter is consistent with a growing body of evidence that air pollution can affect mental and cognitive health and that children are particularly vulnerable to poor air quality. The research in question examined the pollution exposure of more than 500,000 under-18s in Sweden and compared this with records of medicines prescribed for mental illnesses, ranging from sedatives to anti-psychotics. There have also been several earlier studies that found associations between air pollution and autism spectrum disorders and learning and development in children\textsuperscript{33}. However, this study adds to evidence that air pollution may have detrimental effects on the brains of children and adolescents.

### 1.2.3 Skin contact

Chemicals can also enter the body through skin contact. For instance, organic and caustic chemicals can soften the skin, and through this layer reach the dermis; from there they can enter the veins and eventually access the blood stream. Chemicals can also enter the body through cuts, punctures or scrapes of the skin, where the protective layer of the skin is weakened. Moreover, contact with detergents or solvents are of particular concern as they can penetrate the skin and thus = circulate directly into body\textsuperscript{34}.

It is worth noting that chemicals can penetrate the skin with various degrees. For instance, some solvents such as trichloroethylene, naphtha and toluene may soften the keratin layer of the skin, but are not capable of going further unless the contact is delayed. Chemicals such as benzene, carbon tetrachloride, carbon disulphide and methyl alcohol, instead, can quickly damage the epidermis and hence enter the blood stream. Corrosive chemicals can burn the skin immediately, allowing infection or other chemicals to enter. In given circumstances, certain chemicals may enter the body by injection. This can occur in hospital settings. Once chemicals are in the blood stream, chemicals circulate into

\textsuperscript{25} Plascencia-Villa G et al, 2016.
\textsuperscript{26} Jung CR et al., 2015.
\textsuperscript{27} Calderón-Garcidueñas L et al., 2012.
\textsuperscript{28} Power MC et al., 2011.
\textsuperscript{29} Weuve J et al., 2012.
\textsuperscript{30} Canha N et al., 2011.
\textsuperscript{32} Oudin A et al., 2016.
\textsuperscript{33} Wang S et al., 2009.
\textsuperscript{34} Canadian OSH website, 2016.
the body and can spread their effects\textsuperscript{35}. After absorption, chemicals are also capable of causing poisoning or diseases such as cancer\textsuperscript{36}.

Adolescents, pregnant women, children and workers are particularly vulnerable to chemical absorption through the skin.

1.2.4 Other routes of exposure

The placenta

The placenta is a semi-permeable barrier which regulates the exchange of nutrients, gases, waste and molecules between the mother and the foetus. It is an essential organ as it allows the foetus to grow and develop\textsuperscript{37}. While originally the placenta was thought to shield the cord blood and the developing foetus from most chemicals and pollutants in the environment, this has now proved to be untrue\textsuperscript{38}. The thalidomide crisis demonstrated the vulnerability of the foetus and the permeability of the placenta to toxic exposures\textsuperscript{39} (see box 2). Another example of a crisis, before which the placenta was thought to protect the foetus against toxicants, is the ‘Minamata disaster’ (see box 3).

Box 2: The thalidomide crisis

In 1953, the anti-morning sickness drug ‘thalidomide’ was developed in Germany. In 1956, it was licensed for over-the-counter sale in Germany and most European countries. Doctors prescribed the drug for several years, before determining in 1961 that it caused many babies to be born with malformed limbs. Over 10,000 children were born with thalidomide-related disabilities worldwide.

Afterwards, doctors discovered that other chemicals, such as instance, lead, mercury, polychlorinated biphenyls (PCBs), and nicotine could also cross the placenta and cause adverse health effects on the foetus.


Box 3: The Minamata disaster

The Minamata disaster, which affected thousands of individuals, was the first large-scale incident of methylmercury poisoning. Between 1932 and 1968, large amounts of this highly toxic chemical were released in the industrial wastewater from the Chisso Corporation’s chemical factory, and bioaccumulated in shellfish and fish in Minamata Bay. When eaten by the local population, it resulted in mercury poisoning; a condition later referred to as the ‘Minamata disease’ or the ‘Chisso-Minamata disease’.

Minamata disease is a neurological syndrome, and symptoms including ataxia, tremor, memory loss, loss of peripheral vision, and vision and hearing problems. In certain cases, death can follow the previously mentioned symptoms. Minamata showed the neurotoxic effects that mercury can have on the general population, and especially on foetuses, infants, and young children. Before Minamata, the placenta was thought to shield the foetus against toxic chemicals.

Sources: Spheres of Influence, 2013.

It is worth noting that since the foetus has an immature metabolism and is thus unable to detoxify substances efficiently, the role played by the placenta is crucial insofar it determines the substance exchanged between the mother and the foetus. In fact, any toxic substances that the mother is exposed to might be transferred to the foetus. Carbon-dioxide, lead, ethanol, and cigarette smoke, are substances likely to be transferred through the placenta\textsuperscript{40}.

\textsuperscript{35} Canadian OSH website, 2016.
\textsuperscript{36} EU-OSHA, 2008.
\textsuperscript{37} Prouillac C & Lecoeur S, 2010.
\textsuperscript{38} Grandjean P, 2013.
\textsuperscript{39} Konkel L, 2016.
\textsuperscript{40} ATSDR, official webpage.
Breast milk

Human breast milk provides wide benefits for the growth, immunity, and development of the foetus\textsuperscript{41}. Breast milk in fact help infants to fight infection, contribute to brain development, and strengthen resistance to certain diseases such as asthma, allergies, and diabetes\textsuperscript{42}. However, breast milk can be also a source of chemical exposure. Since the 1950s, scientists are aware of the widespread contamination of human breast milk, as a consequence of decades of inadequately controlled pollution of the environment by toxic chemicals\textsuperscript{43}. Polychlorinated biphenyls, dioxins, dibenzofurans, polybrominated diphenyl ethers, and heavy metals are among the toxic chemicals frequently found in breast milk\textsuperscript{44}. These compounds are encountered among women in both developed and developing countries\textsuperscript{45}.

Some of the higher level of contamination is found among women in agricultural settings exposed to pesticides, as well as among women whose diet is heavily based on fish and marine food, as this accumulates persistent organic pollutants\textsuperscript{46}. The level of risk for infants and children of being exposed to chemicals in human milk can vary and ultimately depends on the diet of the mother, the class and amount of chemicals present in the milk, as well as on the toxicological potency of the chemicals\textsuperscript{47}.

Occupational exposure

Many occupations involve the exposure to hazardous chemicals. Health effects can span from eye irritation to serious diseases, such as cancer\textsuperscript{48}. Adverse health effects can occur both as a result of a single episode of persistent exposure or from a constant, long-lasting exposure. Workers can be exposed to toxic chemicals for long period and showing no pathological symptoms for years. Yet, in some cases, symptoms appear only when irreversible harm has already occurred. While certain chemicals can be easily recognised as dangerous substances (e.g. lead, arsenic), others may not appear harmful on a first check. For instance, exposure to flour dust may result in various adverse health outcomes from conjunctivitis to baker’s asthma\textsuperscript{49}.

The types of industry where the risk to chemical exposure is highest include\textsuperscript{50}:

- mining, quarrying, oil and gas drilling, where there is high risk of exposure to respirable crystalline silica, as well as lubricants and drilling muds;
- manufacturing industries, where there is a risk of being exposed to solvents, as well as paints and lubricants);
- farming, as the chance to be exposed to toxic pesticides is high;
- service industries, where the risk of exposure to cleaning products, asbestos, and bioaerosols is relevant;
- healthcare sector, there is risk of exposure to pharmaceuticals and disinfectants;
- hairdressing sector and beauty salon industry, where there is a constant exposure to a wide range of hazardous chemicals used in products such as sprays and paints;
- recycling industry, where there is the risk of exposure to dusts and biohazards.

\textsuperscript{41} U.S. Institute of Medicine, 1991.
\textsuperscript{42} Oddy WH, 2001.
\textsuperscript{43} Lang EP, \textit{et al.}, 1951.
\textsuperscript{44} Hooper K & McDonald TA, 2000.
\textsuperscript{45} Landrigan PJ, \textit{et al.}, 2002.
\textsuperscript{46} Landrigan PJ, \textit{et al.}, 2002.
\textsuperscript{47} Landrigan PJ, \textit{et al.}, 2002.
\textsuperscript{48} Ekenga CC, \textit{et al.}, 2015.
\textsuperscript{49} Stobnicka A & Górny RL, 2015.
\textsuperscript{50} Keen C, 2016a.
1.3 WHAT ARE THE MAIN ADVERSE HEALTH EFFECTS IN VULNERABLE POPULATIONS?

As described above, chemicals can enter the human body through a variety of routes, and can have different health effects on certain population groups depending on their susceptibility. A chemical exposure can produce a health effect directly at the site of contact (local) or elsewhere in the body (systemic), and that effect can be either immediate or delayed. The specific health effects and main routes of exposure most relevant to different vulnerable groups are described in Chapters 2 to 6. The purpose of this section is to set out an overview of the main adverse health effects of chemical exposure among vulnerable populations.

Different organ systems can be affected by chemical exposure, resulting in a range of health effects. This table is not a comprehensive overview but, rather, provides illustrative examples of the adverse health effects which may be caused by some of the chemicals listed.

Table 1: Examples of health effects of chemicals on different organ systems

<table>
<thead>
<tr>
<th>Chemical System</th>
<th>Possible Health Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous system</td>
<td>Adverse health effects caused by neurotoxins include: narcosis, nausea, dizziness, vertigo, irritability, euphoria, movement coordination problems, impaired memory and behaviour, as well as autism, Attention Deficit Hyperactivity Disorder (ADHD), cerebral palsy, and mental retardation. Exposure has also been associated with neurodegenerative diseases like Alzheimer’s disease and Parkinson’s disease. Other health effects include decreased speech, sight and muscle strength, ataxia, and seizures. Damage to the developing nervous system of the foetus may result in neural tube defects, decreased intelligence and increased likelihood of behavioural problems.</td>
</tr>
<tr>
<td>Reproductive system</td>
<td>Early or delayed puberty, early pregnancy loss, premature birth, foetal death, impaired foetal growth, decreased fertility/subfertility, increased foetal mortality, increased birth defects (structural, e.g. cardiac defect, or functional, e.g. learning disability), infertility, low birth weight, menstrual irregularities. The impact of exposure to a reproductive toxicant may not be immediately evident but instead emerge at key life transitions (e.g. adult fertility, pregnancy, embryonic development, puberty, etc.). Examples of possible contaminants: Many chemicals cause mild CNS depression that may be misdiagnosed as inebriation and, if undetected, can progress to psychosis or dementia, such as: Retinoic acid, arsenic, valproic acid, lead, cadmium, carbon monoxide, cyanide, methanol, mercury, PVC, PCBs, toluene.</td>
</tr>
<tr>
<td>Endocrine system</td>
<td>Maternal smoking causes decreased birth weight and increased risk for the baby of diabetes and osteoporosis later in life. Lead poisoning causes abnormal bone structure and poor growth. EDCs have also been associated with the onset of conditions such as diabetes and obesity, as well as cardiovascular disease and hypertension. Certain EDCs have been described as affecting the function of beta cells in the pancreas, which are responsible for insulin production and, therefore, crucial for maintenance of glucose levels. Examples of possible contaminants: An increased risk of Type 2 diabetes has also been reported after exposure to persistent organic pollutants (POPs) (including PCBs, DDE, dioxin, organochlorine pesticides, and hexachlorobenzene), arsenic and some flame retardants.</td>
</tr>
<tr>
<td>Respiratory system</td>
<td>Asbestos, lung cancer, chronic bronchitis, fibrosis, emphysema, and decreased oxygen supply in the blood. In the foetus, it can alter airway growth with increased collagen deposition in airway walls as a result of exposure to maternal smoking, and neonates may experience an increased incidence of respiratory mortality following exposure to particulates in the air. Children may exacerbate pre-existing asthma from exposure to particulates in the air and workers may develop work-aggravated and work-related asthma. More than 100 toxicants have been shown to cause asthma, and many more can exacerbate it. Examples of possible contaminants: Asbestos, radon, cadmium, benzene, carbon monoxide, soot, aluminium, ammonia, arsenic.</td>
</tr>
<tr>
<td>Renal system</td>
<td>Decreased formation of urine, decreased blood flow to kidneys, decreased ability to filter the blood, prevented urine flow, kidney tissue damage, and kidney cancer. The environment, the workplace and, especially, taking medicines, represent potential sources of nephrotoxicity. Examples of possible contaminants: Organic solvents and heavy metals known to adversely affect renal function. Cadmium, lead, mercury, uranium, chlorinated hydrocarbon solvents (TCE, PCE, PCT).</td>
</tr>
<tr>
<td>Cardiovascular system</td>
<td>Study for the strategy for a non-toxic environment of the 7th EAP, Brussels. Sub-study c: the protection of vulnerable groups, August 2017/24</td>
</tr>
</tbody>
</table>
**Possible health effects:** The cardiovascular and haematological systems are frequent targets of toxicants, producing adverse effects in the cardiovascular system by acting on the myocardial cells or the autonomic nervous system (ANS). This can result in various issues, including problems with heart rate, blood pressure or cardiac contractility, heart failure, aplastic anaemia, acute leukaemia and chronic myelogenous leukaemia.

**Examples of possible contaminants:** Carbon monoxide, carbon disulphide, nitrates, methylene chloride, methylmercury, lead, arsenic, cadmium, ozone, vinyl chloride, benzene.

<table>
<thead>
<tr>
<th>Thyroid system</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Possible health effects:</strong> Hypothyroidism or hyperthyroidism, thyroid autoimmune disease, neurodevelopmental effects with changes in circulating levels of thyroid hormones.</td>
</tr>
<tr>
<td><strong>Possible contaminants:</strong> PCBs, BPA, perchlorate, dioxins, pentachlorophenol, triclosan and the PBDE flame retardants. Animal evidence of thyroid disruption exists for the phthalates DEHP, DIDP, DnHP, DBP, resorcinol and the flame retardant TBBPA.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Immune system</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Possible health effects:</strong> Allergies, immune system inhibition or failure, auto-immunity. Early-life exposure to chemicals commonly found in households has been associated with the occurrence of allergic airway diseases, asthma and rhinitis (hay fever). Positive relations have been found between phthalates in dust or phthalate-related products, such as PVC flooring, and asthma or allergic symptoms. Associations between BBzP and DEHP concentrations in dust and selected allergies and asthma have also been found. Also of concern is the finding that exposure to perfluorinated compounds can suppress antibody response to routine childhood immunisations.</td>
</tr>
<tr>
<td><strong>Examples of possible contaminants:</strong> Mercury, lead, pesticides, polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs).</td>
</tr>
</tbody>
</table>

**Sources:** WHO, 2011a; ATSDR, webpage.

In recent years, there has been an increased focus on the effects of exposure to chemicals on both human health and the environment. Humans are simultaneously exposed to numerous chemical substances present in food, water, medicines, air, cosmetics, health care and consumer products. The effects of such chemical mixtures are referred to as combination effects, mixture effects or cocktail effects.

Studies focusing on the health effects of mixtures of chemicals have, however, been limited, for a variety of reasons. Firstly, it is easier to study a single compound in an animal study and to obtain traditional dose–response information. Secondly, an almost infinite number of combinations of contaminants is possible, and it is often difficult to know which is the most important, which dose ranges should be investigated, or which biological end point should be studied. Thirdly, many factors must be taken into account: the amount of chemical the person was in contact with; the duration of the contact; the frequency of exposure; pathway of the chemical through the body of the person; and his/her prior general health. In addition, susceptibility of an individual to the toxic and carcinogenic effects of a chemical mixture is believed to have a significant genetic component.

In the EU, current risk assessments (RA) of chemicals focus on exposure to individual chemicals and do not provide a comprehensive and integrated assessment of cumulative effects of different chemicals, taking into account different routes of exposure. The 2012 Commission Communication on Combination effects of Chemicals (Chemical mixtures) recognised the disadvantage of the EU current RA, which only assess chemicals one by one and launched a new process to develop an effective way to assess exposure stemming from combination effects of chemicals. The new Commission approach arises from the 2012 opinion on “Toxicity and Assessment of Chemical Mixtures”, issued by the scientific committees SCHER, SCENIHR and SCCS. The report notes that the number of possible combinations of toxic substances is enormous and suggests risk assessors focus only on circumstances of a particular concern. The report also highlights that although data gaps limit the assessment of chemical mixtures, the information collected via the REACH Regulation can contribute to reducing some of the challenges risk assessors are facing.

International bodies have also developed other frameworks for the assessment of chemical mixtures in recent years. For instance, a WHO/IPCS workshop resulted in framework for risk assessment of combined exposure to multiple chemicals that could be adapted to the needs of specific users.

---

51 Kienzler et al., 2016.
52 Communication from the Commission to the Council, 2012.
53 SCHER, SCENIHR, SCCS, 2011.
However, its use is often limited by large data gaps on exposure as well as hazard information\(^\text{54}\).

Even though new frameworks for assessing cumulative effects are thus being developed and applied\(^\text{55}\), an overarching, comprehensive approach across different EU acts is still lacking. While frameworks such as the ones described above may provide reference for further development, their concrete application is limited due to lack of exposure data\(^\text{56}\).

Yet, recent studies have pinpointed the detrimental effects caused by combined exposure to certain chemicals on the foetus which can ultimately lead to persistent pathological diseases later in life\(^\text{57}\). As such, these studies stressed that risk assessment based on single substances alone is not to sufficient to interpret the effects that combined exposure may cause on human health and thus urged policymakers to develop a cumulative risk assessment which could take into account all chemicals, spanning from pesticides, to industrial chemicals, and environmental contaminants (e.g. food, cosmetics, dust, and other sources)\(^\text{58}\).

In addition to combination effects from chemical mixtures, another area of concern is the issue of environmentally induced epigenetic toxicity. An epigenetic trait has been described as: ‘a stably heritable phenotype resulting from changes in a chromosome without alterations in the DNA sequence’\(^\text{59}\). Epigenetic programming is fundamental for normal mammalian development, and provides a more subtle mechanism by which the environment can rapidly alter gene expression within single or multiple generations. It is the complex interaction between our genome, epigeome and environment that shapes development into unique individuals, and thus influences human health and potentially the health of future offspring\(^\text{60}\).

While regulatory bodies have developed comprehensive testing procedures and safety guidelines to protect human health against the adverse effects of environmentally induced genetic mutations causing, for example, cancer, there are few established regulatory procedures in chemical safety programmes for determining environmentally induced epigenetic toxicity\(^\text{61}\). Such changes can influence people’s health, with numerous adult onset diseases associated with abnormal epigenetic changes, including cancer, diabetes, and neurological, renal, cardiac and respiratory conditions\(^\text{62}\). Epigenetic processes also play a key role in initiating the onset of puberty, changes to which can also increase the risk of some of these adult onset diseases\(^\text{63}\).

Certain stages in development and cell types can be thought of as particularly sensitive to epigenetic change due to the severity of the outcome for the individual, or the potential to affect multiple generations\(^\text{64}\). For example, in utero exposure could result in environmentally induced epigenetic changes during early embryo and germ line development. Such changes could have far-reaching consequences on embryo viability and development, and thus subsequent future health and fertility. It is also important to consider ex utero exposures, as early childhood and adolescence are also periods of significant growth and development. Environmentally induced epigenetic changes during these stages could also have detrimental effects on future health and fertility\(^\text{65}\).

\(^{54}\) Kienzler \textit{et al.}, 2016
\(^{55}\) Price, 2012.
\(^{56}\) Kienzler \textit{et al.}, 2016.
\(^{57}\) Govarts E., \textit{et al.}, 2016.
\(^{59}\) Berger SL \textit{et al.}, 2009.
\(^{60}\) Marczylo EL \textit{et al.}, 2016.
\(^{61}\) Reproductive generation studies (such as EOGRTS) are partly design to address some of these conditions, such as sexual maturation and neurological developmental aspects. See for more info: Saghir SA & Dorato MA, 2016.
\(^{62}\) Hamm CA & Costa FF, 2015.
\(^{63}\) Rzeczkowska PA \textit{et al.}, 2014.
\(^{64}\) Marczylo EL \textit{et al.}, 2016.
\(^{65}\) Ibid.
A recent study concluded that research in the area of epigenetic toxicity is largely in its infancy, and is incomplete with respect to the specific mechanisms of epigenetically mediated environmentally induced toxicity in humans at doses relevant to human exposures. There is, however, sufficient information to perform retrospective epigenetic analysis of existing regulatory studies and to identify future research needs. Collaboration between scientists from academia, industry, and governmental and regulatory bodies will promote further research within a regulatory context, and drive the development and implementation of epigenetically relevant integrated testing strategies or policies for the continued protection of public health.

In order to bridge the gap between science, the general public and policy makers, in 2010 the EU launched the FP7 European Community-funded Network of Excellence: EpiGeneSys. The goal of this initiative, which ended in March 2016, was to address fundamental epigenetic mechanisms, both spatially and temporally, in quantitative terms, using systems biology approaches. It helped to build a bridge between the fields of epigenetics and systems biology, facilitated communication of the underlying science in an accessible and interesting manner, and built public support for scientific research, changing the public’s perception of science through education.

66 Ibid.
2 CHILDREN: FROM THE DEVELOPING FŒTUS TO LATE ADOLESCENCE

Foetuses, infants, children and adolescents are especially susceptible to chemical exposures, owing to developmental stage-specific exposure patterns and physiological and toxicodynamic factors. They possess distinct characteristics and/or behavioural tendencies that contribute to a particular susceptibility to chemical exposures. A report published in 1993 by the American National Research Council entitled *Pesticides in the Diets of Infants and Children* was the first publication to highlight the unique risk of chemical exposure faced by children. Prior to this, little attention was paid to the impact of chemicals on children.

The following sections further analyse the vulnerability of children according to their developmental stages and outlines the reasons for their increased vulnerability compared to the general population.

2.1 FOETUS

As explained in paragraph 1.2.4, scientific studies demonstrated that the placenta does not shield the foetus from the exposure to certain toxic chemicals. In particular, research has shown that chemicals in pregnant women can cross the placenta; in addition, chemicals such as with lead, mercury, polychlorinated biphenyls (PCBs) and nicotine, can accumulate inside the foetus, resulting in higher exposure doses for the latter compared to the mother.

The developing foetus is considered to be one of the most vulnerable groups in the population for chemical exposure. Their increased exposure and risk is mainly due to factors such as:

- Fast cell reproduction rates, which make the developing organs of the foetus particularly susceptible to toxic aggression;
- Different development stages of sensitive organs, which make the foetus highly sensitive to harmful chemicals;
- Immature ability of the foetus’ body to expel toxicants;
- The undeveloped blood-brain barrier, which does not shield the developing brain from transport of toxic chemicals.

The vulnerability of the foetus, linked to increased exposure and absorption, can be further increased by socioeconomic conditions such as poverty and poor nutrition. If, for instance, the foetus does not receive the adequate intake of protein, calcium, and iron, the absorption of toxic substances such as lead is likely to increase. Given the above, the exposure to neurotoxicants such as lead, arsenic, mercury, PCBs, pesticides and solvents during this unique sensitive life stage can cause lifelong damages. For these reasons, research has developed the concept of ‘windows of vulnerability’, which describes the critical periods in early development when exposures to even minimal doses of toxic chemicals - which would not have any adverse effects on adults - are able to cause long-lasting hazardous health effects on the

---

69 KEMI, 2012.
72 Grandjean P, 2013; Rollin HB et al., 2009.
75 Landrigan PJ & Goldman LR, 2011.
76 Diamanti-Kandarakis E et al., 2009; Grandjean P, 2013
77 Diamanti-Kandarakis E et al., 2009.
foetus and, more in general, children. 

- In fact, prenatal exposure to environmental chemicals is linked to adverse health consequences, including: pre-term birth; low birth weight (due to intrauterine growth retardation); congenital abnormalities (birth defects); pregnancy loss (miscarriage); childhood morbidity; and neurodevelopmental defects.

A focus of recent studies has been the developing human brain, which is uniquely vulnerable to toxic chemical exposures, with critical windows of developmental vulnerability occurring in utero, as well as during infancy, childhood and early adolescence. Toxic substances can contribute to neuropsychiatric disorders in children, with disorders of neurobehavioral development affecting 10–15% of all births, and prevalence rates of autism spectrum disorder and ADHD appeared to have spread worldwide. It is worth noting that all of these clinical conditions have profound consequences for the society in its entirety, as they lead to reduced academic performance and behavioural disorders, thus strongly reducing overall quality of life.

According to a 2006 study, among the chemicals which can be more harmful for the developing brains there are the following neurotoxicants: lead, methylmercury, arsenic, polychlorinated biphenyls (PCBs), and toluene.

For instance, studies have demonstrated that exposure to lead – which can be found in the paint of old houses and water pipes - may cause neurological effects, strain development, behavioural difficulties and learning problems, as well as loss of IQ, hyperactivity and inattention. In addition, exposure to lead during early childhood can decrease school performance and lead to antisocial behaviour later in life.

Methylmercury is formed from inorganic mercury and is common contaminant of fish. It is a strong neurotoxin which is formed primarily from mercury emitted by coal-fired power plants, waste incineration, and other industrial processes. Exposure to methylmercury can reduce cognitive performance and attention, as well as cause psychomotor deficiencies in children. Even post-birth exposure can cause negative health effects; in fact, children which consumed contaminated seafood have experienced deficits in attention, motor function, language, and memory impairments. It is also important to notice that developmental neurotoxicity in the foetus occurs at much lower exposures than the one that would affect adults.

As far as PCBs are concerned, despite being banned, they can still be found in certain products such as electrical transformers. They are pollutants with endocrine disrupting properties. Evidence strongly suggest that exposure to PCBs can negatively affect brain development.

With regard to arsenic, prenatal and early postnatal exposures to this chemical are associated with neurological disease appearing in adult life.

---

79 Kim H & Cizmadia P, 2010; Gluckman PD & Hanson MA, 2004; Stillerman KP et al., 2008.
81 Landrignan PJ et al., 2012.
84 CHEM Trust, 2017.
86 Fergusson DM, et al., 2008.
87 CHEM Trust, 2017.
90 WHO, Regional Office for Europe, 2014
91 Hamadani, JD, et al., 2011.
Finally, concerning toluene, maternal consumption of alcohol during pregnancy, even in very small quantities, has been linked to several neurobehavioural diseases in children, spanning from reduced IQ, antisocial behaviour, and sensory problems\textsuperscript{92}.

In addition to the above five chemicals, recent epidemiological studies have documented six additional developmental neurotoxicants, i.e. manganese, fluoride, chlorpyrifos, dichlorodiphenyl-trichloroethane, tetrachloroethylene, and the polybrominated diphenyl ethers\textsuperscript{93}. In particular, recent studies showed that exposure to manganese is associated with reduced performance at school, hyperactivity, and impaired functions of the motor system\textsuperscript{94}.

Furthermore, scientific research demonstrated that exposure fluoride in drinking water, lead to a decrease of IQ\textsuperscript{95}. As far as solvents are concerned, exposure to these chemicals during pregnancy has been linked to hyperactivity and anti-social behaviour, as well as psychiatric disorders\textsuperscript{96}.

In addition to these chemicals, other 200 chemicals are known to cause neurotoxic effects; moreover, many additional chemicals have shown neurotoxic properties in laboratory\textsuperscript{97}. The entire picture of neurotoxicity is thus not yet known, and further research is required to fully understand the impact of chemicals on the developing human brain.

Other than neurotoxicants, a large variety of pervasive chemicals, such as dioxin-like compounds, certain flame retardants, PCBs, bisphenol A (BPA), perchlorate, pentachlorophenol and several other common contaminants have been shown to have thyroid-disrupting properties\textsuperscript{98}. Thyroid hormones play a significant role in the development of the CNS, pulmonary system, cardiovascular system, and other organs. Small modifications in thyroid serum levels during pregnancy – particularly during the first trimester - have been associated with cognitive deficits and other damaging effects on neurological outcome. Various studies have shown that hypothyroidism in the mother can result in impaired intellectual development in her children, as well as hearing loss. Perinatal exposure to thyroid-disrupting chemicals such as PCBs has also been associated with poorer neurodevelopment in neonates, toddlers and school-aged children\textsuperscript{99}.

Endocrine-disrupting chemicals (EDCs) are exogenous substances or compounds that cause adverse health effects in the organism by disrupting the endocrine functions. Compared to adults, infants and children are not only exposed to chemical toxins in the environment but may also be exposed indirectly during their intrauterine life\textsuperscript{100}. The foetus can also be exposed to toxic chemicals through the placental cord\textsuperscript{101}. In particular, exposure to endocrine toxic chemical components can impair the hormonal, neurological and immunological development of the foetus\textsuperscript{102}. Studies have demonstrated that foetuses, exposed to EDCs are not only born with congenital abnormalities, but may also experience a wide range of neurological diseases later in life\textsuperscript{103}. This explains why certain adult diseases are the results of prenatal exposure\textsuperscript{104}.

Few studies exist on human exposure to chemical carcinogens during early life, with most concerning animal studies. One such study showed that acute exposure of juvenile animals to several carcinogens

\textsuperscript{92} Grandjean P & Landringer PJ, 2014.  
\textsuperscript{93} Grandjean P & Landringer PJ, 2014.  
\textsuperscript{94} Bouchard, M, et al., 2007; Khan, K, et al., 2012; Lucchini, RG, et al., 2012.  
\textsuperscript{95} Choi, AL, et al., 2012.  
\textsuperscript{96} Janulewicz, PA, 2012.  
\textsuperscript{97} Grandjean P & Landringer PJ, 2006.  
\textsuperscript{98} CHEM Trust, 2017.  
\textsuperscript{99} Grandjean P, et al., 2011.  
\textsuperscript{100} Ünüvar, T., & Büyükgebiz, A., 2012.  
\textsuperscript{101} Ünüvar, T., & Büyükgebiz, A., 2012.  
\textsuperscript{102} Ünüvar, T., & Büyükgebiz, A., 2012.  
\textsuperscript{103} Crinnion WJ, 2009.  
\textsuperscript{104} Barker DJ, 2003.
with the same intensity, showed a greater sensitivity compared to adult animals\textsuperscript{105}. Moreover, certain chemicals, such as benzo[a]pyrene, showed a nine-fold increase in risk for liver cancer when administered to neonatal animals compared to adult animals\textsuperscript{106}.

Bioaccumulation is another important factor to consider. It refers to the accumulation of (possibly toxic) substances at a faster rate than the rate at which the substances are expelled from the body. Children are at particular risk to this process, as they have more years, compared to adults, to accumulate environmental chemicals, such as persistent organic pollutants (POPs), pesticides, and flame retardants. Exposure to these toxic chemicals early in life can lead towards the development of cancer during adult life\textsuperscript{107}.

Maternal exposure to atmospheric contaminants, in particular, can have several negative health consequences on the foetal development, as the risk of low birth weight increases. The timing of maternal exposure is also important, as a developing foetus is more susceptible to exposure during the first trimester. Maternal exposure to pesticide exposure has also shown to contribute to growth retardation\textsuperscript{108}.

The following table provides a non-exhaustive overview of the commonly identified environmental chemical exposures and birth defects.

**Table 2: Commonly identified environmental chemical exposures and birth defects in the developing foetus.**

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Birth Defect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic</td>
<td>Cardiac defects</td>
</tr>
<tr>
<td>Bisphenol A (BPA)</td>
<td>Reproductive system anomalies</td>
</tr>
<tr>
<td>Dioxin</td>
<td>Neural tube defects</td>
</tr>
<tr>
<td></td>
<td>Neurobehavioral problems</td>
</tr>
<tr>
<td></td>
<td>Hypospadias</td>
</tr>
<tr>
<td></td>
<td>Oral clefts</td>
</tr>
<tr>
<td>Lead</td>
<td>Neural tube defects</td>
</tr>
<tr>
<td></td>
<td>Neurobehavioral problems</td>
</tr>
<tr>
<td></td>
<td>Hypospadias</td>
</tr>
<tr>
<td></td>
<td>Oral clefts</td>
</tr>
<tr>
<td>Methylmercury</td>
<td>Neural tube defects</td>
</tr>
<tr>
<td></td>
<td>Neurobehavioral problems</td>
</tr>
<tr>
<td>Particulate matter in air</td>
<td>Vascular defects</td>
</tr>
<tr>
<td>PCBs</td>
<td>Impaired hearing</td>
</tr>
<tr>
<td>Sulphur dioxide</td>
<td>Musculoskeletal defects</td>
</tr>
<tr>
<td></td>
<td>Cardiac defects</td>
</tr>
<tr>
<td>Environmental tobacco smoke</td>
<td>Low birth weight</td>
</tr>
<tr>
<td></td>
<td>ADHD</td>
</tr>
<tr>
<td>Air pollution</td>
<td>Low birth weight</td>
</tr>
<tr>
<td>Pesticides</td>
<td>Low birth weight</td>
</tr>
<tr>
<td></td>
<td>Congenital anomalies</td>
</tr>
</tbody>
</table>

\textit{Source:} Kim H & Cizmadia P, 2010

HELIX is a collaborative project funded through the European Commission 7th Framework Programme. It is intended to exploit new tools and methods for characterisation of early-life exposure to environmental hazards. The ‘exposome’ concept was coined to map the totality of human environmental exposures. The objectives of Project HELIX include measurement of a range of chemical and physical environmental hazards in food, consumer products, water, air, noise and the built environment, pre- and postnatal early-life periods, definition of multiple exposure patterns and individual exposure variability, and quantification of uncertainty in exposure estimates. Six prospective birth cohort studies contribute to HELIX as ‘the only realistic and feasible way to obtain

\textsuperscript{105} Ginsberg, GL, 2003.
\textsuperscript{106} Carpenter DO & Bushkin-Bedient S, 2013.
\textsuperscript{107} Carpenter DO & Bushkin-Bedient S, 2013.
\textsuperscript{108} Kim H. & Cizmadia P., 2010
the comprehensive, longitudinal, human data needed to build this early-life exposome’. The project is intended to lead to major improvements in health risk and impact assessments and thus to improved prevention strategies for vulnerable populations\textsuperscript{109}.

### 2.2 CHILDREN

Children have an increased susceptibility to chemicals in the environment for various reasons. Firstly, children have greater exposure to toxic chemicals in proportion to their bodyweight\textsuperscript{110}. They are constantly growing, breathing in more air, consuming more food, and drinking more water than adults\textsuperscript{111}. Moreover, children have larger respiratory ventilation rate compared to adults. Consequently, they absorb more air pollutants and/or toxic air compounds per body weight\textsuperscript{112}.

Secondly, children’s behaviour is different than adults, resulting in different routes of exposure. For instance, children crawl on the ground where they can be exposed to chemicals present on floors, soils, and household dust. Their hand-to-mouth behaviour also magnifies their exposure\textsuperscript{113}. Furthermore, children’s immature behaviour may lead them to take poor choices regarding their health and safety (e.g. touching caustic chemicals). In addition, they are often not able read warning labels on products thus being exposed to higher risks compared to adults\textsuperscript{114}.

The following table shows the behavioural factors that are likely to affect children’s exposures and the associated developmental windows.

### Table 3: Behavioural factors by age group that can affect children’s exposure to chemicals

<table>
<thead>
<tr>
<th>Age group</th>
<th>Characteristics relevant to oral and dermal exposure</th>
<th>Characteristics relevant to inhalation exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to &lt;3 months</td>
<td>Breastfeeding and bottle feeding. Hand-to-mouth activities</td>
<td>Time spent sleeping/sedentary</td>
</tr>
<tr>
<td>3 to &lt;6 months</td>
<td>Solid food may be introduced. Contact with surfaces increases. Object/hand-to-mouth activities increase</td>
<td>Breathing zone close to the floor</td>
</tr>
<tr>
<td>6 to &lt;12 months</td>
<td>Food consumption expands. Floor mobility increases (surface contact). Children are increasingly likely to mouth non-food items</td>
<td>Development of personal dust clouds</td>
</tr>
<tr>
<td>12 to &lt;24 months</td>
<td>Children consume full range of foods. They participate in increased play activities, are extremely curious and exercise poor judgement. Breastfeeding and bottle feeding cease</td>
<td>Children walk upright, run and climb. They occupy a wider variety of breathing zones and engage in more vigorous activities</td>
</tr>
<tr>
<td>2 to &lt;6 years</td>
<td>Children begin wearing adult-style clothing. Hand-to-mouth activities begin to moderate</td>
<td>Occupancy of outdoor spaces increases</td>
</tr>
<tr>
<td>6 to &lt;11 years</td>
<td>There is decreased oral contact with hands and objects as well as decreased dermal contact with surfaces</td>
<td>Children spend time in school environments and begin playing sports</td>
</tr>
<tr>
<td>11 to &lt;16 years</td>
<td>Smoking may begin. There is an increased rate of food consumption</td>
<td>Increased independence (more time out of home). Workplace exposure can begin</td>
</tr>
<tr>
<td>16 to &lt;21 years</td>
<td>Alcohol or drugs consumption may begin. High rate of food consumption begins</td>
<td>Independent driving begins. Expanded work opportunities</td>
</tr>
</tbody>
</table>


Thirdly, children’s central nervous, immune, reproductive, and digestive systems are still developing and are thus immature. The developing organs are particularly susceptible to toxic aggression, given

\textsuperscript{109} HELIX project, official webpage: http://www.projecthelix.eu/index.php/en
\textsuperscript{110} U.S. National Research Council, 1993.
\textsuperscript{111} Ershow AB & Cantor KP, 1989.
\textsuperscript{112} Bennett WD et al., 1996.
the increased rate of cell division and immaturity of some functional excretion systems. Another consequence of their immature organs and systems is that children’s ability to metabolise and expel toxic chemicals from their body is weaker than adults. Given the above, exposure to toxicants during this sensitive life stage can lead to lifelong irreversible damage.

Finally, children have more time than adults to develop chronic diseases. In fact, research has demonstrated that cancer and many neurological diseases appearing during adult life are the results of early childhood exposure.

These observations are summarised in the following table.

Table 4: Characteristics, exposure and vulnerability to environmental health hazards by developmental stage

<table>
<thead>
<tr>
<th>Developmental stage</th>
<th>Developmental characteristics</th>
<th>Exposure</th>
<th>Vulnerability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preconception</td>
<td>Lack of awareness of gonadal exposure</td>
<td>All environmental exposures</td>
<td>Potential for genotoxicity</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>High calorie intake Permeable placenta</td>
<td>All environmental exposures Ad-hoc diagnostic investigations</td>
<td>Potential for teratogenicity due to embryonic development of various organs and apparatuses</td>
</tr>
<tr>
<td>First three years</td>
<td>Oral exploration Beginning to walk Stereotyped diet</td>
<td>Food (milk and baby foods) Air (indoor) Water Mattress/ carpets/ floor</td>
<td>Potential for damage to brain (synapses) and lungs (developing alveoli) Allergic sensitisation Injuries</td>
</tr>
<tr>
<td>Preschool and school-age child</td>
<td>Growing independence Playground activities</td>
<td>Food (milk, fruit, vegetables) Air (indoor and outdoor)</td>
<td>Potential for damage to brain (specific synapse formation, dendritic trimming) and lungs (volume expansion) Injuries</td>
</tr>
<tr>
<td>Adolescence</td>
<td>Puberty Growth spurt Risk-taking behaviour Youth employment</td>
<td>Food (any) Air (indoor and outdoor) Water Occupational exposure</td>
<td>Potential for damage to brain (continued synapse formation), lungs (volume expansion) and pubertal development Injuries</td>
</tr>
</tbody>
</table>


The table above introduces the concept of ‘windows of susceptibility’, and shows which health effects can be triggered by chemical exposure during a particular period of time. Windows of susceptibility in children are broad, as they span from the preconception period until to the end of adolescence.

The European Environment and Health Strategy, adopted in 2003, includes a strong focus on children as a section of the population with particular susceptibility to environmental agents. Covering the first cycle of the Strategy, the European Environment & Health Action Plan 2004-2010 maintains a focus on concerns related to children. The first cycle aims at understanding the link between environmental factors and (1) childhood respiratory diseases, asthma, allergies; (2) neurodevelopmental disorders; (3) childhood cancer; (4) endocrine-disrupting effects. It also aims at identifying and preventing new health diseases caused by environmental factors.

The items selected for the first cycle include the following:

- European Integrated Environment & Health Monitoring and Response system, which includes:

116 Diamanti-Kandarakis E et al., 2009.
(a) Establishing an EU Biomonitoring Framework, which aims to assess environmental and health linkages insofar as they relate to children;
(b) Pilot projects on dioxins, heavy metals and endocrine disruptors (the choice of the specific pollutants was made on the basis of significant health effects in children)
(c) Developing harmonised environment and health indicators.

- Research on environment and health issues, including:
  (a) Application of research results arising from activities funded under the EU research Framework Programmes and other sources, such as progress in genomics research by the Joint Research Centre (JRC) and the research by the European Science Foundation networks on genetic susceptibility to environmental toxicants and their impacts on human health, with particular attention to the interaction between nutritional, environmental and genetic factors in early human development;
  (b) Annual research meetings and reports organised by the Commission, and research supported by the Policy Interpretation Network on Children’s Health and the Environment which operates in the context of the European Health Forum;
  (c) Development of methodologies to identify exposures and to perform combined exposure analysis of environmental factors connected to particular diseases, and risk assessment which takes account of individual susceptibilities and genetic predisposition;
  (d) Strengthening the research base for the economic valuation of the health impact of policies, measures and technologies, with a particular focus on the environment and children’s health.

- Reducing exposure, including:
  (a) Improvement of air quality (indoors and outdoors), linked to the evidence showing that exposure to environmental smoke causes increased risks of several illnesses in children and reduced foetal growth;
  (b) Adoption of a strategy and measures on heavy metals;
  (c) Studying possible health effects of exposure to electro-magnetic fields;
  (d) Adoption of a thematic strategy on the urban environment, including biomonitoring of children in an urban environment.

The Third WHO International Conference on Children’s Health and the Environment in Busan, Republic of Korea (June 2009), resulted in the Busan Pledge, asking the WHO to facilitate the development of a global plan of action to improve children’s environmental health and to regularly monitor and report on its progress. The Pledge recognised that the activities of the plan should be implemented in close interactive partnerships with all sectors. Five target areas of work are included in the Global Plan of Action, including: (1) data collection and analysis; (2) collaborative research; (3) advocacy; (4) clinical service delivery; and (5) awareness raising and education. Among the more detailed actions listed in the Plan, those related to chemicals include ‘promotion of human biomonitoring and human tissue measurements in order to enable better measurement of children’s exposure to chemicals, as well as urging national and global efforts to clean the air, water and soil of contaminants and to properly manage chemicals in the environment’.

The Danish Chemicals Action Plan for 2010-2013 aims to ensure that no products which can be harmful for human or the environment should be available on the market. The plan consists of two parts: general initiatives, and challenges relating to specific target groups or specific substances and groups of substances. Vulnerable groups are explicitly considered in the context of a number of the listed initiatives. For example, continued efforts in the consumer field will focus more studies on consumer products, including product groups such as toys, cosmetics, hobby products and textiles, as

---

well as examining the overall exposure of specific population groups, such as children. The plan also mentions targeted information campaigns for particularly vulnerable or at-risk groups, as well as institutions and parents. It specifically targets endocrine disruptors and combination effects through knowledge acquisition and information sharing, as well as a voluntary phasing-out of EDCs in medical equipment.

The previous Swedish Action Plan for a Non-toxic Everyday Environment (2011-2014) focused on safeguarding the reproduction of human beings and child health, and this remains the focus for the current plan (2015-2020). The national level measures in the plan include information campaigns on sustainable consumption targeted at pre-school and school pupils. The impact of chemicals on children and young people is listed as one of the main challenges, with the Swedish Chemicals Agency placing considerable importance on a national action plan for endocrine disruptors and a national action plan for allergenic substances during 2015-2020124. The plan includes activities to influence chemicals policy at EU and international level.

The French strategy on endocrine disruptors125 targets the prevention of health risks and the exposure of vulnerable populations, pregnant women and young children. The strategy makes reference to several research projects, with a goal to increase expertise and improve measures to evaluate the dangers and risks of EDCs through a programme of expertise carried out by Anses and ANSM. Based on their conclusions, EDCs are subject to appropriate regulatory measures prioritised at EU level in order to reduce exposure. France strongly promotes the adaptation of EU regulations to the specificities of EDCs. The strategy also envisages educational and information-sharing activities.

Adopted in 2010, the UK Children’s Environment and Health Action Plan (CEHAP) aims to identify a set of indicators that appropriately describes the burden and distribution of hazards and risks of childhood disease and injury due to environmental factors at a sub-national level. One of the indicators is the potential exposure to chemical incidents, defined as ‘an acute event in which there is, or could be, exposure of the public to chemical substances which cause, or have the potential to cause ill health’. It is noted that the impact of such exposure will likely be acute and short-term rather than chronic. The numerator for the indicator is the number of uncontained chemical incidents occurring within the West Midlands between January and December 2007. The source of the information is the Chemical Incident Surveillance System hosted and managed by the CRCE of the HPA. Another indicator is exposure to air pollutants, measured as the annual mean levels of nitrogen oxide (NO\(_2\)) and particles (PM\(_{10}\)) at background locations. It is noted that children living in the more urban/industrial areas experience poorer air quality, and that ambient air pollution is associated with a range of health impacts in children.

### 2.2.1 Neonates and infants

Neonates, i.e. children of less than four weeks old, are especially vulnerable to toxic chemical exposures because of the immaturity of their anatomy and physiology.126 In fact, after delivery, all newborns’ systems and organs are immature – a circumstance that exposes them to higher risks stemming from chemical exposure. In particular, their gastrointestinal tract is more permeable and thus absorbs more toxins compared to older children or adults. Moreover, having a larger respiratory rate, infants are exposed to higher intake of chemical compounds per body weight compared to adults. Infants also need more water and food per body weight than adults. This circumstance increases their exposure to toxic compounds (e.g. pesticides) which are present in food and water. In addition, newborns spend the majority of their time in the same environment (e.g. hospital or home), and are thus constantly exposed to indoor contaminants.128 It is worth noting that vulnerability to chemical

---

124 KEMI, 2014.
126 Sattler B et al., 2012.
exposure through inhalation may be highest during the first six months after birth. Air pollutants may in fact cause a wide range of clinical conditions spanning from asthma to bronchitis, as well as infant mortality due to respiratory diseases. Infants are also extremely sensitive to lead and environmental tobacco smoke.

The research project FACET, originally designed to create a food chemical exposure surveillance system, is intended as a tool for post-market monitoring. The concept for the project originated in an attempt to harmonise monitoring methods and to provide a scientific standardised approach to food chemical exposure assessment in Europe – an area where efforts tended to be orientated towards specific groups of chemicals in isolation. The FACET project draws on scientific expertise in the areas of food additives, flavourings and FCMs, together with expertise in food intake, exposure assessment methodologies and software development. A number of the food categories chosen for the study are relevant to children’s health, e.g. baby foods and fennel tea. Limitations in the amount of available data in certain countries were observed during the project, such as the lack of food consumption data on children under five years, younger adults between 18-25 years and older adults over 65 years.

In a study carried out in the U.S., over 200 toxic chemicals were detected in the umbilical cord blood, including pesticides, chemicals found in food packaging, chemical by-products from burning coal and flame retardants. It is worth taking into account that as infants are delivered in hospitals, they are exposed to chemicals used in nursery and hospital settings, such as polyvinyl chloride (PVC), di 2-ethylhexyl phthalate (DEHP), BPA, phthalates, and parabens. The sections below analyse the chemicals of special concerns for infants.

**Bis (2-ethylhexyl phthalate) (DEHP)**

Bis (2-ethylhexyl phthalate) (DEHP) is a common plasticiser. Its aim is to make plastics more flexible. Medical products used in hospitals which contain DEHP include IV tubing and bags, respiratory equipment, and haemodialysis equipment. Research suggests that exposure of ill infants to DEHP may negatively affect male reproductive tract development and function. As a consequence of these concerns – not specifically limited to medical products - the European Chemicals Agency (ECHA) has recently proposed a restriction on DEHP and other phthalates.

**Bisphenol A (BPA)**

BPA is an organic compound used to make polycarbonate plastic, food can linings and epoxy resins. Exposures to this chemical occur when consuming liquids and canned foods stored in BPA-containing vessels. BPA is an EDC. Additionally, recent evidence shows that BPA has developmental neurotoxic (DNT) properties.

A number of animal studies have associated BPA exposure to neurological risks in infants. Moreover, perinatal exposure to low doses of BPA may increase the risk of developing breast

---

129 Ginsberg G et al., 2004.
133 EWG, 2005.
134 Sattler B, et al., 2012.
135 SCENIHR, 2015
137 Sattler B, et al., 2012.
139 EFSA, 2015;
cancer\textsuperscript{140}. According to recent scientific evidence, newborn rats which have been exposed to low doses of BPA, have developed prostate cancer in adulthood\textsuperscript{141}. Several recent studies also link obesity with BPA exposure\textsuperscript{142}. Currently, the European Food Safety Authority (EFSA) is re-evaluating the potential toxicity of BPA on the immune system in light of new evidence highlighted in a recent publication issued by the Dutch National Institute for Public Health and the Environment (RIVM) which raised concerns about the effects of BPA on the immune system of foetuses and young children\textsuperscript{143}.

**Body care products containing fragrances and parabens**

Body care products such as baby soap, shampoo and lotion usually contain several synthetic chemical compounds. While some of the ingredients such as surfactants and fragrances may have some positive features, they may also cause hazardous health effects to humans.

For instance, fragranced products may contain parabens which have shown to have hormone disrupting properties by mimicking and binding to oestrogen receptors on cells. Exposure to these compounds early in life is linked to an increased risk of breast cancer and reproductive toxicity\textsuperscript{144}.  

### 2.2.2 Toddlers and school-aged children

The term ‘toddler’ refers to children who are learning to walk; it is often used for children aged one to two years, but sometimes also up to three years\textsuperscript{145}. During this life stage, children start moving, crawling, touching and testing, and, as such, they have higher chances of being exposed to toxic chemicals present at home such as pesticides, cleaners or chemical which accumulate in carpet or household dust\textsuperscript{146}. It is worth considering that given their specific exploring and hand-to-mouth behaviour, together with their incapacity to read warning labels, the main danger to which toddlers are exposed is the ingestion of toxic chemicals that may cause permanent damage to their health\textsuperscript{147}.

A recent study reported that a two-year old girl who accidentally ingested endosulphan - a polychlorinated hydrocarbon pesticide used in agriculture – presented with clinic-status epilepticus\textsuperscript{148}. This study also highlighted the importance of considering the relevant framework of the poisoning, as in the case in question it happened in a rural agricultural environment. It is also worth noting that often the socioeconomic status is an indicator of possible unsafe childcare practices which may be the cause of hazardous episodes of poisoning.

Another study reported the case of a male child, aged one year and nine months, who swallowed a computer lithium battery cell. The lithium battery cell is potentially dangerous due to its ability to cause chemical damage to the mucosa and cause early inflammation and oedema, leading to dysphagia and respiratory obstruction\textsuperscript{149}. This study also shows that insufficient supervision of children may increase their risk of exposure and subsequent accidental poisoning\textsuperscript{150}.

In addition to this, toddlers spend a large part of their time at home, making them particularly vulnerable to indoor pollution and increasing the likelihood of exposure to household dust. In particular, house dust is an important route of exposure for many chemical contaminants, with various...
levels of pesticides, PCBs, PAHs, plasticisers (phthalates, phenols), flame retardants, other organic xenobiotics, and inorganic constituents. Among the toxic substances that a toddler is likely to inhale are cleaning products, home improvement supplies, gas stoves and heaters. In addition, as young children breathe rapidly and are smaller, they are more likely to absorb large doses of any chemicals present in the air. Furthermore, at home, toddlers can come into contact with several dangerous household products, such as pesticides, ammonia, chlorine bleach, glue, shoe polish, and gasoline.

### 2.3 ADOLESCENCE

Puberty and adolescence are vulnerable life stages as far the exposure to chemicals is concerned. Although adolescents are able to take more independent choices compared to children, their immature behaviour may increase their exposure to toxic substances such as tobacco and alcohol, substances likely to be abused, and chemicals in some personal care products.

Moreover, during adolescence, all organs and systems are subject to changes and development, a circumstance which make them particularly vulnerable to the exposure of toxic chemicals and especially to carcinogens and EDCs.

Another factor which contributes to higher risks during adolescence is their life expectancy. In fact, adolescents have more time to absorb environmental chemicals, and especially air contaminants. An example is dioxin, a known human carcinogen, which has a half-life of about seven years.

For instance, persistent organic pollutants (POPs), including polychlorinated biphenyls (PCBs), chlorinated pesticides, and brominated flame retardants – which are able to accumulate in the adipose tissue – may explicate their negative effects on human health several years after the initial exposure. Hence, exposures occurring during vulnerable phases such as adolescence may lead towards the development of a wide range of hazardous diseases (e.g. cancer) later in life.

In addition, adolescents tend to increase the consumption of personal care products thus intensifying their exposure to toxic chemicals, such as phthalates, parabens, and phenols. For instance, one study found that the average adult woman uses approximately 12 individual personal care products each day, while the average teenage girl uses 17. In particular, cosmetics, fragrances, and other personal care products are a possible source of human exposure to potential EDCs.

Furthermore, according to a recent study, ‘Reducing Phthalate, Paraben and Phenol Exposure from Personal Care Products in Adolescent Girls: Findings from the HERMOSA Intervention Study’, when teens stop using personal care products, even briefly, levels of these EDCs drop significantly. Scientists took urine samples from 100 teenage participants before and after they used products with lower levels of phthalates, parabens, triclosan and oxybenzone for three days. Even after a brief lapse in exposure to these EDCs, there were substantial differences. Cosmetic preservatives methyl and propyl parabens dropped 44% and 45% respectively. Triclosan, found in soaps and toothpastes, and

---

151 Mitro SD et al., 2016.
153 SCCS, 2011.
154 Mills KL et al., 2014.
157 Flesch-Janys D et al., 1996.
159 Braun JM et al., 2014; Meeker JD et al., 2013.
160 EWG, 2008.
161 Braun JM et al., 2014.
162 Harley KG et al., 2016.
benzophenone-3, used in sunscreen, dropped 33%. Levels of metabolites of diethyl phthalate commonly used in fragrances fell 27%\(^{163}\).

During this phase, adolescents are also likely to be employed – a situation that increases their risks to be exposed to workplace chemicals. It should also be borne in mind that adolescents can also work as entrepreneurs, thus creating their own working environments which do not always comply with health and safety rules. In addition, adolescents may be unaware of hazardous materials to which they might exposed, such as tobacco smoke, solvents, and other cleaning agents\(^{164}\). It has also been noted that more than two million young people are exposed to farm-related chemicals, such as fertilisers and pesticides, some of which are known to be carcinogenic, neurotoxicants and hormone disruptors\(^{165}\).

\(^{163}\) Ibid.
\(^{164}\) Ibid.
3 REPRODUCTIVE HEALTH AND PREGNANT WOMEN

Since the mid-20th century, numerous studies have reported an increasing incidence of human reproductive diseases and a consequent decline in reproductive function worldwide. The following trends, related to changes of the reproductive system, have been described in the literature:

- Data from the U.S. show that the percentage of women who have difficulty in achieving and maintaining pregnancy has increased between 1982 to 2002, and is slightly lower in 2006-2010 (though still higher than in 1995 and earlier). While some of this increase is likely due to people starting families later in life (fertility decreases with age and miscarriage rates increase with age), this does not explain why the sharpest increase in reported infertility between 1982 and 2002 was among younger women.

- In the U.S., UK and Scandinavia, the preterm birth rate has increased by more than 30% since 1981. Since 1990, the percentage of infants born in the U.S. with low birth weight also rose by 16% to 8.1% of births in 2004.

- There is a trend toward earlier onset puberty among American and European girls. Premature puberty can lead to reduced adult height and is also associated with a higher risk of breast cancer and polycystic ovary syndrome. It can also have psychological consequences, such as greater likelihood of engaging in risky behaviours (smoking, unprotected sex, alcohol and drugs).

Given the short time frame, the above described developments cannot be explained by genetic changes alone. Environmental and other non-genetic factors, including nutrition, age of mother and viral diseases are also at play, and the exposure to environmental substances may play a part in the trends observed.

A large body of research exists on the adverse effects of EDCs on the reproductive system. This, together with the consistent detection of endocrine-disrupting residues in human serum, seminal plasma and follicular fluid, has raised concern that environmental exposure to EDCs is affecting human fertility. EDCs may affect the development and functioning of the reproductive system in both sexes, causing infertility, as well as developmental and reproductive disorders in foetuses. As male sexual differentiation is androgen-dependent (and potentially oestrogen-dependent) and female differentiation occurs largely independently of oestrogens and androgens, it is expected that different disorders are seen in males and females as a result of EDC effects.

Many EDCs are known to act as agonists (triggers) of oestrogen receptors, e.g. bisphenol A and alkylphenols, with several antagonising androgen receptors, such as the dicarboximide fungicides. Progesterone receptors are also a potential target for many chlorinated EDCs, such as DDT and derivatives. Other examples of EDCs that have shown to have an effect on the reproductive system are: diethylstilbestrol (DES), tributyltin, phytostrogens, alkylphenolethoxylates, phthalate esters (DEHP, BBP, DiNP, DBP), dioxins, polychlorinated biphenyls, herbicides, lead, cadmium, and manganese.

Experimental studies with rodents have widely studied the adverse effects of EDCs on the reproductive system. These animal studies, which enable the investigator to measure hormone action at various times during development and thus to accurately interpret the relationship between exposure and each of the effects on the endocrine system, indicate that early prenatal and/or perinatal exposure to EDCs can lead to long-term effects on reproduction and development which become evident later.

---

166 Woodruff TJ, 2011.
168 Younglai EV et al., 2002.
169 Diamanti-Kandarakis E et al., 2009.
170 Caserta D, 2008.
even at sexual maturity and/or at adulthood. The identification and characterisation of this ‘early exposure—late effect’ pattern of EDCs represents a challenge for scientists and risk assessors. Additionally, EDCs can have varying effects throughout development because of variations in tissue hormone receptor isoforms and concentrations at different developmental stages.

With regard to the EU legislative framework, the Commission adopted its first Strategy on Endocrine Disruptors in 1999. The EU legislation in force already takes account of endocrine disruptors and, as such, consumers are protected from endocrine disruptors via the authorisation of chemical substances to be used in plant protection products, biocidal products, chemicals falling within the scope of REACH, and cosmetics. However, no formal criteria have been established, internationally or at EU level, to identify substances with endocrine-disrupting properties. For this reason, on 15 June 2016, the EC issued two draft legal acts – one under the Biocidal Products legislation, the other under the Plant Protection Products legislation – which set out the criteria to identify endocrine disruptors. The two draft legal acts containing the criteria now need to be adopted by the Parliament and the Council under the relevant procedures.

The acts were also subject to the feedback mechanism procedure which closed on 28 July 2016. The Commission received 260 public responses to the draft act for plant protection products and 126 responses to the draft act for biocidal products. In particular, the chemical industry denounced the lack of inclusion of potency – the capacity of a substance to induce adverse effects depending on its concentration – as part of these criteria. Nevertheless, if adopted, the EU regulatory system will be a global first in defining scientific criteria for endocrine disruptors in legislation.

The use of certain chemicals such as alkylphenols, some of the phthalate plasticisers, PCBs and the pesticide DDT, in addition to DES, are now prohibited in many countries, as they are considered to have hormone-disrupting properties. In the EU, paragraph 50 of the 7th EAP notes the potential of EDCs to cause adverse effects on health, including children’s development. Efforts must be stepped up to ensure that, by 2020, all relevant substances of very high concern, including those with EDC properties, are placed on the REACH candidate list. According to paragraph 54, the 7th EAP must also ensure that, by 2020, the combination effects of chemicals and safety concerns related to endocrine disruptors are effectively addressed in all relevant EU legislation, and risks to the environment and health associated with the use of hazardous substances, including chemicals in products, are assessed and minimised.

In 1999, the Commission adopted the Communication ‘Community strategy for endocrine disruptors – A range of substances suspected of interfering with the hormone systems of humans and wildlife’. As a short-term action the document indicated that the Commission intended to establish a priority list of substances for further evaluation of their role in endocrine disruption – the so-called ‘ED priority list’. The priority list was meant to be used, inter alia, to identify specific cases of consumer use (e.g. more vulnerable groups of consumers, such as children) for special consideration from a consumer policy point of view. In such cases, insofar as the substances are not covered by the methodology agreed under existing legislation, the Commission would consult the relevant scientific committees for independent scientific advice and consider potential restrictions on use through Community legislative instruments. The possibility of using existing instruments such as Directive 92/59/EEC for short-term emergency action was also mentioned.

It is intended that the priority list of chemicals developed within the EU-Strategy for Endocrine Disruptors

172 Caserta D, 2008.
173 Crain DA et al., 2008.
175 European Commission, 2016, Communication on endocrine disruptors.

Milieu Ltd
Brussels

Study for the strategy for a non-toxic environment of the 7th EAP.
Sub-study c: the protection of vulnerable groups, August 2017/14
Disruptors will be used to prioritise further detailed review of the information. However, it is important that the listings produced are not regarded as final and unchangeable: addition and removal of chemicals may be required in response to either developments in scientific knowledge or changes in chemical usage patterns.

A Communication on the implementation of the Community strategy was adopted in 2001, with a number of Staff Working Documents subsequently produced, the most recent in August 2011\textsuperscript{178}. This last Staff Working Document mentions ongoing large-scale projects in the field of endocrine disruption and food, relevant to vulnerable groups: NEWGENERIS\textsuperscript{179} focusing on the role of exposure to genotoxic substances (including endocrine disruptors) in the development of childhood cancer and immune disorders; PHIME\textsuperscript{180} focusing on public health impact of long-term, low level mixed element exposure in susceptible population strata; NECTAR cluster\textsuperscript{181} (Network for Environment Chemical Toxicants Affecting Reproduction) comprising four projects (and receiving over EUR 10m in EU funding) focusing on the impact of early life exposures to endocrine disrupting substances on foetal testes development and male reproductive disorders in newborns and young adults (DEER\textsuperscript{182}); the impact of foetal exposure to mixtures of endocrine disrupting substances on human reproductive health (CONTAMED\textsuperscript{183}); and the impact of endocrine disrupting substances on female reproductive tissue and consequent effects on conception, maintenance of pregnancy, and hormonal processes that regulate reproduction (REEF).

\subsection{3.1 REPRODUCTIVE HEALTH}

The female reproductive tract depends on specific biological processes that, if altered during critical development periods, can have critical negative effects on women’s health and reproductive system\textsuperscript{184}. Worldwide, women today are mainly affected by the following three reproductive disorders, as causes of infertility or sub-fertility\textsuperscript{185}.

\begin{itemize}
  \item \textit{Polycystic ovary syndrome} (PCOS) can affect between 3\% and 15\% of women of reproductive age. It is the leading cause of sub-fecundity and anovulatory infertility, and women with this disorder are more likely to have gestational diabetes, endometrial cancer, preterm labour, and pre-eclampsia.
  \item \textit{Uterine fibroids} (also termed leiomyomata) are the most common tumour of the female reproductive tract, affecting up to 25-50\% of pre-menopausal women. They are a significant cause of pelvic pain, abnormal uterine bleeding, menorrhagia, infertility and complications of pregnancy, including preterm labour.
  \item \textit{Endometriosis} occurs in 10-15\% of women of reproductive age (15-49 years) and a minimum of 176 million women worldwide, and in up to 50\% of women with infertility and/or chronic pelvic pain. The prevalence of endometriosis is higher in infertile or sub-fertile women than in the general population, and the pelvic pain associated with endometriosis is a major cause of disability and compromised quality of life.
\end{itemize}

In Europe, uterine fibroids and endometriosis are the two most common conditions, affecting an estimated 70\% of women and are the leading causes of female infertility\textsuperscript{186}. While most female reproductive disorders are well described in terms of clinical presentation, histological evaluation of

\begin{itemize}
  \item \textsuperscript{178} Commission Staff Working Paper SEC(2011) 1001 final.
  \item \textsuperscript{179} NEWGENERIS, project summary.
  \item \textsuperscript{180} PHIME, 2011.
  \item \textsuperscript{181} NECTAR, project abstract.
  \item \textsuperscript{182} DEER, webpage, available at: \url{http://www.eu-deer.net/}.
  \item \textsuperscript{183} CONTAMED, project summary.
  \item \textsuperscript{184} Diamanti-Kandarakis \textit{et al.}, 2009.
  \item \textsuperscript{185} UNEP \& WHO, 2013.
  \item \textsuperscript{186} Diamanti-Kandarakis \textit{et al.}, 2009.
\end{itemize}
the involved tissue and diagnostic classification, their causes and the factors influencing them are often not well understood. Environmental factors, including diet, age, exercise habits, sexually transmitted infections, and access to good health care, play a role in a woman’s overall reproductive health and thus could contribute to the abovementioned disorders.\textsuperscript{187}

Research shows that EDCs play a role in the pathogenesis of several female reproductive disorders, including PCOS, aneuploidy, Premature Ovarian Failure (POF), reproductive tract anomalies, uterine fibroids, endometriosis, and ectopic gestation.\textsuperscript{188} In a recent study, researchers determined that 56,700 cases of fibroids among women in Europe were probably due to DDE exposure, and 145,000 cases of endometriosis were probably caused by phthalates.\textsuperscript{189} The researchers arrived at these estimates through studies that looked at typical DDE exposures in women of reproductive age in Europe and the association between DDE levels in the blood and fibroid diagnoses.

The most well-known case, showing the ability of synthetic chemicals to alter reproductive function and health in females, is the case of diethylstilbestrol (DES) (see box below).

Box 4: DES case

In the adult female, the first evidence of endocrine disruption was provided through observations of uncommon vaginal adenocarcinoma in daughters born to women treated with Diethylstilbestrol (DES) during pregnancy. DES is an oestrogenic compound that was prescribed to prevent miscarriages in women until 1971. It was initially given to women at-risk pregnancies, but ultimately it was also prescribed to women with normal pregnancies to make babies ‘healthier’.

Apart from the link between women exposure to DES and genital tract cancers in their babies, other abnormalities have been observed as the daughters have also experienced decreased fertility and increased rates of ectopic pregnancy, increased breast cancer and early menopause.

The DES case shown that the female foetus is susceptible to environmentally induced reproductive abnormalities that certain diseases may occur even decades after the first exposure, and that exposure to DES may lead to several female reproductive disorders.

Sources: Crain et al., 2008; Diamanti-Kandarakis E et al., 2009; Giusti et al, 1995.

Research also shows that endocrine disruptors could cause an increasing variety of reproductive health problems in women, including altered mammary gland development, irregular or longer fertility cycles, and accelerated puberty. These changes indicate a higher risk of later health problems such as breast cancer, changes in lactation, or reduced fertility. EDCs can also have an effect on the development of female reproductive disorders, particularly those occurring during critical windows of susceptibility (in utero, neonatally, in childhood, during puberty, and during adulthood).\textsuperscript{190}

Most of the information on the effects of endocrine disruption on female reproductive health comes from molecular, cellular and animal studies. In addition to DES, these studies have shown that the following EDCs could be linked to female reproductive health problems: BPA, PCBs, dioxins, DDT, DDE and phthalates.\textsuperscript{191} The table below sets out an overview of some of the EDCs that have been shown capable of interfering with the female reproductive system and which are possibly implicated in the development of some gynaecological pathologies.

\textsuperscript{187} Ibid.
\textsuperscript{188} Diamanti-Kandarakis E et al., 2009.
\textsuperscript{189} Hunt PA et al., 2016.
\textsuperscript{190} UNEP & WHO, 2013.
\textsuperscript{191} Bredhult C et al., 2008; Buck Louis GM et al., 2013; UNEP & WHO, 2013; Upson K et al., 2014.
## Table 5: Overview of EDCs, their pathways of exposures, mechanisms of action and observed health impacts in relation to female reproductive health

<table>
<thead>
<tr>
<th>Chemical(s)</th>
<th>Pathways of exposure</th>
<th>Mechanisms of action</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent Organic Pollutants (POPs)</td>
<td></td>
<td>Alteration steroid hormone metabolism/transport, ability to bind with the thyroxin transport protein, transthyretin (TTR), interaction with thyroid hormone receptors, neuroendocrine effects</td>
<td></td>
</tr>
<tr>
<td>Polychlorobiphenyls (PCB)</td>
<td>Food chain (fat-rich food, e.g. milk and derivatives, fatty fish, etc.), living environment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dioxins and 'dioxin-like' PCBs</td>
<td>Food chain (fat-rich food, e.g. milk and derivatives, fatty fish, etc.), living environment</td>
<td>Aryl hydrocarbon receptor interaction leading to altered steroid hormone metabolism and neuroendocrine effects, including on the thyroid</td>
<td></td>
</tr>
<tr>
<td>DDT and metabolites</td>
<td>Food chain (fat-rich food, e.g. milk and derivatives, fatty fish, etc.), living environment and workplaces (in developing countries)</td>
<td>Mainly oestrogenic activity</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Substances used in agricultural and farm animal production</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Organochlorine insecticides (e.g. Lindane)</td>
<td>Food chain (fat-rich food, e.g. milk and derivatives, fatty fish, etc.), living environment, workplaces (mainly in developing countries)</td>
<td>Homeostasis of steroid hormones (oestrogenic and/or anti-androgenic effects, interaction with progesterone receptor)</td>
<td></td>
</tr>
<tr>
<td>Triazoles, Imidazoles</td>
<td>Food chain (agricultural and zootechnical fungicides), living environment and workplaces (agricultural areas)</td>
<td>Inhibition of steroid hormone biosynthesis</td>
<td></td>
</tr>
<tr>
<td>Triazines</td>
<td>Food chain (herbicides), living environment and workplaces (agricultural areas)</td>
<td>Effects on hypothalamo-hypophysis-gonadal axis</td>
<td></td>
</tr>
<tr>
<td>ETU (metabolite of ethylene bisdithiocarbamates, e.g. manebe), benzimidazoles</td>
<td>Food chain (agricultural and zootechnical fungicides), living environment and workplaces (agricultural areas)</td>
<td>Thyreostatic effects</td>
<td></td>
</tr>
<tr>
<td>Industrial products and daily-use products</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonyl-phenols and octyl-phenols</td>
<td>Detergent by-products: food chain (seafood) and consumer products</td>
<td>Oestrogen agonists—oestrogen receptor alpha</td>
<td>Animal models: Uterine abnormalities; reduced fertility</td>
</tr>
<tr>
<td>BPA</td>
<td>Food chain (e.g. plastics in contact with food), consumer products (e.g. dental sealant, plastic additive, etc.)</td>
<td>Oestrogen agonist—oestrogen receptor alpha</td>
<td></td>
</tr>
<tr>
<td>Several phthalates (di-2-ethylhexyl, di-n-butyl, etc.)</td>
<td>Food chain (e.g. plastics in contact with food), consumer products (e.g. PVC, deodorants, adhesives, etc.)</td>
<td>Agonists of pregnane X receptor, effects on steroid hormone biosynthesis</td>
<td></td>
</tr>
<tr>
<td>Polybrominated flame retardants</td>
<td>Food chain (fat-rich food, e.g. milk and derivatives, fatty fish, etc.), living environment, workplaces</td>
<td>Interaction with pregnane X receptor</td>
<td></td>
</tr>
</tbody>
</table>
### Chemical(s) | Pathways of exposure | Mechanisms of action | Observations
--- | --- | --- | ---
Organotins | Food chain (seafood), consumer products (e.g. anti-fouling agents) | Aromatase inhibition | leading to altered steroid and thyroid hormone homeostasis
Perfluorooctane sulphonate | Food chain (bioconcentration in animal tissues), consumer products (e.g. plastics, carpets, materials, etc.) | Alteration hypothalamic-hypophysis-gonadal axis | etc.
Parabens | Main cosmetic, toiletries and pharmaceutical preservatives | Oestrogen agonist—oestrogen receptor alpha and beta | etc.
UV-screen (benzophenone 2, 4-methylbenzylidene camphor, etc.) | Mixture for protection against UV radiation | Oestrogen oestrogen receptor alpha | etc.
Cadmium | Food chain (e.g. refined food as flour, rice, sugar; seafood), cigarette smoking | Oestrogen oestrogen receptor alpha | Animal models: Perturbed oestrous cycles; Reduced number of differentiating germ cells and the size of the ovary in 16.5-day embryos; Tendency towards delayed timing of vaginal opening; Earlier onset of vaginal opening; Increased the epithelial area and the number of terminal end buds in the mammary glands and decreased the number of alveolar buds
Phytoestrogens | Food chain (e.g. vegetables, soy-based food), consumer products (e.g. cosmetics) | SERMs, high affinity for oestrogen receptor beta | Animal models: Decreased pituitary responsiveness to GnRH; increased the size of sexually dimorphic nucleus of the preoptic area; increased/decreased the weight of uterus; decreased the weight of ovaries; reduced serum oestradiol levels; reduced serum progesterone levels; irregular oestrous cycle; histopathological changes in the ovaries and uterus; induced permanent oestrous; decreased the age of vaginal opening
| Isoflavones, lignans, etc. | etc. | etc. | etc.

**Source:** Adapted from Caserta, D., 2008, and UNEP & WHO, 2013

In 2016, Hunt et al estimated the cost of female reproductive disorders and diseases as a result of exposure to ECDs. The study was based on epidemiological evidence, which, in Europe, is mostly available for diphenyldichloroethene (DDE)-attributable fibroids and phthalate-attributable endometriosis in Europe. Across the EU, attributable cases were estimated to be 56,700 and 145,000 women, respectively. The authors concluded that EDCs (DDE and phthalates) contribute substantially to the almost EUR 1.5 billion annual cost of these reproductive diseases. The estimated cost for fibroids was EUR 163 million, while the costs related to endometriosis accounted for EUR 1.25 billion. Cost estimation was carried out from a societal perspective and included direct costs (e.g., treatment costs) and indirect costs, such as productivity loss. Other health problems that could be caused by the conditions, such as infertility, cancer and autoimmune disorders, were not factored in,

---

leading researchers to conclude that the costs are probably even greater.

### 3.2 PREGNANCY

During pregnancy women are particularly vulnerable to chemical exposure\(^\text{193}\). This is due to the numerous physiological changes occurring during this unique stage, such as weight gain and increases in blood and plasma volume, both of which can influence chemicals absorption and thus lead to a greater exposure to toxins\(^\text{194}\). Behavioural changes, such as diet modification (e.g., quantity and food type), may also influence the degree of chemical exposure during pregnancy\(^\text{195}\). For instance, according to scientific evidence there is an inverse relationship between weight gain during pregnancy and levels of POPs in pregnant women\(^\text{196}\). Certain behaviours, such as smoking, may also influence chemicals body burden in pregnant women thus triggering adverse health effects for the foetus\(^\text{197}\). In particular, a recent study demonstrated that drinking alcohol or smoking during pregnancy can lead to the development of the attention deficit hyperactivity disorder (ADHD) in children\(^\text{198}\).

Avoiding toxic exposure during this vulnerable stage is particularly difficult for women, as chemicals are found in everyday products. Food, for instance, can contain DDT and PVC, which can accumulate in adipose tissues of pregnant women. They are also exposed to the chemicals contained in cosmetics/personal care products, such as sunscreens, cosmetics, fragrances, shower gels and hairsprays\(^\text{199}\), as well as to some medicines, that are linked to adverse health outcomes. A recent Spanish birth cohort study found that mothers using acetaminophen (an over-the-counter medication widely used by pregnant women as an antipyretic and analgesic) were more likely to give birth to boys with autism\(^\text{200}\).

It is also worth noting that, according to scientific research, pregnant women can be exposed to multiple chemicals at one time. These chemicals may lead to severe health outcomes for both the mother and the child. In particular, exposure to perchlorate, PCBs, polybrominated diphenyl ethers (PBDEs), and triclosan can lead to maternal thyroid hormone disruption, while exposure to mercury, lead and PCBs can damage the developing brain\(^\text{201}\).

Significant evidence exists to consider EDC exposure as a risk factor for women's fertility and fecundity, as well as for the trans-generational transfer of undesirable, potentially toxic compounds\(^\text{202}\). The disorders stemming from EDC exposure include disorders of the ovary: aneuploidy\(^\text{203}\); PCOS\(^\text{204}\); endometriosis\(^\text{205}\) and altered cyclicity\(^\text{206}\); disorders of the uterus: uterine fibroids\(^\text{207}\); disorders of placental function and adverse pregnancy outcome: early pregnancy loss, recurring abortion, foetal growth restriction\(^\text{208}\); disorders of the breast: breast cancer, reduced duration of lactation\(^\text{209}\) and, finally, the timing of puberty\(^\text{210}\).

---

\(^{193}\) Woodruff TJ et al., 2011.
\(^{195}\) Mirel LB et al., 2009.
\(^{196}\) Bradman A et al., 2006.
\(^{198}\) NHS choices, webpage, 2016.
\(^{199}\) Wittorsch RJ & Thomas JA, 2010.
\(^{200}\) Avella-Garcia BC et al., 2016.
\(^{201}\) National Research Council, 2008.
\(^{202}\) Caserta D et al., 2011.
\(^{203}\) Crain DA et al., 2008.
\(^{204}\) Takeuchi T et al., 2004.
\(^{205}\) Cobellis L et al., 2003.
\(^{206}\) Lu LJ et al., 2000.
\(^{207}\) McLachlan JA et al., 2006.
\(^{208}\) Chiaffarino F et al., 2006.
\(^{209}\) Crain DA et al., 2008.
\(^{210}\) Krstevka-Kostantinove M et al., 2001.
Pregnant women can be particularly vulnerable to toxicants absorbed through the skin due to the increased vascularity and vasodilatation associated with pregnancy. In fact, chemicals used in cosmetics and personal-care products have been shown to have endocrine-disrupting properties. Ethanolamine compounds, commonly found in shampoos, soaps and facial cleaners, have been demonstrated to be carcinogenic; exposure to synthetic ‘fragrances’ has been shown to affect the CNS; heavy metals like lead, arsenic and mercury that can be found in personal care products including lipstick, whitening toothpaste and nail polish can also cause various adverse health effects. Note that the risk assessments carried out in the context of the Cosmetics Regulation concerning the use of substances classified as CMR 1A and 1B are supposed to take into account the exposure to those substances of vulnerable population groups, such as pregnant and breast-feeding women, as well as children.

An analysis of National Health and Nutrition Examination Survey data from 2003–2004 found that virtually every pregnant woman in the U.S. is exposed to at least 43 different chemicals. As recalled in paragraph 2.1, prenatal exposure is linked to a range of adverse health effects which can affect the neurological and reproductive system of the child later in life. For instance, prenatal exposure to certain pesticides can increase the risks of developing cancer during childhood. It was also observed from the French ELFE study that pregnant women are particularly exposed to phthalates, and findings from the South Korean MOCEH study suggested that prenatal exposure to phthalates may cause neurologic diseases on infants.

The FLEHS study demonstrated that lead, arsenic, and thallium are transported to the foetus from the mother. Moreover, prenatal exposure to these chemicals can cause serious adverse health effects on newborns. The MOCEH study showed that the higher the exposure to lead and cadmium s during pregnancy and the lower the children scored on neurodevelopment. The Norwegian MoBa cohort study reported a negative association between maternal exposure to mercury and birth weight. The Japanese Tohoku HBM study also demonstrated the existence of link between maternal exposure to mercury, and motor deficits in infants.

All these studies showed the importance of monitoring chemical levels in pregnant women in order to reduce risks of developing hazardous health disorders in newborns.

211 ATSDR, 2014.
213 Woodruff TJ et al., 2011.
214 Sutton P et al., 2011.
215 Zeman FA et al., 2013.
216 Kim Y et al., 2011.
217 Baeyens W et al., 2014.
218 Kim Y et al., 2013.
219 Vejrup K et al., 2014.
220 Suzuki K et al., 2010.
4 THE ELDERLY AND AN AGEING SOCIETY

The elderly are vulnerable to chemical exposure due to the ageing process, which imposes both physiological and metabolic limitations. Their weakened nervous system limits their ability to absorb or eliminate toxic substances from their bodies. Furthermore, decreased liver and kidney function increases the likelihood of absorbing toxic substances and thus triggering psychiatric and neurological disorders.

As the life expectancy has drastically raised in Europe, a higher percentage of the population is expected to face higher risks stemming from chemical exposure. It is also worth considering that, if concurred to certain medical conditions, chemical exposure can have particular negative effects on the elderly’s health. Human biomonitoring programmes have shown that certain metals appear to accumulate in the elderly throughout their lives. For instance, the FLEHS study showed that the highest levels of mercury were found in elderly’s blood; the PROBE study also demonstrated that lead and palladium concentrations in blood intensified with age. The Slovenian HBM study found that the blood cadmium, blood lead, and hair mercury levels were highest among older women compared to other adults. Apart from metals, urinary levels of phthalates also appeared to be higher among the elderly population.

Furthermore, a scientific HBM study from Australia observed that PFOS concentration was higher in the portion of the population aged 60 or older. These findings suggest that the elderly population is highly vulnerable to chemicals as they have more time to absorb toxic compounds during their life which are known to cause a wide range of negative effects on human health. It is therefore paramount to monitor chemical levels within this subgroup of the population through human biomonitoring programmes.

A significant problem among this category of the population is accidental poisoning, either through medication or toxic chemicals. The following factors are likely to increase the risks of swallowing hazardous compounds:

- The elderly’s olfactory and gustatory perception is impaired. This problem is particularly relevant among the elderly over 80 years old.
- The elderly’s impaired vision makes it difficult for them to read warnings and ultimately enhance the risks of ingesting hazardous chemicals.
- A study taking into account 45 older adults showed that 55% of respondents reported motor difficulties in handling products, 42% reported memory difficulties, 40% perceptual difficulties, and 29% difficulties with symbol comprehension and text comprehension. All these circumstances may increase the risks for elderly of being exposed to toxic chemicals.
- Unlike young children, the elderly are often alone and under no supervision for prolonged periods of time, which makes difficult to intervene promptly in case of accidental ingestion.
- In case of accidental ingestion of toxic chemicals, the elderly may not seek for help immediately, for reasons of shame or uncertainty.
- When disoriented - due to illnesses or medications - elderly often lack the ability to distinguish.

---

221 Wagner W et al., 2008.
222 Ibid.
223 Croes K et al., 2014.
224 Alimonti A et al., 2011.
225 Lee KM et al., 2011.
226 Toms LML et al., 2009.
227 SCCS, 2011.
228 Doty RL et al. 1984.
229 Parsons SO et al. 1999.
230 Mayhorn CB et al., 2004.
231 SCCS, 2011.
232 SCCS, 2011.
between hazardous and not hazardous products.\textsuperscript{233}

In addition, the elderly often spend the majority of their time indoors, which is the main site contributing to exposure to air pollutants\textsuperscript{234}. Furthermore, inadequate ventilation in elderly care centres further increases the degree of absorption of toxic substances\textsuperscript{235}.  

\textsuperscript{234} Shusterman D \textit{et al}., 2003.  
\textsuperscript{235} Almeida-Silva M \textit{et al}., 2014.
5 OCCUPATIONAL GROUPS

Several substances used at the workplace can have toxic properties and are thus capable of causing lifelong damages to workers. Moreover, these substances may not always be easy to identify. Toxic compounds can be found in paints and glues, cleaning fluids, as well as in food being left exposed at the workplace. For instance, according to recent scientific evidence, exposure to flour dust may cause adverse health outcomes ranging from conjunctivitis to baker's asthma\textsuperscript{236}.

In order to protect workers from these risks, the European legislation sets out health and safety measures, and especially rules to limit the exposure to hazardous chemicals at the workplace\textsuperscript{237}.

Moreover, in the EU, supplied chemicals must have accompanying safety data sheets, which include information about the properties of the substance, its hazards, instructions for handling, as well as exposure control measures\textsuperscript{238}. However, many harmful substances are process-generated materials, and as such can’t require safety data sheets. For example, stone dust contains respirable crystalline silica, which can cause irreversible effects on workers’ lungs, while wood dust can cause asthma. Both of these types of dust can also cause cancer\textsuperscript{239}.

It is worth noting that certain categories of workers are intrinsically more vulnerable than others, such as migrant workers, young workers and those with certain medical conditions. Other workers, instead, can be vulnerable only during specific period of time, for instance when conducting work activities (e.g. maintenance work) which expose them to particularly hazardous chemicals\textsuperscript{240}.

Among the reasons which make certain workers more vulnerable to the risks of chemical exposure there are\textsuperscript{241}:

- constant exposure to hazardous chemicals in certain occupation;
- language barriers which may hamper access to health and safety information;
- Poor working conditions which increase the likelihood to be exposed to toxic chemicals;
- conduction of high-risk, non-routine activities involving chemical exposure;
- exposure to multiple lower level exposures;
- Lack of training or experience on safety standards;
- Lack of access to preventative services;
- Working at client premises with unregulated conditions.

The most significant route of exposure is inhalation, i.e. breathing air contaminated with dangerous substances. Dangerous substances can become airborne through several ways. For instance, liquid can become easily vapour if the temperature at the workplace is high. Moreover, solvents can quickly contaminate the working environment, if the latter is not sufficiently ventilated. Others examples according to which indoor air might be contaminated include: spray applications or fusion of metals at elevated temperatures\textsuperscript{242}.

Dermal (skin) exposure to hazardous chemicals is another common route of exposure at the workplace, either as a result of direct effects on the skin, or through the absorption of chemicals into the body. Dermal exposure often happens via direct contact to contaminated items, surfaces or objects. Jobs where the risks of dermal exposure are higher including degreasers, painters, hairdressers, and

\textsuperscript{236} Stobnicka A & Górny RL, 2015.
\textsuperscript{237} Council Directive 98/24/EC.
\textsuperscript{238} For more information, see: REACH Regulation (EC) No 1907/2006.
\textsuperscript{239} IARC, 1995.
\textsuperscript{240} EU-OSHA, oshwiki.
\textsuperscript{241} EU-OSHA, oshwiki.
\textsuperscript{242} Keen C, 2016a.
fruit pickers. The degree of exposure may vary according to the circumstances. Well known chemicals that are capable of being absorbed through the skin are mercury, isocyanates, polychlorinated biphenyls (PCBs), acrylates, and nicotine.

Work-related ingestion of hazardous substances usually occurs in one of the following ways:

- ingestion of contaminated food or beverages;
- (contamination via hand-to-mouth or object-to-mouth contact;
- contaminants which accumulate around the mouth and into the oral cavity.

Substance groups which are of particular concern as far as ingestion at the workplace is concerned are metals, pesticides, pharmaceuticals, infectious agents, radionuclides, as well as certain molecular weight materials which can cause allergenic reactions. Some of the substances are also suspected to be carcinogens.

**Secondary Exposure**

Secondary exposure refers to situations where work activities may cause exposure to toxic compounds to people which are not directly employed. For instance, secondary exposure happens when workers inadvertently transfer toxic compounds outside of their workplace. Secondary exposure is of a particular concern insofar it can increase hazardous exposure for the general population, and especially for certain groups which are already intrinsically vulnerable.

One of the most common cases of secondary exposure happen when workers bring contaminated clothing home. This situation has the potential to extend exposure to toxic compounds to vulnerable groups such as young children, elderly and pregnant women.

Scientific findings demonstrate that workers who were in contact with asbestos and brought contaminated clothing at home, increased the risks for their families of contracting asbestos related cancer. The same situation, but with different health effects, has been registered in the case of workers exposed to lead who brought contaminated food or objects into their homes. Farmers exposed to pesticides created secondary exposure and thus triggering a wide range of negative health effects for their families through overspray or spray drift.

The sections below analyse the categories of workers that need special attention and protection.

**Migrant workers**

According to the International Labour Organisation (ILO) migrant workers are particularly vulnerable to chemicals for a variety of reasons:

- Higher risks: migrant workers usually work in poorer conditions than local workers. For instance, migrant workers are often employed in higher risk sectors, such as farming and construction. These jobs involve working with dangerous substances, such as pesticides or silica dust, that further increase the risk of toxic exposure.
- Language barriers: migrant workers usually work in environments where the language employed is not their native one; this circumstance creates language barriers which can significantly hamper.

---

244 Cherrie JW et al., 2006.
245 Keen C, 2016b.
246 Keen C, 2016b.
247 Thompson B et al., 2003.
248 Keen C, 2016b.
communication of written and verbal occupational safety and health (OSH) information. If migrant workers are not in the position to understand safety regulations, they will likely receive higher exposure to toxic chemicals.\textsuperscript{251}

- Cultural issues: workers moving to more developed countries may not be used to different health and safety standards. This may result in a different culturally based risk perception which may ultimately increase their exposure to dangerous substances.\textsuperscript{252}

- Longer working hours and a tendency to regularly work overtime: the longer the time workers spend with dangerous substances, the higher their chances of being exposed to toxic substances.\textsuperscript{253}

**Young workers**

According to the ILO, young workers are those within the age group of 15 to 24 years.\textsuperscript{254} This subgroup thus includes adolescents. All of the categories included in this subgroup have one thing in common: they are all relatively immature and lack experience in the workplace, which means they may not always be fully aware of OSH regulations and the risks around them. As a result, young workers are 50% more likely to experience accidents at work.\textsuperscript{255} In order to protect this category, which is uniquely vulnerable to chemical exposure, specific EU legislation was adopted.\textsuperscript{256}

The reasons for the increased risk among young people when working with dangerous substances are given below:

- Unique vulnerability: during this particular stage young people are still developing their mental and physical conditions.\textsuperscript{257}

- Increased susceptibility: data indicate that allergic reactions (such as asthma) and work-related skin disorders are higher among young workers. Moreover, lead exposure may be especially harmful to young people, given its effects on the development of the nervous system.\textsuperscript{258}

- Employment in high-risk sectors: young workers are often employed in temporary or precarious jobs and in industries that are acknowledged to be more hazardous than others, such as agriculture, construction, transport, and hairdressing. For instance, young workers tend to be employed on farms, where they could be exposed to toxic substances such as pesticides. Young workers are also employed in low-skilled manufacturing jobs or the construction sector, with the potential for exposure to a range of dangerous substances.\textsuperscript{259}

- Lack of awareness of health and safety issues: young people lack experience in the workplace and are often unfamiliar with safety standards. This leads them to take greater risks than older people, magnifying their exposure to chemical substances. The risks stemming from toxic exposure are also exacerbated in situations where young workers receive little or no appropriate supervision or training.\textsuperscript{260}

**Maintenance workers**

Maintenance is defined as a ‘combination of all technical, administrative and managerial actions during the life cycle of an item intended to retain it in, or restore it to, a state in which it can perform the required function’\textsuperscript{261}. Since maintenance operations take place in various sectors, from the chemical industry to manufacturing and agriculture, maintenance workers may come into contact with

\begin{footnotesize}
\begin{itemize}
\item \textsuperscript{251} Guldenmund FW \textit{et al.}, 2010.
\item \textsuperscript{252} Renn O & Rohrmann B, 2000.
\item \textsuperscript{253} ILO, 2004.
\item \textsuperscript{254} ILO, 2012.
\item \textsuperscript{255} EU-OSHA, webpage ‘young workers’.
\item \textsuperscript{256} Council Directive 94/33/EC.
\item \textsuperscript{257} See Chapter 3.
\item \textsuperscript{258} EU-OSHA, 2016.
\item \textsuperscript{259} EU-OSHA, 2007.
\item \textsuperscript{260} EU-OSHA, 2016.
\end{itemize}
\end{footnotesize}
wide range of dangerous substances. Generally, the following three major sources of exposure can be identified:

- Exposure through products that need to be used in certain operations (e.g. detergents, solvents, acids, etc.)\(^{262}\);
- Exposure via contact with substances that are generated by the products during the maintenance operations, such as welding fumes, diesel exhaust, and dust\(^{263}\);
- Exposure through compounds that may be encountered during the maintenance process, such as lubricants and hydraulic fluids, dusts, ammonia, poisonous gases, etc.\(^{264}\).

As a consequence, maintenance workers may be exposed to all of the substances that have been identified as ‘emerging chemical risks’ by EU-OSHA: ultrafine particles, diesel exhaust, nanoparticles, man-made mineral fibers, isocyanates, epoxy resins silica and wood dust\(^{265}\). Among the maintenance activities which involve exposure to hazardous substances are\(^{266}\):

- Cleaning activities (exposure to detergents and acids);
- Metal degreasing (exposure to solvents);
- Painting (exposure to dust, ammonia, solvents and detergents);
- Welding (exposure to gases);
- Vehicle repair activities (exposure to solvents, isocyanates, and polyester resin);
- Maintenance of façades of buildings (exposure to acids, solvents, lyes);
- Maintenance of refrigeration and cooling systems (exposure to acids, solvents, lyes);
- Maintenance of swimming pools (exposure to toxic chlorine gas);
- Road maintenance (exposure to asphalt fumes, and traffic exhaust);
- Maintenance of diesel motor exhaust (exposure of gases and particles).

As the toxic substances to which a maintenance worker may be exposed are various, so too are the health effects associated with such exposures. For instance, skin contact with acids or dyes may lead to acute irritation or burns; detergents, epoxy resins, isocyanates, cement, oils and greases may cause irritant contact dermatitis (eczema). Inhalation of chlorine or ammonia may result in acute irritation of the airways. Wood dust exposure may also lead to bronchitis\(^{267}\); exposure to isocyanates may cause asthma\(^{268}\). Exposure to silica and diesel motor exhaust may contribute to the development of lung cancer\(^{269}\). Additionally, the inhalation of hazardous substances in maintenance activities might lead other additional health effects. For instance, exposure to solvents may lead to neurological diseases, such as chronic toxic encephalopathy\(^{270}\).

Given the several routes of exposure, as well as the multiple substances that they may encounter, maintenance workers are a subcategory of the population which is particularly vulnerable to chemicals.

**New workers**

New workers are also particularly sensitive to chemical exposure. The reasons of their highly vulnerability is explained below:

---

\(^{262}\) EU-OSHA, 2012.

\(^{263}\) EU-OSHA, 2012.

\(^{264}\) EU-OSHA, 2012.

\(^{265}\) EU-OSHA, 2009.

\(^{266}\) EU-OSHA, 2012.

\(^{267}\) EU-OSHA, 2009.


\(^{269}\) Tjoe Nij E, 2003.

\(^{270}\) Meyer-Baron M, 2008.
- Lack of training: new workers are often not sufficiently equipped with the necessary information about the possible routes of exposure through which toxic for the substances may enter in their body, as well as the associated negative health consequences. New workers also lack of the adequate level of supervision; this circumstance further increases their risks of being exposed to hazardous compounds.\textsuperscript{271}

- Increased susceptibility: new workers may experience symptoms at levels of exposure which do not cause any effects to more established workers.\textsuperscript{272}

\textsuperscript{271} EU-OSHA, oshwiki.
\textsuperscript{272} EU-OSHA, oshwiki.
The following chapter sets out some of the other vulnerable groups that should be considered when putting in place protection measures against chemical exposure.

**Lower socioeconomic groups**

According to research in the U.S., some communities (e.g., low income, minority, indigenous groups) bear multiple sources of chemical exposure associated with where they live, work, or play which can increase their risk of adverse health outcomes. For instance, some studies have found that low-income or indigenous populations often live in areas where the concentration of pollution is higher (e.g., near high-traffic roadways, industrial site, hazardous waste site) than the average population, which increases their risk of being exposed to hazardous chemicals. Hence, factors such as level of income, and/or occupation) together with lifestyle may have indirect effects on the degree of exposure to toxic compounds and consequently on health status. It is also worth noting that people with low incomes may not have the same level of education or access to health care as those in higher socioeconomic groups.

These results are also confirmed by the findings of the Environmental Justice Movement, according to which chemical concentrations in the body are higher where people face hazards in their social environments. The Environmental Justice Movement emerged in the 1980s and believes that all citizens, regardless of their socioeconomic status, should equally share burdens of environmental hazardous chemicals. The major focus of the Environmental Justice Movement is individuals in lower socioeconomic groups, as, according to research, they are the category of the population which are particularly vulnerable to environmental toxicants. In fact, certain diseases – such as cancer, asthma and diabetes - appear more within the population having a low socioeconomic status. Evidence also suggests that there is social disparity concerning certain chemicals, with higher exposure to lead, pesticides and polychlorinated biphenyls identified in specific sub-groups of the population.

A recent study has further investigated the link between socioeconomic status and chemical concentrations in the body, finding that chemicals concentration affects the whole population across the poverty spectrum, and not just those from economically deprived backgrounds as previously thought. These findings also contradict the environmental justice hypothesis, which states that the lower is the socioeconomic status, the higher is the concentration of chemicals in the body. Instead, this study shows that lifestyle and diet are the factors which play a major role as far the accumulation of chemicals in the body is concerned.

While this study should be taken into account, recent research also shows link between two chemicals and socioeconomic status. Poor people are in fact more likely to accumulate higher levels of BPA, while wealthier people are more likely to show concentration of perfluorinated compounds (PFCs). BPA exposure is particularly harmful for the human body, as it may lead to behavioural impacts, developmental changes that increase the risk of mammary and prostate tumours, decreased sperm count and increased risk of Type 2 diabetes and obesity. These results also reflect the findings...
published in a study issued in 2007\textsuperscript{283}.

**People with medical conditions and/or disabilities**

People with medical conditions, or those with a disability, may also have particular susceptibilities to chemical exposure. In fact, certain medical conditions can make people more vulnerable to hazardous chemical exposure.

For instance, atopic people have higher risks of developing respiratory diseases after inhaling irritant materials\textsuperscript{284}. People suffering from cardiovascular diseases are more vulnerable to particles\textsuperscript{285}, and people having respiratory diseases are more susceptible to several air pollutants\textsuperscript{286}.

Furthermore, medical conditions may result from occupational exposure. For example, certain substances can cause sensitisation if individuals are constant exposed to them. The skin or respiratory system are often affected by such substances which can trigger dermatitis, asthma and allergic alveolitis. Respiratory sensitization, in few cases, can also cause death\textsuperscript{287}.

Lastly, transient medical conditions, which are medical conditions that are not permanent and are not necessarily caused by work, can make affected workers more vulnerable. For instance, workers with damaged skin are more susceptible to dermal exposure. Through the damaged skin chemicals can easily enter into the body and circulate into the blood stream thus causing adverse health effects on human health\textsuperscript{288}.

\textsuperscript{283} Calafat AM \textit{et al}., 2008.
\textsuperscript{284} Droste J \textit{et al}., 2003.
\textsuperscript{285} WHO, 2003b.
\textsuperscript{286} WHO, 2005.
\textsuperscript{287} EU-OSHA, oshwiki.
\textsuperscript{288} EU-OSHA, oshwiki.
7 REGULATING AND ASSESSING CHEMICAL EXPOSURE OF VULNERABLE POPULATIONS

The protection of vulnerable groups from the health risks of chemical exposure has been addressed at the EU and global level through a variety of initiatives and actions. The following sections set out the state of play with regard to the current legislative framework and assessment methods, such as risk assessment and biomonitoring.

7.1 LEGISLATIVE FRAMEWORK

7.1.1 Regulation of chemicals and the exposure of vulnerable groups

Chemicals are regulated through a dense network of legislation at a number of levels. At the international level, chemicals are primarily addressed by the Strategic Approach to International Chemicals Management, which defines a policy framework to foster sound global management of chemicals; the Globally Harmonised System of Classification and Labelling of Chemicals, which provides for uniform physical, environmental, and health and safety information on hazardous chemical substances; the Stockholm Convention, a global treaty to protect human health and the environment from persistent organic pollutants (POPs); the Rotterdam Convention, a multilateral treaty promoting shared responsibility and cooperative efforts among parties in the international trade of certain hazardous chemicals in order to protect human health and the environment from potential harm; the Basel Convention, an international treaty to reduce the movements of hazardous waste between nations, and specifically to prevent transfer of hazardous waste from developed to less developed countries; and the Montreal Protocol, which was designed to reduce the production and consumption of ozone-depleting substances.

The EU has compiled a comprehensive legal and regulatory framework to ensure a high level of protection for human health and the environment, while preventing barriers to trade. EU chemicals legislation applies to all industry sectors dealing with chemicals and along the entire supply chain, making companies responsible for the safety of chemicals they place on the market. The legislation put in place consists of rules governing the marketing and use of chemical products, major accidents and exports of dangerous substances, as well as restrictions on marketing of specific hazardous substances.

Substantial progress has been achieved in the management of chemical substances in Europe since 2006, when the EU adopted its flagship regulation concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). The Classification, Labelling and Packaging Regulation also ensures that the hazards presented by chemicals are clearly communicated to workers and consumers in the EU through classification and labelling of chemicals. EU chemicals legislation is spearheaded by REACH and CLP, which address chemicals horizontally. Particular groups of chemicals, such as biocides, pesticides, pharmaceuticals or cosmetics, are regulated through

---

295 European Parliament, webpage, EU Fact Sheets, Chemicals.
specific pieces of legislation\textsuperscript{298}. No single comprehensive legal framework exists that specifically addresses the protection of vulnerable groups from the risks of chemical exposure. Instead, a range of provisions, spread across different legal sources, refer to the importance of protecting vulnerable people from chemical exposure. Most of these provisions stress the need to protect vulnerable groups in a general way, such as recital 12 of the REACH Regulation, or recital 8 of the Plant Protection Products Regulation\textsuperscript{299}. Other provisions are more specific, and require concrete actions to be taken, such as Article 33 of the CLP Regulation which establishes that ‘packaging containing a hazardous substance or a mixture supplied to the general public shall not have either a shape or design likely to attract or arouse the active curiosity of children’\textsuperscript{300}, or article 6 of Council Directive 92/85/EEC on the introduction of measures to encourage improvements in the safety and health at work of pregnant workers and workers who have recently given birth or are breastfeeding, which prevents pregnant and breastfeeding workers to be obliged to perform duties for which the assessment has revealed a risk of exposure to toxic chemicals\textsuperscript{301}.

Other than these, often vague, references to vulnerable groups included in chemicals legislation, there is no clear definition of the groups in society that require specific attention and/or protection. At international level, the WHO uses the following definition for vulnerable groups in relation to chemicals\textsuperscript{302}:

**Box 5: WHO Definition of ‘vulnerable groups’ in relation to chemical exposure**

'Susceptible subpopulations exist in all groups of individuals. Such susceptible subpopulations may have a greater inherent risk of suffering adverse health effects from a chemical incident, for example, because:

- their exposure thresholds for health effects are lower;
- they receive a relatively high exposure;
- their mobility is reduced or their ability to protect themselves from exposure is reduced.

Some common examples of populations that must be considered when evaluating population susceptibility are children, pregnant women, elderly persons, hospital patients and people with low socioeconomic status. The actual list will vary by location and by toxic end-point to be considered.'

While this definition offers a strong basis for describing those population groups that are particularly vulnerable to chemical exposure, it does not encompass all groups identified in this study. For example, women of childbearing age are not covered by the WHO definition. Secondly, the definition does not refer to specific windows of vulnerability, which are especially important when considering the vulnerability of the foetus and children.

At EU level, specific definitions of vulnerable groups in relation to chemical exposure have been defined in two regulations: The Plant Protection Products Regulation\textsuperscript{303} and the Biocidal Products Regulation\textsuperscript{304}. Again, while these definitions offer a good basis, they do not cover all vulnerable groups identified by the literature review conducted as part of sub-study c.

**Box 6: EU legislation definition of ‘vulnerable groups’ in relation to chemical exposure**

**Article 3 of the Plant Protection Products Regulation:**

\textsuperscript{298} For more information, see Table 2 below.
\textsuperscript{299} More information is available in Table 2 below.
\textsuperscript{300} CLP Regulation (EC) N0 1272/2008.
\textsuperscript{301} Council Directive 92/85/EEC of 19 October 1992 on the introduction of measures to encourage improvements in the safety and health at work of pregnant workers and workers who have recently given birth or are breastfeeding.
\textsuperscript{302} WHO, 2009.
\textsuperscript{303} Regulation (EC) No 1107/2009 concerning the placing of plant protection products on the market.
\textsuperscript{304} Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products.
A review of the relevant international and EU chemicals legislation was conducted for the current study, which analysed which pieces of legislation refer to the importance of protecting or considering vulnerable groups. The results of this review are described in the following two sections. In the first instance, the regulations and other legislative documents that refer to vulnerable groups are described and set out, followed by an overview of the chemicals legislation that does not consider vulnerable groups even though it would be relevant to do so.

### 7.1.2 Chemical legislation containing reference to vulnerable groups

The following table lists the chemical legislation – both international and European – which makes specific reference to vulnerable groups. It sets out the general legal framework, as well as specific pieces of legislation that are relevant to certain types of vulnerable groups: children, pregnant and breastfeeding women, the elderly, workers, people with medical conditions and/or disabilities, and lower socioeconomic groups. The table shows for each of the pieces of legislation described, the category of vulnerable groups addressed. More specifically, those provisions that refer to vulnerable groups directly, or that include a reference relevant to the protection of vulnerable groups, have been listed in the right-hand column.
Table 6: Overview of relevant EU and international chemicals legislation and their provisions concerning vulnerable groups

<table>
<thead>
<tr>
<th>Chemicals legislation</th>
<th>G</th>
<th>C</th>
<th>PB</th>
<th>E</th>
<th>W</th>
<th>O</th>
<th>Comments/Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General chemicals framework, international level</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2001, Stockholm Convention on Persistent Organic Pollutants (POPs)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>Non-binding provision recognising the health concerns stemming from the impact of women’s exposure to POPs (recital)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Provision on the development of educational and public awareness programmes and training – especially for children, women, workers and the least educated – on POPs, their health and environmental effects and the alternatives (Art. 10(c)).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2004, Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
<td>General non-binding provision on the need to protect human health of consumers and workers (preamble); Provision on the requirements for notifications of the procedures for banned or restricted chemicals. The notification shall include a summary of the hazards and risks presented by the chemical to the health of consumers and workers (Annex I, point 2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006, Strategic Approach to International Chemicals Management (SAICM)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>General provisions on the need to protect vulnerable groups by reducing the risks from hazardous chemicals and making scientific information available for appropriate risk assessments (point 9 and 23 Dubai Declaration; point 7 and 15 of the Overarching Policy Strategy)</td>
<td></td>
</tr>
<tr>
<td>2013, Minamata Convention on Mercury</td>
<td>x</td>
<td>x</td>
<td>Provisions on: Adopting science-based health guidelines relating to exposure to mercury (Art. 16); Setting targets and developing strategies to reduce mercury exposure (Art. 16 + Annex C); Promoting education, training and public awareness of the effects of exposure to mercury (Art. 16); Monitoring the levels of mercury in vulnerable populations (Art. 19);</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>General framework, EU level</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regulation (EC) 1907/2006 (REACH)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>General non-binding provisions on the need to protect vulnerable groups (recital 12, 69); Provisions on identifying different DNELs for certain vulnerable groups (Annex I, point 1.4.1); Provisions on the restriction of marketing substances that might be harmful for children or workers (Annex VII, point 30, 31, 52, 59); Provisions on the standard information requirements for certain substances that might be harmful for the foetus (Annex VIII, point 8.7.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regulation (EC) No 1272/2008 (CLP)</td>
<td>x</td>
<td>x</td>
<td>Provision stressing that packaging containing a hazardous substance or a mixture supplied to the general public shall not have either a shape or design likely to attract or arouse the active curiosity of children (Art. 33); Special rules for labelling and packaging of mixtures or substances that can harm children, such as lead, cyanoacrylates (Annex II, 2.1, 2.2); Provision on precautionary statements to be used in labelling of hazardous substances in order to protect children (Annex IV); Classification and labelling requirements for hazardous substances and mixtures and the need to protect newborns (Annex I, point 3.7.1.4.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regulation (EC) 1107/2009 on plant protection products (PPP)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>General non-binding provisions on the need to protect vulnerable groups (recital 8, 24); Provision on the definition of vulnerable groups (Art. 3, point 14); Binding provision specifying that the residues of PPP shall not have any harmful effects on vulnerable groups (Art. 3(2) and (3)); Provisions on the advertising of PPP and the need to protect children (Art. 66); Provisions on the requirements of the authorisation of the PPP and the need to protect workers (Art. 31); Provision on different risk assessments for workers (Annex IV, point 2);</td>
<td></td>
</tr>
<tr>
<td>Regulation (EU) 528/2012 on biocidal products</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>General provisions on the need to protect vulnerable groups (recital 3, Art. 1, Annex VI, point 24, 32, 59); Provision on the definition of vulnerable groups (Art. 3); Provision on conditions for granting an authorisation and the need to protect vulnerable groups (Art. 19); Provision on the possibility for a Member State to derogate from mutual recognition to protect vulnerable groups (Art. 37); Provision on the obligation for notification of new data on adverse effects for vulnerable groups (Art. 47); Provision on the possibility for a competent authority to derogate from Art. 19 – while always preventing harmful effects for vulnerable groups (Art. 55(3)).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

305 G: Reference to vulnerable groups in General; C: Reference to Children (and/or the foetus) as a vulnerable group; PB: Reference to Pregnant or Breastfeeding women as a vulnerable group; E: Reference to the Elderly as a vulnerable group; W: Reference to Workers as a vulnerable group; O: Reference to Other types of vulnerable groups.
### Chemicals legislation

<table>
<thead>
<tr>
<th>Regulations</th>
<th>G</th>
<th>C</th>
<th>PB</th>
<th>E</th>
<th>W</th>
<th>O</th>
<th>Comments/Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Directive 2001/83/EC on the Community code relating to medicinal products</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>Provision on the obligation to review safety data taking into account guidelines published by the Commission, with particular attention to events resulting in changes of dose or need for concomitant medication, serious adverse events, events resulting in withdrawal, and deaths. In these cases, particular attention shall be given to vulnerable groups (Annex I, point 5.2.5.1). Provision on the labelling, packaging and advertising of medicinal products and the need to protect vulnerable groups (Art. 54, 59, Art.90).</td>
</tr>
<tr>
<td>Directive 2008/50/EC on ambient air quality and cleaner air for Europe</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>Provision on the need to include specific measures as well as drawing up short-term action plans to protect vulnerable groups (Art. 23, 24, Annex XV, letter B, point 3(h)).</td>
</tr>
<tr>
<td>Regulation (EC) 850/2004 on Persistent Organic Pollutants (POPs)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Provisions on developing awareness programmes and training on POPs for vulnerable groups (recital 19, Art. 10).</td>
</tr>
<tr>
<td>Regulation (EC) 1223/2009 on cosmetic products</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>Provisions on substances classified as carcinogenic, mutagenic or toxic for reproduction (CMR) should also take into account the exposure to those substances of vulnerable groups (recital 34, Art. 15); Provision on the information contained in the cosmetic product safety report and the need to protect vulnerable groups (Annex I); Provision on substances prohibited in cosmetic products in order to protect children (Annex II and Annex III).</td>
</tr>
<tr>
<td>Directive 2001/95/EC on general product safety</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>Provisions which specify that the safety of products should be assessed, taking into account the categories of consumers which can be particularly vulnerable to the risks posed by the products, such as children and the elderly (recital 8, Art. 2(b)).</td>
</tr>
<tr>
<td>Regulation (EU) 1169/2011 on the provision of food information to consumers</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Specific provision for foods with certain chemicals that may not be nutritionally appropriate for breastfeeding women and children under the age of 5 years (Annex III).</td>
</tr>
<tr>
<td>Directive 93/42/EEC on medical devices</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Specific provision on the requirements for the design and construction of the medical device, and the need to reduce to a minimum the risks posed by toxic substances leaking from the device for children or pregnant women (Annex I, point 7.5)</td>
</tr>
<tr>
<td>Regulation (EC) 1333/2008 on food additives</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>Binding provision specifying that food additives shall not be used in foods for infants and young children except where specifically provided for in Annex II to this Regulation (Art. 1A) Binding provision in the Annex specifying the list of food colours for which the labelling of foods shall include additional information (Annex V).</td>
</tr>
<tr>
<td>Regulation (EC) 1881/2006 setting maximum levels for certain contaminants in foodstuffs</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Non-binding provision on setting lower maximum level for certain food contaminants to which vulnerable groups are exposed in order to protect them (recital 4, 23, 45, 56); Non-binding provision which suggests that targeted consumer advice is an appropriate approach in the case of methyl mercury for protecting vulnerable groups of the population (recital 43); Specific provision on setting maximum levels for certain contaminants in foodstuffs to which children are exposed (Annex).</td>
</tr>
<tr>
<td>Regulation (EC) 396/2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Non-binding provision which specifies that maximum residue levels should be set at the lowest achievable level consistent with good agricultural practice for each pesticide, with a view to protecting vulnerable groups such as children and the unborn (recital 5); Specific provision defining maximum residue level (MRL) which is the upper legal level of a concentration for a pesticide residue in or on food or feed set in accordance with this Regulation, based on good agricultural practice and the lowest consumer exposure necessary to protect vulnerable consumers (Art. 3(d)).</td>
</tr>
</tbody>
</table>

### Specific legal framework for children, international and EU level

<p>| 1990, UN Convention on the rights of the child                | X |   |   |   |   |   | General provision on the right of the child to enjoy the highest attainable standard of health and to facilities for the treatment of illness and rehabilitation of health. Since States Parties shall pursue full implementation of this right, this provisions can be considered a legal basis to protect children from the harmful effects of chemicals (Art. 24). |</p>
<table>
<thead>
<tr>
<th>Chemicals legislation</th>
<th>G</th>
<th>C</th>
<th>PB</th>
<th>E</th>
<th>W</th>
<th>O</th>
<th>Comments/Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Directive 2009/48/EC on the safety of toys</strong></td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>Non-binding provision on the need to adopt specific safety requirements to protect children against risks caused by carcinogenic, mutagenic and reproto-toxic (CMR) substances in toys (recital 21, 25); Provision which oblaste manufacturers to carry out assessment procedures before placing a toy on the market [Art. 18 + recital 35, 47]; Provision specifying that the Commission may adopt specific limit values for chemicals used in toys intended for use by children under 36 months or in other toys intended to be placed in the mouth [Art. 44(2) + recital 22, 24 + Appendix C]; Provisions setting out particular safety requirements for the chemical properties of toys intended for use by children (Annex II, point II and III); Provisions on warnings and indications of precautions to be taken when using certain categories of toys (Annex V, part B, point 4).</td>
</tr>
<tr>
<td><strong>Regulation 609/2013 on food intended for infants and young children, food for special medical purposes, and total diet replacement for weight control</strong></td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Non-binding provision on setting the MRL of pesticides in food for infants at the lowest achievable level to protect vulnerable population groups (recital 21); Non-binding provision stressing the need to take into account the restriction and prohibitions of certain pesticides classified in accordance with Regulation (EC) No 1272/2008 in the delegated acts adopted pursuant to this Regulation (recital 22); Non-binding provision stressing that, in the interest of protecting vulnerable consumers, labelling requirements should ensure accurate product identification for consumers (recital 26).</td>
</tr>
</tbody>
</table>

**Specific legal framework for pregnant women, international and EU level**

<p>| | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Directive 92/85/EEC pregnant workers</strong></td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>Provision preventing pregnant and breastfeeding workers to be obliged to perform duties for which the assessment has revealed a risk of exposure to toxic chemicals [Art. 6]; Provision obliging the employer to assess the nature, degree and duration of exposure for all activities likely to involve a specific risk of exposure to the agents, processes or working conditions for which a non-exhaustive list is given in Annex I [Art. 4 + Annex I, point 3].</td>
</tr>
</tbody>
</table>

**Specific legal framework for the elderly, international and EU level**

<p>| | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Directive 98/24/EC on risks related to chemical agents at work</strong></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>Provision on labelling hazardous chemicals in a manner that is easily understandable to workers [Art. 7]; Provisions on the responsibilities of employers, notably in respect of identification [Art. 10], transfer of chemicals [Art. 11], exposure [Art. 12], operational control [Art. 13], information and training [Art. 15]; Provisions on the duties and rights of workers concerning chemicals [Art. 17 and 18].</td>
</tr>
</tbody>
</table>

**Specific legal framework for workers, international and EU level**

<p>| | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1990, ILO Chemicals Convention No. 170, concerning Safety in the use of Chemicals at Works</strong></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Directive lays down minimum requirements for the protection of workers from risks to their safety and health arising, or likely to arise, from the effects of chemical agents present at the workplace or as a result of any work activity involving chemical agents. Specific provisions include: Occupational exposure limit values and biological limit values [Art. 3]; Employers’ obligations, e.g. determination, assessment, prevention of risk associated with hazardous chemical agents, as well as specific protection and prevention measures and information and training that the employer shall carry out [Art. 4, 5, 6, 7, 8]; Prohibition of certain chemical agents at work [Art. 9 and Annex III]; Health surveillance [Art. 10 and Annex III].</td>
</tr>
</tbody>
</table>

<p>| | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Directive 2004/37/EC carcinogens or mutagens at work</strong></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Directive laying down the minimum requirements for the protection of workers against risks to their health and safety, including the prevention of such risks, arising or likely to arise from exposure to carcinogens or mutagens at work. Specific provisions include: Employers’ obligations [Art. 4, 5, 6, 7, 8, 9, 10, 11, 12, 13]; Health surveillance [Art. 14 and Annex III]; Limit values for occupational exposures [Art. 16 and Annex III].</td>
</tr>
</tbody>
</table>

<p>| | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Directive 94/33/EC on young people at work</strong></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Provisions on the general obligations on employers to adopt the measures necessary to protect the safety and health of young people, also taking into account the nature, degree and duration of exposure to physical, biological and chemical agents [Art. 6]; Provision prohibiting Member States from employing young people for work involving harmful exposure to chemicals [Art. 7 and Annex].</td>
</tr>
</tbody>
</table>
### Chemicals legislation

<table>
<thead>
<tr>
<th>G</th>
<th>C</th>
<th>PB</th>
<th>E</th>
<th>W</th>
<th>O</th>
<th>Comments/Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>x</td>
<td></td>
<td></td>
<td>Directive laying down the minimum requirements for the protection of workers against risks to their health, including the prevention of such risks, arising or likely to arise from exposure to asbestos at work.</td>
</tr>
</tbody>
</table>
The table shows that, currently, only two pieces of EU legislation provide a definition of the term ‘vulnerable groups’. These are the Plant Protection Products Regulation and the Biocidal Products Regulation. It could be worth considering adding provisions defining which particular ‘vulnerable groups’ may need special protection to relevant EU legislation. For instance, while the CLP Regulation refers to children and pregnant women as vulnerable categories, other relevant categories such as the elderly and workers are not mentioned and therefore arguably not given adequate attention in the Regulation.

Another area that could be considered in EU legislation are the specific windows of vulnerability that exist for certain vulnerable groups. For instance, the different EU Regulations and Directives analysed only refer to children as a general category, without distinguishing between neonates, infants, toddlers and adolescents. Referring to these different windows of vulnerability in the legislation seems an option worthy of consideration, given the particular vulnerability of foetuses, neonates and infants. At the very least it would seem important to provide sufficient safety margins to foetuses and neonates, the most vulnerable among the vulnerable categories, particularly for those chemicals suspected of being neurotoxins or endocrine disrupters. As shown by the scientific evidence described in this report, there is a need to protect children from hazardous chemical exposure from the very early stages of their development. Particular exposure of the foetus can result in significant health impacts that affect their entire life.

The types of protection from chemical exposure that can be offered to vulnerable groups by EU legislation can be grouped into four different categories: (1) legislation related to work, (2) legislation related to food, (3) legislation related to products; and (4) legislation related to the environment (air). This grouping is not incidental but, rather, reflects the routes through which vulnerable groups are exposed. In each of these groups there is EU legislation that considers vulnerable groups, as well as other EU legislation that, while sharing the same objectives, does not include vulnerable groups in its provisions. For instance, in the ‘food’ group, there are pieces of EU legislation which refer to vulnerable groups (e.g. Food Additives Regulation) and other EU legislation that - despite being directly related to specific circumstances or environments in which the protection of vulnerable groups is a consideration - do not provide any references to vulnerable populations (e.g. Novel Food Regulation, and Food Contact Materials Regulation). For the sake of consistency, therefore, it would be worth reviewing these groupings of legislation in order to identify if references to vulnerable groups should be included in all legislation belonging to the four categories mentioned above.

This study identified the following types of provisions to protect vulnerable groups:

- Lowering the level of exposure or setting maximum levels of exposure;
- Marketing restrictions and general prohibitions;
- Authorisation procedures;
- Risk assessment rules;
- Information requirements (labelling/packaging/advertising);
- Manufacturing obligations and safety requirements (design and construction);
- Obligations for employers (training and awareness raising programmes);
- Member States’ obligations and rights (e.g. notifications procedures, possibility to enact provisional measures, etc.).

This list could be used by the Commission to add provisions belonging to these areas to both the EU legislation which refers to vulnerable groups, as well as those that do not.

---

307 See paragraph 1.2 above.
7.1.3 Chemical legislation that could contain references to vulnerable groups

Numerous pieces of legislation were identified that, despite dealing with chemicals and having the protection of human health as a general objective, nonetheless do not contain any direct references to vulnerable groups. As demonstrated by the literature review, the scope of these regulations and legislative documents is directly related to specific circumstances or environments in which the protection of vulnerable groups should be an important consideration. An overview of the most relevant pieces of legislation that could include provisions to protect vulnerable groups from the risks of chemical exposure are listed below. An exhaustive list of all legislation considered can be found in the list of references (Chapter 10).

- Regulation (EC) No 648/2004 on detergents;
- Regulation (EC) No 1935/2004 on materials and articles intended to come into contact with food (Food Contact Materials);
- Regulation (EU) No 10/2011 on plastic materials and articles intended to come into contact with food;
- Directive 98/79/EC on in vitro diagnostic medical devices;
- Directive 2008/98 on waste;
- Directive 2006/66/EC on batteries & accumulators;
- Regulation (EC) No 1334/2008 on flavourings and certain food ingredients with flavouring properties for use in and on foods and amending Regulation (EC) No 2232/96;
- Directive 2004/107/EC relating to arsenic, cadmium, mercury, nickel and polycyclic aromatic hydrocarbons in ambient air;

Three of the above-mentioned pieces of legislation offer, in particular, significant opportunities to improve the protection of vulnerable groups, as indicated by EU institutions and civil society organisations\(^308\). They are described in further detail below, together with an argument for the inclusion of the protection of vulnerable groups in these contexts.


The main aim of the Drinking Water Directive (DWD) is to protect the health of EU consumers as well as ensuring the water is healthy. The Directive obliges Member States to regularly monitor the quality of drinking water and to provide consumers with adequate information on the quality of the water. In order to ensure that drinking water everywhere in the EU is healthy, clean and tasty, the DWD sets standards for the most common substances (parameters) that are found in drinking water. A total of 48 microbiological and chemical parameters must be monitored and tested regularly.

The parameters and parametric values are included in Annex I of the DWD. Part A of this Annex refers to microbiological parameters, while part B refers to chemical parameters. With regard to the latter, only 25 chemicals have been listed in part B of the Annex. While the list contains chemicals of concerns for both general and vulnerable populations - such as arsenic, cadmium, chromium, lead and mercury - there are other chemicals of concern, such as the perfluorooctanoic acid (PFOA), that are not included in the list\(^309\). In particular, foetuses and newborns are highly vulnerable to exposure of PFOA through umbilical cord blood or via breast milk after birth.

---


\(^309\) For more information about the main concerns regarding PFOA see Vierke, L. et al., 2012.
In line with the general scope of the Directive, i.e. the protection of human health from the adverse effects of any contamination of water intended for human consumption, it seems relevant to study the number of chemicals listed in Annex I, part B, and to update the list based on the latest scientific evidence available, in order to protect the general population and, especially, certain vulnerable categories, such as foetuses, pregnant women and children.

Regulation (EC) No 1935/2004 on materials and articles intended to come into contact with food (Food Contact Materials)

Food contact materials (FCMs) encompass all materials and articles intended to come into contact with food, such as packaging and containers, processing machinery, kitchen equipment, cutlery and dishes. 15,000 different substances are estimated to be present in FCMs. These substances can migrate into food thus triggering hazardous health effects on human health. Hence, the safety of FCMs should be assessed; they also have to be manufactured in compliance with EU Regulations.

General requirements for all FCMs are laid down in Framework Regulation EC 1935/2004. The principles set out in the Regulation require that FCMs do not release their harmful constituents into food or change food composition, taste and odour in an unacceptable way. The Regulation also allows the European Commission to adopt specific measures for 17 materials listed in its Annex. So far, specific EU measures have only been adopted for five of these, notably plastics (including recycled plastic), ceramics, regenerated cellulose film and active and intelligent materials.

The FCMs Regulation has recently been under the spotlight of the EU legislator. According to a European Parliament study, food contamination from FCMs is an under-estimated issue. In particular, studies have indicated that further harmonisation of legislation governing FCMs is required, as the level of enforcement is inconsistent across the EU. Specific EU measures could thus be adopted for non-harmonised materials, giving priority to those that constitute a particular risk to human health. Moreover, harmonisation of FCMs would also make the level of public health protection homogeneous in the EU.

Critics have also underlined a gap which exists between legal requirements and a de facto situation where risk assessment is not possible, because the identity of substances present in FCMs is unknown. A recent report from the European Parliament highlighted that FCMs with a higher risk of migration, are of a particular concern. The report also stressed that more research is needed about non-intentionally added substances (NIASs), whose composition is often unknown. The report also highlighted that current EU risk assessment does not take into account the effects of chemical mixtures. Finally, the report pointed out that FCMs are a significant source of human exposure to EDCs, such as phthalates and bisphenols (BPA). EDCs are chemicals of particular concern; which recent research has linked to various diseases which are particularly harmful for vulnerable groups.

Given the above, the FCMs Regulation offers several opportunities for improvement. Firstly, while the current FCMs Framework Regulation allows for more particular rules to be set for any of the 17 types of FCMs, specific EU laws have only been set for five of the 17 types. Therefore, 12 types of FCMs are not covered by any specific legislative measures at EU level. Such rules are particularly important to consider as they usually involve more specific requirements for risk assessment and set limits for the maximum migration of chemicals into food. There is therefore scope for the EU to address these

---

313 Ibid.
12 uncovered types of FCMs, starting with those whose chemical contamination problems have already been established, e.g. printing inks migrating into food, bisphenol A, fluorinated substances, and other hazardous chemicals in paper/board packaging.

Secondly, further harmonisation of the legislation governing FCMs, and in particular the provision concerning EDCs, seems an option worth exploring. For instance, the majority of Member States do not have specific legal measures on the food contact uses of certain phthalates and BPA. These chemicals are particularly harmful for both the general population and vulnerable groups. In light of this, consideration should be given to the inclusion of specific provisions to protect vulnerable groups in the FCMs Framework Regulation. Provisions identifying safe levels for EDCs for the protection of both the general population and specific vulnerable groups would be a good starting point.\(^\text{317}\)

Thirdly, the issue of mixtures of chemicals in FCMs has not yet been assessed. Safety levels are, in fact, determined without taking into account multiple exposure to different FCMs at the same time. Addressing the issue of safety levels arising from exposure to such mixtures could be beneficial for both the general population and specific vulnerable groups.

Finally, the NIASs are chemicals present in FCMs as impurities or as the consequence manufacturing processes. Currently, the majority of NIASs in FCMs have not yet been identified; this circumstance makes risk assessments particularly difficult to be performed.\(^\text{318}\) Addressing the issue of NIAS, for instance by proving guidance on how companies should carry out the risk assessment, seems an option worth considering, in light of the exposure risk to both the general population and vulnerable groups.

**Regulation (EC) No 648/2004 on detergents**

Regulation (EC) No 648/2004 establishes a set of rules designed to achieve the free movement of detergents and surfactants for detergents in the internal market while, at the same time, ensuring a high degree of protection of the environment and human health. The Regulation harmonises the rules on the biodegradability of surfactants, their restrictions and bans, the information that manufacturers must provide, and the labelling of detergent ingredients.

The Regulation was amended several times in order to include all classes of surfactant. With respect to product labelling, Regulation (EC) No 907/2006 extends the rules to include fragrance ingredients that could cause allergies.

Within the scope of the Regulation on detergents, consideration could be given to the inclusion of specific provisions to protect certain categories of vulnerable groups who may either be more exposed to detergents compared to the general population (e.g. workers in the cleaning industry, clothing industry, soap industry, laundries, etc.), or those who are more vulnerable to these substances (children, especially toddlers, the elderly) and who may experience higher risk should they accidentally come into contact with these substances. Pregnant women, whose condition implies an intrinsic vulnerability of the foetus, may also need special protection.

### 7.2 RISK ASSESSMENT

Risk assessment is an integral part of the EU legal framework, aiming to protect people, including vulnerable groups, from the health risks associated with chemicals. Risk assessment combines the intrinsic potential of chemicals to cause adverse health effects with knowledge of human exposure to chemical substances via the possible routes. Chemical risk assessment usually encompasses four steps: hazard identification (e.g. carcinogen, endocrine disruptive etc.), hazard characterisation (dose-response relationship, mode of action etc.), exposure assessment (external or internal) and risk

\(^\text{317}\) Geuweke B et al., 2014.

\(^\text{318}\) HEAL, 2016.
characterisation. From the perspective of protecting vulnerable groups, it is particularly important that risk assessment considers windows of susceptibility.

Hazard identification is the identification of the adverse effects which may result from contact with a given substance. Hazard characterisation (an alternative name for effects assessment or dose-response assessment) is the estimation of the relationship between dose or level of exposure to a substance, and the incidence and severity of an effect. Exposure assessment is the determination of the emissions, pathways and rates of movement of a substance and its transformation or degradation in order to estimate the concentrations/doses to which human populations or environmental compartments are, or may be, exposed. Risk characterisation is an estimate of the incidence and severity of the adverse effects likely to occur in a human population or environmental pocket due to actual or predicted exposure to a substance, and may include a quantitative ‘risk estimation’. Risk management is the decision-making process based on the risk assessment, which develops, analyses and compares regulatory options and selects the appropriate regulatory response.

Three scientific committees of the Commission have noted that the protection of vulnerable populations is a major challenge in risk assessment. Vulnerability is understood in this context as the combination of higher susceptibility and higher levels of exposure, together with additional factors, including social and cultural parameters such as socioeconomic status and location of residence, as well as risk awareness and risk education. Given that the level of chemical exposure may vary significantly during different stages of life, and that inherent biological differences may make certain groups more susceptible to chemicals, the evaluation of exposure to chemicals and the related health risk requires population-specific information which in itself may be subject to significant variation. For example, a 2010 study measuring packaged food intake by British children aged 0-6 years showed that children, on average, consumed 1.6-3 times (depending on the more specific age group) as much plastic food packaging as estimated by the current EU model, indicating a proportionally higher exposure to substances leaching from plastic food contact materials for children than adults.

The International Programme on Chemical Safety (IPCS) has issued a number of publications and projects on risk assessment methodology, including principles for evaluating health risks for specific populations, such as children and older adults, as well as for babies born following exposure to chemicals during pregnancy. They have also published a document on the need for a special approach to chemical risk assessment applying to children, one which takes into account the special characteristics of infants and young children.

In 2013, the OECD carried out a survey on the tools and methodologies for chemical risk assessment process in the context of children’s health. The survey addressed the methodologies and tools currently available for assessing the risk of chemicals to children’s health, as well as the need for additional guidance. Respondents were asked to identify the need for guidance and whether or not such methodologies and tools exist in the following areas: the definition of terms, hazard assessment, exposure assessment, risk characterisation, cohort studies, and combined exposure to multiple chemicals. The results showed that 49% of the respondents assess the risks generically, as part of the assessment of consumers and the general public, with only 45% assessing the risks specifically for children. 6% indicated that they do not conduct risk assessments for children, or that such assessments depend on the chemical being assessed. The chemicals reviewed by respondents included pesticides.

319 Choi J et al., 2015b.
321 SCHER, SCENIHR & SCCS, 2013.
322 Muncke J, 2011.
323 IPCS, 2006.
324 IPCS, 1993.
325 IPCS, 1984.
326 IPCS 1986.
327 OECD, 2013.
chemicals in consumer products, cosmetics and nanomaterials. The survey results also demonstrated that the definitions of ‘children’ and sub-categories such as ‘toddlers’ varies by respondent and type of chemical assessed. With regard to hazard assessments specific to children, respondents provided six endpoints: developmental toxicity, carcinogenicity, neurotoxicity, generic alterations, reproductive toxicity and endocrine disruption. Other respondents, including ECHA, reported that they perform specific hazard assessments for children and gave the titles of existing guidance (e.g. ‘Guidance on information requirements and chemical safety assessment (R7 and R8)’ for REACH and ‘Guidance for chemical safety assessment (R8.4.3.1)’ (for REACH) were given by ECHA, while the EHC 237 ‘Principles for Evaluating Health Risks in Children Associated with Exposure to Chemicals’ were referred to by IPCS). Respondents also reported that they perform specific exposure assessments for children, including the use of specific exposure scenarios. Specific risk characterisations for children were also performed, with some respondents (including the EC Joint Research Centre and the German Human Biomonitoring Commission of the Federal Environment Agency) referring to guidance documents or tools used for this purpose. Cohort studies of children (e.g. by the RIVM in the Netherlands) are also undertaken. Other programmes assess the risks to children from combined exposure to multiple chemicals (e.g. the ‘Expert Workshop on Combination Effects of Chemicals’ report by the Danish EPA).

In addition to the tools currently available, respondents highlighted a need for additional guidance on risk assessment for children. These include, firstly, harmonised definitions for assessing the risks of chemicals to children’s health. With regard to hazard assessment, the respondents’ pointed to the following needs:

- Guidance or methodologies on extrapolation from adults to children, including age-dependent adjustment factors;
- Sensitivity guidance or studies related to children’s level of development, developing markers of outcome assessment for children;
- Tools which take account of developing country scenarios;
- Epidemiological outcomes to show correlation between human biomonitoring (HBM) and health outcomes;
- Harmonisation of end-points;
- Focus on specific areas such as: adult onset effects resulting from early life exposures; effects of chemicals in psychoneuro-development and immune development; endocrine modulators and low-dose effects; developmental programming and/or epigenetics; markers of outcome assessment for children; and prenatal exposure to specific chemicals such as PCBs.

In the context of exposure assessment, the OECD concluded that there is a significant need for more tools. Respondents highlighted a variety of needs in this regard, including:

- General exposure scenarios for children (including time of exposure, number of hand-to-mouth events/activities, contact with pets, body weight and inhalation);
- Specific exposure behaviour or situations for children;
- Exposure scenarios from specific sources (e.g. biocides, consumer products, insecticides in domestic environments, etc.);
- Specific exposure factors, data or models (e.g. standard values for body weight and breathing volume, indoor guide values).

For risk characterisation, the suggestions included:

- Harmonisation of risk characterisation methodologies such as uncertainty factors, in order to account for the specificity of children and/or deviation;
- Identification of people/groups with mixed/multiple exposures;
- Risk characterisation which takes account of developing country scenarios;
- More information regarding toxicokinetics and dynamics between children and adults.
In relation to the combined exposures to chemicals, the following needs were described:

- Tools/methodologies for both children and adults;
- Guidance on combined exposure for all age groups (one response suggested harmonised guidance for cumulative/combined exposure to pesticides, including for infants and children);
- Common definitions and a common methodology to assess combined exposure;
- Guidance for assessment of uncertainty;
- Specific information on co-use scenarios, prenatal exposure to PCBs and combined exposure, and real-life scenarios in developing countries;
- Case studies employing the WHO Framework.

Finally, additional responses suggested that the following are needed:

- Identification and assessment of other pathways, such as behaviour and lifestyle;
- Harmonised approach for calculating and handling exposures for children when conducting cancer risk assessments, such as age-specific adjustment factors;
- Exchange of information on factors of exposure measurements and outcome measurements in child health;
- Data extrapolating to children, for all steps in risk assessment processes;
- Assessment of risk from engineered and non-engineered nanoparticles which are already dispersed in the environment.

The literature reviewed for this sub-study indicates that specific challenges remain in respect of chemical risk assessment for vulnerable groups, particularly in relation to certain types of substances. For example, according to the latest scientific knowledge, endocrine substances are typically subject to an ‘early exposure – late effect’ pattern, which poses difficulties for risk assessors.

Assessing the risks of chemical mixtures poses another specific challenge. The variety of possible chemical combinations is too vast to allow for an individual risk assessment of each combination. Also, the combination effects may vary in their level of seriousness.

Efforts to harmonise methodologies for chemical risk assessment continue, with the WHO’s International Programme on Chemical Safety leading a project to harmonise approaches to a number of specific risk assessment areas, such as combined exposures to multiple chemicals, exposure assessment and mutagenicity testing. A challenge here is the harmonisation of chemical risk assessment and the need to cater for the diverse circumstances of vulnerable populations, whose consumption patterns and exposure levels may differ significantly depending on age group, geographical location and lifestyle factors.

### 7.3 BIOMONITORING

Human Biomonitoring (HBM) is a scientific technique that allows a systematic standardised measurement of human exposures to chemical contaminants entering the body through the various possible routes. This method involves analyses of human tissues and fluids, using biomarkers (BM) as measurable indicators of changes or events in biological systems. Biomarkers are measurements of the concentrations of chemical substances, their metabolites, or reaction products in the human tissues or specimens used for analysis, such as blood, urine, hair, saliva, breast milk and semen. Cord blood and placenta are also often used to measure exposure in utero. The measured concentrations are

---

329 Choi J et al., 2015a.
commonly referred to as ‘body burdens’ of the relevant chemical substances.\textsuperscript{330}

The strength of HBM as a method is that it is the only available tool which integrates exposures from all sources. Biomonitoring data reflect the internal dose of the measured chemicals in the test participant at a given point in time. With modern analytical methods, it is possible to measure a wide range of chemicals in the human body even at very low levels.\textsuperscript{331} The use of biomarkers also enables scientists to detect early health effects.\textsuperscript{332} According to the EU-level COPHES programme,\textsuperscript{333} HBM surveys can highlight spatial trends, help to uncover cultural and lifestyle contributing factors, and indicate specific at-risk groups, such as given age cohorts. Repeated surveys can reveal increases or decreases in chemical exposures over time, making HBM a valuable tool in tracking the results of policy initiatives.

HBM data alone cannot be used to track the source of exposure or the length of time a chemical has been in the body. In many HBM programmes, complementary questionnaires are used to collect information on factors such as occupation and lifestyle, in order to estimate potential sources of exposure. In combination with a detailed understanding of the potential analytical/methodological pitfalls and the toxicokinetics of individual chemicals, HBM data could be translated into daily exposure estimates.\textsuperscript{334}

In the context of this sub-study, a number of resources were identified that outlined the uses and value of HBM in several stages of risk assessment, from hazard identification and characterisation to risk characterisation and exposure assessment. At the hazard identification stage, HBM has a role in some toxicological studies, where the actual in vivo exposure can only be found via biological monitoring. HBM can also allow observation of an increased individual or group level of a potentially toxic chemical, or its metabolites, in human biological samples. Forward or reversed dosimetry comparing human and experimental animal concentrations can be used to bridge toxicology and human effects.\textsuperscript{335} At the hazard characterisation level, HBM can provide useful data for either or both sides of the dose-response equation: it may help to measure the biological level of a chemical or its metabolite(s) corresponding to a given level of exposure (the dose), or it can be used to assess the proportion of individuals showing some early adverse effects at a given level of exposure (the response).

The most critical function of HBM is the provision of data on actual exposure to chemical substances, making it indispensable in exposure assessment. HBM data reflects the total exposure from all sources, including environmental and lifestyle exposures, as well as individual susceptibility based on gender, age, genetic background and body composition.

Risk characterisation combines the hazard identification information with exposure assessment. HBM has a role in performing or validating risk assessment where environmental monitoring and health surveillance are unavailable, or inadequate, due to an intrinsically low sensitivity and/or specificity. With HBM it is also possible to assess certain specific components of risk that would otherwise not be accessible, such as metabolic polymorphism, enzymatic inhibition or induction of the metabolising enzymes and other susceptibility factors that could cause a different response to chemicals. HBM data also has a role in risk management when combined with HBM-related guidance values, such as those under development in the USA and Germany (HBM-I and HBM-II in Germany and Biomonitoring Equivalents (BE) in the USA).

Researchers suggest that risk assessment and risk management without HBM could lead to inaccurate risk estimates and thus inadequate measures.\textsuperscript{336} Based on this, it appears that HBM is an invaluable

\begin{flushleft}
\textsuperscript{330} Choi J et al., 2015b.
\textsuperscript{331} Ibid.
\textsuperscript{332} Choi J et al., 2015a.
\textsuperscript{333} COPHES, project website, available at: \texttt{www.eu-hbm.info/cophes}.
\textsuperscript{334} Choi J et al., 2015b.
\textsuperscript{335} Choi J et al., 2015a.
\textsuperscript{336} Ibid.
\end{flushleft}
source of complementary data. Its major limitation in risk assessment, however, is the inability to differentiate exposures from different sources, with data collected by other methods needed to provide this information. As HBM results represent a snapshot of exposure for a specific time, the data is subject to significant variation and may not show past exposure for short-lived substances.

In occupational medicine, HBM has long been associated with vulnerable groups, due to its value in providing data of the body burden of toxic substances and their metabolites. Through the detection of exposure, HBM can indicate adverse health risks and thereby provide an incentive for risk management measures. It is also useful for assessing the effectiveness of preventative measures and for controlling workplace limit values. HBM is also relevant for other vulnerable groups. In fact, its ability to identify vulnerable groups and populations with higher exposures and emerging chemical risks, as well as to establish the distribution of exposure among the general population is a key strength. Additionally, HBM data can be used to provide supporting evidence of the higher susceptibility of certain population groups. For example, several HBM studies have provided support for the proposition that prenatal exposure to chemicals in infants could result in some adverse health effects. Some HBM programmes have also demonstrated higher body burdens of phthalate metabolites, PAH metabolites and PBDEs and fluorocarbons in children, highlighting these substances as a major concern for children. Many existing HBM studies emphasise the need for this methodology in children in order to generate the data required for accurate risk assessment and management.

A range of HBM studies (e.g. the FLEHS and PROBE programmes outlined below) noted that several metals appear to accumulate in the elderly population. The KorSEP study also attributed higher body burdens of phthalates to older subjects. The clearance of chemicals out of the body is slower in the elderly, which increases the risk of developing adverse effects. This further supports the need for biomonitoring in the elderly to gain accurate exposure data.

The collection of complementary information from HBM programme participants through questionnaires enables researchers to combine exposure data with historical factors such as gender, living environment (urban, rural), lifestyle habits, medical history, etc. These factors have been used to determine the additional risk factors of higher body burdens of chemicals.

Box 7: Examples of relevant HBM programmes

<table>
<thead>
<tr>
<th>Country</th>
<th>Programme</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S.</td>
<td>National Health and Nutrition Examination Survey (NHANES)</td>
</tr>
<tr>
<td>Canada</td>
<td>Canadian Health Measures Survey (CHMS)</td>
</tr>
<tr>
<td>Germany</td>
<td>German Environmental Survey (GerES)</td>
</tr>
<tr>
<td>Belgium</td>
<td>Flemish Environment and Health Study (FLEHS)</td>
</tr>
<tr>
<td>France</td>
<td>French National Survey on Nutrition and Health (ENNS)</td>
</tr>
<tr>
<td>Spain</td>
<td>BIOAMBIENT.ES</td>
</tr>
<tr>
<td>Italy</td>
<td>Programme for Biomonitoring the Italian Population Exposure (PROBE)</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>Human Biomonitoring Project (CZ-HBM)</td>
</tr>
<tr>
<td>South Korea</td>
<td>Korean National Survey for Environmental Pollutants in the Human Body</td>
</tr>
</tbody>
</table>

337 Choi J et al., 2015b.
338 Choi J et al., 2015b.
339 Choi J et al., 2015a.
340 Becker K et al., 2009; Calafat AM et al., 2011; Frederiksen H et al., 2014.
341 Choi J et al., 2015a.
Participants in HBM programmes are, usually, randomly selected adult volunteers. Children and adolescents (aged 3-12 and 13-17 years, respectively) have also participated in all of the programmes listed, with the exception of PROBE and KoSEP. FLEHS and CZ-HBM also recruited pregnant women and their newborns.

A common approach for human biomonitoring surveys, developed by the EU-funded programme ‘COPHES’, has been tested in 17 European countries. The purpose of this European-level human biomonitoring study, (and its predecessor, ‘DEMOCOPHES’) was to produce comparable data as a step towards European reference values. In line with the themes included in the EU Environment & Health Action Plan 2004-2010, the target population of the project included children aged 6-11 years and their mothers aged 45 years and under. Hair and urine samples were collected from a total of 3,688 volunteers, evenly split between urban and rural areas. Additional details on living environment, nutrition, smoking behaviour and other information were collected from the mothers through questionnaires. While methodological harmonisation and comparability of data remains a challenge for HBM in Europe, the DEMOCOPHES project demonstrates that it is possible to produce comparable data on a European scale.

In the US, the Environmental Working Group (EWG) recently conducted a review of scientific literature and publicly available human biomarker datasets, and then used this data to compile an inventory of known or likely carcinogens that have been measured in people. EWG found more than 400 known or likely carcinogens, measured across a diverse array of populations. In these cases, exposure could not solely be linked to on-the-job contact, meaning that exposure took place in a variety of environments.

---

344 EWG, 2016.
8 GAPS AND DEFICITS

On the basis of the literature review and the issues highlighted during the workshop: ‘Strategy for a Non-toxic Environment of the 7th Environment Action Programme (EAP)’, held at the Committee of the Regions on 8 and 9 June 2016, a number of gaps and deficits have been identified in relation to the protection of those groups in the population that are particularly vulnerable to the negative effects of exposure to chemicals. Different stakeholder groups had different opinions; there was no consensus on how to address the gaps on this matter.

The sections below summarise the gaps and deficits. They are structured around four themes: regulatory issues; insufficient assessment methodologies; research gaps; and information and awareness gaps.

The catalogue of available tools to respond to gaps and deficits identified in this study is a comprehensive inventory of all possible measures identified during the work of this study. The potential impacts of these tools have not been assessed as part of this study. This needs to be done in a further step, taking into account the tools identified in the better regulation agenda.

8.1 REGULATORY ISSUES

1. Lack of provisions in EU legislation defining which vulnerable groups should be ensured special protection, especially for those pieces of legislation that are of particular relevance to the protection of certain groups in society from chemical exposure.

2. Lack of references to specific windows of vulnerability; e.g., EU chemicals legislation may refer to children being a vulnerable group, but it does not distinguish between neonates, infants, toddlers and adolescents.

3. Inconsistencies in the protection of vulnerable groups in relation to specific categories of relevant chemicals legislation, e.g. legislation related to work, food, products, and environment. In each of these categories, there are pieces of legislation that consider vulnerable groups, while other legislation sharing the same objectives does not consider vulnerable groups in its provisions.

4. Annex I, part B of the Drinking Water Directive (chemical parameters) does not provide a comprehensive list of chemicals that should be considered in light of its overall aim to protect human health (and thus vulnerable groups).

5. While the current Food Contact Materials Framework Regulation allows for more particular rules to be set for any of the 17 types of food contact materials, specific EU laws have been set for only five of these 17 types. Therefore, 12 types of food contact materials are not covered by any specific legislative measures at EU level. Such rules are particularly important to consider as they usually involve more specific requirements for safety assessment and limits for the maximum migration of chemicals into the food.

6. In the absence of EU and national law, the majority of Member States do not have specific legal measures on the uses of certain phthalates or BPA in food contact materials.

7. The protection of children from harmful exposure to chemicals is sporadic at best, with a broader approach being necessary, one which takes into account their wider living environment and surroundings.

8. Chemicals having developmental neurotoxic (DNT) properties should be further regulated in order to ensure an adequate level of protection for the foetus and children.

8.2 INSUFFICIENT ASSESSMENT METHODOLOGIES AND CRITERIA

9. Assessment methodologies are not sufficient to measure the combination effects of chemical mixtures and/or environmentally induced epigenetic toxicity. This has resulted in an incomplete
picture of the disease risk, as well as the total impact that chemicals can have on different systems within the human body.

10. EU risk assessments typically focus on single substances and do not consider the risks to children and other vulnerable groups from combined exposure to toxic chemicals. Therefore, a regulatory approach for cumulative risk assessment needs to be developed.

11. Bioaccumulation effects cannot be properly measured and assessed, and thus adult onset effects resulting from early life exposures (latency period) are unknown.

12. Current risk assessment methodologies do not cater for the diverse circumstances of vulnerable populations, whose consumption patterns and exposure levels may differ significantly due to factors such as age, geographical location and lifestyle factors.

13. Certain hazards are not identified due to a lack of classification criteria and data requirements (e.g. EDCs and endocrine modulators).

14. HBM methods are unable to differentiate exposures from different sources; they currently represent a snapshot of exposure for a specific time, thus the data are subject to signification variation and may not show past exposure for short-lived substances.

15. Insufficient cooperation and linkages between risk assessment and HBM.

16. Uncertainty of test methods for screening chemicals for endocrine disrupting effects on reproductive health – the majority of such methods are based on animal models and are focused at the cellular or molecular level.

17. Lack of guidance and evidence on how to effectively perform a general risk assessment for engineered and non-engineered nanoparticles that takes into account particular risks, e.g., exposures of workers.

8.3 RESEARCH GAPS

18. Lack of knowledge of the potentially harmful effects of fragrances and phthalates contained in care products, particularly their impact on the health of female adolescents.

19. Lack of knowledge of the health impacts of the various levels of pesticides, PCBs, PAHs, plasticisers (phthalates, phenols), flame retardants, other organic xenobiotics and inorganic constituents present in furniture at home and household dust.

20. Certain substances including many pesticides and biocides have been found to have neurotoxic properties which can have major negative effects on the brains of foetuses and children. In this case, the precautionary approach should be applied.

21. Knowledge is lacking on the effects that certain toxic chemicals (e.g. NIASs and nanomaterials) can have on vulnerable groups. More research is also needed on how chemicals interfere with brain development.

8.4 INFORMATION AND AWARENESS GAPS

22. Lack of awareness of the potential toxic substances that children are exposed to through inhalation in the household, including cleaning products, home improvement supplies, gas stoves and heaters, as well as the impacts of hand-to-mouth behaviour and the likelihood that they will ingest toxic substances such as non-volatile semi-volatile chemicals, which can accumulate in household dust.

23. Lack of awareness of the impacts of indoor air pollution on the health of children and the elderly, who spend most of their times indoors.

24. Lack of awareness of the chemicals used in products such as personal care products and cosmetics, particularly those that should be avoided during pregnancy, and their associated risks.

25. Lack of awareness of chemical exposure in environments where children spend major time, such as school and playgrounds.

26. Labelling and packaging of all consumer products containing potentially harmful chemicals should be improved; this would require complete information throughout the supply chain.
27. Lack of awareness of the links between changes related to ageing (e.g. impaired vision, motor difficulties, memory problems) and increased risks for chemical exposure.
8.5 AVAILABLE TOOLS TO RESPOND TO GAPS AND DEFICITS IDENTIFIED

On the basis of the gaps and deficits described in the previous sections, a range of available tools have been identified. Some of these measures may be implemented in the short (one or two years) or medium term (three to five years), while others would need a longer time span (five years or more) as they are likely to involve new legislation or amendments to the current legislative framework.

A number of ongoing initiatives within the Commission are currently assessing the performance of chemicals legislation. These include the fitness check of all chemicals legislation except REACH and the REACH review, which are both due in 2017. The results of this study will also provide useful input to those initiatives.

The catalogue of available tools to respond to gaps and deficits identified in this study is a comprehensive inventory of all possible measures identified during the work of this study. The potential impacts of these tools have not been assessed as part of this study. This needs to be done in a further step, taking into account the tools identified in the better regulation agenda.

The following tables set out, by gap or deficit identified, a short reasoning for the gap/deficit, an overview of the possible response(s) to address the issue, a qualification of the possible response (short/medium or long term; type of measure) and a short discussion, explaining the issue and reasoning for the response in further detail.
### Table 7: Overview of gaps in legislation and the responses identified

<table>
<thead>
<tr>
<th>Gap / Deficit</th>
<th>Reason for Gap/Deficit</th>
<th>#</th>
<th>Identified Responses</th>
<th>Qualification</th>
<th>Discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of provisions in EU legislation defining which vulnerable groups should be ensured special protection, especially for those pieces of legislation that are of particular relevance to the protection of certain groups in society from chemical exposure.</td>
<td>Inadequate attention to need for special protection for certain ‘vulnerable groups’.</td>
<td>1</td>
<td>Consider including specific provisions in relevant EU acts to define any categories of vulnerable populations where special protection may be needed, particularly for those pieces of EU legislation relevant to the protection of vulnerable groups from chemical exposure.</td>
<td>Long-term, regulatory.</td>
<td>The inclusion of specific provisions clearly defining which vulnerable groups may need special protection would clarify and improve the scope of EU legislation.</td>
</tr>
<tr>
<td>Lack of references to specific windows of vulnerability; e.g. EU chemicals legislation may refer to children being a vulnerable group but do not distinguish between neonates, infants, toddlers and adolescents.</td>
<td>Not included during development of legislation.</td>
<td>2</td>
<td>Add provisions referring to specific windows of vulnerability in the EU legislation, for instance in the Directive on the safety of toys.</td>
<td>Long-term, regulatory.</td>
<td>References to specific windows of vulnerability would improve the scope of EU legislation and improve the protection of specific vulnerable groups.</td>
</tr>
<tr>
<td>Inconsistencies in the protection of vulnerable groups in relation to specific categories of relevant chemicals legislation (e.g. legislation related to work, food, products, and environment/air). In each of these categories, there are pieces of legislation that consider vulnerable groups, while other legislation with the same objectives does not consider vulnerable groups in its provisions.</td>
<td>Pieces of legislation were developed and implemented at different moments in time and in different contexts.</td>
<td>3</td>
<td>Conduct a review of the four different categories of legislation identified by this study (legislation related to work, food, products, environment/air) and explore opportunities to include references to vulnerable groups to ensure consistency.</td>
<td>Long-term, regulatory.</td>
<td>This would increase level of coherence and consistency among the different pieces of legislation, particularly those belonging to the same category, as identified during this sub-study.</td>
</tr>
<tr>
<td>Annex I, part B of the Drinking Water Directive (chemical parameters) does not provide a comprehensive list of chemicals that should be considered in light of its overall aim to protect human health (and thus vulnerable groups).</td>
<td>Research is evolving, the Directive may not be up to date.</td>
<td>4</td>
<td>Review and update the number of chemicals listed in Annex I, part B of the Drinking Water Directive, e.g. adding PFOA to the list.</td>
<td>Long-term, regulatory.</td>
<td>Adding more chemicals to Annex I, part B of the Drinking Water Directive will better protect the overall population as well as specific vulnerable groups such as the foetus, pregnant women and children.</td>
</tr>
<tr>
<td>While the current Food Contact Materials Framework Regulation allows for more particular rules to be set for any of the 17 types of food contact materials, specific EU laws have been set for only five of the 17 types. Therefore, 12 types of food contact materials are not covered by any specific legislative measures at EU level.</td>
<td>The EU Commission has not yet proposed a ‘legislative text’ to the Parliament and the Council on these matters.</td>
<td>5</td>
<td>Enact specific EU rules for the 12 types of food contact materials which are so far not covered by any specific legislative measures at EU level, starting with those where chemical contamination problems have already arisen, e.g. printing inks migrating into food, bisphenol A, fluorinated substances, and other harmful chemicals in paper/board packaging.</td>
<td>Long-term, regulatory.</td>
<td>Rules for food contact materials are important to consider as they usually involve more specific requirements for safety assessment and limits for the maximum migration of chemicals into the food.</td>
</tr>
<tr>
<td>Gap / Deficit</td>
<td>Reason for Gap/Deficit</td>
<td>#</td>
<td>Identified Responses</td>
<td>Qualification</td>
<td>Discussion</td>
</tr>
<tr>
<td>------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>----</td>
<td>--------------------------------------------------------------------------------------</td>
<td>------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>In the absence of an EU and national specific legal framework, the majority of Member States do not have specific legal measures on the food contact uses of certain phthalates and BPA.</td>
<td>Lack of specific framework for FCMs using BPA or certain phthalates.</td>
<td>7</td>
<td>Further harmonise EU legislation governing FCMs, in particular the provision concerning certain phthalates and BPA.</td>
<td>Long-term, regulatory.</td>
<td>Harmonised measures at EU level will better protect the general population, as well as vulnerable groups.</td>
</tr>
<tr>
<td>The protection of children from harmful exposure to chemicals is sporadic and a wider approach is required, taking into account their wider living environment and surroundings.</td>
<td>Research is evolving, EU legislation may not be up to date.</td>
<td>8</td>
<td>Extend the Toys Directive regime to cover all products aimed particularly at children, such as furniture, bedding, clothing.</td>
<td>Long-term, regulatory.</td>
<td>A more comprehensive scope of protection of children is required to ensure minimal exposure to chemicals.</td>
</tr>
<tr>
<td>Chemicals having developmental neurotoxic (DNT) properties should be further regulated in order to ensure an adequate level of protection for foetus and children.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Although the EU Toys Directive provides standards to protect children as a vulnerable group, other consumer products aimed at children such as clothing and bedding are not covered.</td>
<td>Research is evolving, EU legislation may not be up to date.</td>
<td>8</td>
<td>Extend the Toys Directive regime to cover all products aimed particularly at children, such as furniture, bedding, clothing.</td>
<td>Long-term, regulatory.</td>
<td>A more comprehensive scope of protection of children is required to ensure minimal exposure to chemicals.</td>
</tr>
<tr>
<td>Assessment methodologies are not sufficient to measure the combination effects of chemical mixtures and/or environmentally induced epigenetic toxicity.</td>
<td>New area, not much evidence and research available yet.</td>
<td>10</td>
<td>Encourage further research on the health effects stemming from multiple exposures of chemicals as well as epigenetic toxicity.</td>
<td>Mid-term, research.</td>
<td>New research could help to establish a complete picture of the disease risks, as well as the total impact that chemicals can have on different systems within the human body.</td>
</tr>
<tr>
<td>EU risk assessments typically focus on single substances and do not consider the risks to children and other vulnerable groups from combined exposure to toxic chemicals.</td>
<td>Lack of data</td>
<td></td>
<td>Develop a regulatory approach for cumulative risk assessment</td>
<td>Mid-term, research.</td>
<td>Although specific framework for assessing the combination effects of chemicals are being used, a comprehensive approach across different legislation is still not in place. Developing the appropriate framework can thus guarantee better protection of vulnerable groups stemming from the combination effects of chemicals.</td>
</tr>
<tr>
<td>Safety testing of chemicals often do not include evaluation of developmental neurotoxic (DNT) properties</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 8: Overview of gaps in risk assessment methodologies and criteria and the responses identified
<table>
<thead>
<tr>
<th>Gap / Deficit</th>
<th>Reason for Gap/Deficit</th>
<th>#</th>
<th>Identified Responses</th>
<th>Qualification</th>
<th>Discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioaccumulation effects cannot be properly measured and assessed, and thus adult onset effects resulting from early life exposures (latency period) are unknown.</td>
<td>New area, not much evidence and research available yet.</td>
<td>11</td>
<td>Encourage further research on bioaccumulation effects.</td>
<td>Mid-term, research.</td>
<td>New research could help to establish a complete picture of the disease risks, as well as the total impact that chemicals can have over a lifetime.</td>
</tr>
<tr>
<td>Current risk assessment methodologies do not cater for the diverse circumstances of vulnerable populations, whose consumption patterns and exposure levels may differ significantly due to factors such as age, geographical location and lifestyle factors.</td>
<td>Complex issue, difficult to capture wide range of elements.</td>
<td>12</td>
<td>Develop risk assessment methodologies that consider aspects such as: exposure levels and scenarios; age; consumption patterns; behavioural characteristics; geographical location; lifestyle factors; cultural differences.</td>
<td>Long-term, regulatory.</td>
<td>While it is a difficult task to take such wider elements into consideration, risk assessment methods would significantly improve.</td>
</tr>
<tr>
<td>Certain hazards are not identified due to a lack of classification criteria and data requirements (e.g. EDCs, endocrine modulators, and developmental neurotoxicants).</td>
<td>Complex issue, and hazard assessment methods might not be sufficient to identify a property of very high concern and/or might not be available.</td>
<td>14</td>
<td>Inclusion of new hazard categories in relevant EU regulations (CLP, REACH).</td>
<td>Long-term, regulatory.</td>
<td>New hazard categories would improve information availability (hazards identified and communicated).</td>
</tr>
<tr>
<td>Human biomonitoring methods are unable to differentiate exposures from different sources; they currently represent a snapshot of exposure for a specific time and the data are subject to signification variation and may not show past exposure for short-lived substances.</td>
<td>Complex issue, requires new research.</td>
<td>15</td>
<td>Produce a comprehensive, longitudinal, human data bank, including:</td>
<td>Mid-term, research.</td>
<td>Harmonising the wealth of data and evidence available may facilitate progress in this important area.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Harmonised environment and health indicators;</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- HBM data and human tissue measurements translated into daily exposure estimates;</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- HBM data that reflects the total exposure from all sources, and complement this with data on individual susceptibility based on gender, age,</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Further strengthen the link between risk assessment and HBM

<table>
<thead>
<tr>
<th>Reason for Gap/Deficit</th>
<th>Identified Responses</th>
<th>Qualification</th>
<th>Discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>It exists but there are opportunities to improve.</td>
<td>Ensure that HBM plays a role in several stages of risk assessment, from hazard identification and characterisation to risk characterisation and exposure assessment.</td>
<td>Long-term, regulatory.</td>
<td>HBM can be a valuable source of complementary information. Its main strength is to the ability to identify vulnerable groups and populations with higher exposures and emerging chemical risks, as well as establish the distribution of exposure among the general population.</td>
</tr>
</tbody>
</table>

Lack of availability of test methods for screening chemicals for endocrine-disrupting effects on reproductive health.

<table>
<thead>
<tr>
<th>Identified Responses</th>
<th>Reasons for Deficit</th>
<th>Qualification</th>
<th>Discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test methods are currently mainly based on animal models and focused at the cellular or molecular level.</td>
<td>Explore innovative methods in order to test the effects of EDCs, particularly low doses of EDCs, on human health.</td>
<td>Mid-term, research.</td>
<td>This would result in better protection of reproductive health across the life-cycle.</td>
</tr>
</tbody>
</table>

Lack of guidance and evidence on effective general risk assessment for engineered and non-engineered nanoparticles.

<table>
<thead>
<tr>
<th>Identified Responses</th>
<th>Reasons for Deficit</th>
<th>Qualification</th>
<th>Discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encourage further research on the development of new risk assessment methods on engineered and non-engineered nanoparticles.</td>
<td>Relatively new area; needs to be explored further.</td>
<td>Mid-term, research.</td>
<td>This is a relatively new area and a lot of uncertainty exists about the risks of (non)engineered nanoparticles.</td>
</tr>
</tbody>
</table>

Lack of knowledge on the potentially harmful effects of fragrances and phthalates contained in care products and particularly their impact on the health of female adolescents.

<table>
<thead>
<tr>
<th>Identified Responses</th>
<th>Reasons for Deficit</th>
<th>Qualification</th>
<th>Discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encourage further research on the potential harmful effects of chemicals used in care products (e.g. phthalates, parabens, triclosan and oxybenzone), particularly for the health of female adolescents.</td>
<td>Research area so far not yet explored (extensively).</td>
<td>Mid-term, research.</td>
<td>Will help to build the evidence around the potential harmful effects of chemicals used in care products.</td>
</tr>
</tbody>
</table>

Lack of knowledge of the health impacts of the various levels of pesticides, PCBs, PAEs, plasticisers (phthalates, phenols), flame retardants, other

<table>
<thead>
<tr>
<th>Identified Responses</th>
<th>Reasons for Deficit</th>
<th>Qualification</th>
<th>Discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encourage research into the possible health implications of chemicals in household dust, particularly for young</td>
<td>Research area so far not yet explored (extensively).</td>
<td>Mid-term, research.</td>
<td>Will help to build the evidence around the potential harmful effects of chemicals present in household dust.</td>
</tr>
</tbody>
</table>

Table 9: Overview of gaps in research and evidence and the responses identified
**organic xenobiotics and inorganic constituents present in furniture at home and household dust.**

**Certain substances including many pesticides and biocides have been found to have neurotoxic properties which can have major negative effects on the brains of foetuses and children. In this case, the precautionary approach should be applied.**

**Knowledge is lacking on the effects that certain toxic chemicals (e.g. NIASs and nanomaterials) can have on vulnerable groups. More research is also needed on how chemicals interfere with brain development.**

<table>
<thead>
<tr>
<th>Gap / Deficit</th>
<th>Reason for Gap/Deficit</th>
<th>#</th>
<th>Identified Responses</th>
<th>Qualification</th>
<th>Discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of awareness of the potential toxic substances that children are exposed</td>
<td>Evidence not known among wider audience.</td>
<td>23</td>
<td>Awareness raising about chemicals in household products and how to avoid exposure</td>
<td>Short-term,</td>
<td>Will help to raise awareness and knowledge among policy makers and the general public, particularly parents, of the</td>
</tr>
<tr>
<td>to through inhalation in the household, including cleaning products, home</td>
<td></td>
<td></td>
<td>of heavily treated textiles, including stain-resistant treatments for carpets and</td>
<td>awareness</td>
<td>potential dangers of toxic substances in the household and how their child(ren) can be exposed to these. May also</td>
</tr>
<tr>
<td>improvement supplies, gas stoves and heaters, as well as the impact of</td>
<td></td>
<td></td>
<td>furniture, as well as the positive impact of frequent handwashing, vacuuming, etc.</td>
<td>raising.</td>
<td>support the implementation of prevention measures.</td>
</tr>
<tr>
<td>hand-to-mouth behaviour and the likelihood that children will ingest toxic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>substances, such as non-volatile semi-volatile chemicals, which can</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>accumulate in household dust.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lack of awareness of the impact of indoor air pollution on the health of</td>
<td>Research area so far not yet explored (extensively).</td>
<td>24</td>
<td>Explore ways to reduce chemicals in indoor environments where the elderly live,</td>
<td>Short-term,</td>
<td>Will help to raise awareness among policy makers and the general public on the potential dangers of indoor air</td>
</tr>
<tr>
<td>children and the elderly, who spend most of their times indoors.</td>
<td></td>
<td></td>
<td>e.g., through better ventilation systems.</td>
<td>awareness</td>
<td>pollution, particularly for children and the elderly. May also support the implementation of prevention measures.</td>
</tr>
<tr>
<td>Lack of awareness of chemicals used in products such as personal care</td>
<td>Evidence not known among wider audience.</td>
<td>25</td>
<td>Educate women, particularly those who are pregnant or of child-bearing age, about</td>
<td>Short-term,</td>
<td>Will help to raise awareness among policy makers and the general public, particularly women who are pregnant or of</td>
</tr>
<tr>
<td>products and cosmetics, particularly those that should be avoided during</td>
<td></td>
<td></td>
<td>chemicals and products to avoid, e.g. personal care products with phthalates,</td>
<td>awareness</td>
<td>child-bearing age, on the</td>
</tr>
<tr>
<td>pregnancy, and their associated risks.</td>
<td></td>
<td></td>
<td>deodorant with aluminium</td>
<td>raising.</td>
<td></td>
</tr>
</tbody>
</table>

Table 10: Overview of gaps in awareness raising and information distribution and the responses identified
<table>
<thead>
<tr>
<th>Gap / Deficit</th>
<th>Reason for Gap/Deficit</th>
<th>#</th>
<th>Identified Responses</th>
<th>Qualification</th>
<th>Discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of awareness of the chemical exposure in environments where children</td>
<td>Evidence not known among wider audience.</td>
<td>26</td>
<td>Make schools, playgrounds and other areas where children spend major time into</td>
<td>Long-term, regulatory.</td>
<td>Will help to raise awareness among policy makers and the general public on the potential dangers of chemicals in children’s daily environments. May also support the implementation of prevention measures.</td>
</tr>
<tr>
<td>spend major time, such as school and playgrounds.</td>
<td></td>
<td></td>
<td>chemical-free zones</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Labelling and packaging of all consumer products containing potentially</td>
<td>Lack of awareness among consumers as well as producers.</td>
<td>27</td>
<td>Information and labelling of the content of products should be ensured across the</td>
<td>Short-term, awareness raising.</td>
<td>Will help to increase knowledge on the content of products across the entire supply chain among consumers and producers. May also support the implementation of prevention measures.</td>
</tr>
<tr>
<td>harmful chemicals should be improved; this would require complete information</td>
<td></td>
<td></td>
<td>entire supply chain; this would improve awareness of consumers as well as producers.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>throughout the supply chain.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lack of awareness of the links between changes related to ageing (e.g.,</td>
<td>Research area so far not yet explored (extensively).</td>
<td>29</td>
<td>Raise awareness of the impact of an ageing population and the increased risk of</td>
<td>Short-term, awareness raising.</td>
<td>Will help to increase awareness among the general public and policy makers on the need to address the risks related to population ageing and chemical exposure. May also support the implementation of prevention measures.</td>
</tr>
<tr>
<td>impaired vision, motor difficulties, memory problems) and increased risks of</td>
<td></td>
<td></td>
<td>chemical exposure, as well as increased levels of chemical-related health problems</td>
<td></td>
<td></td>
</tr>
<tr>
<td>chemical exposure.</td>
<td></td>
<td></td>
<td>due to rising life expectancy.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Potential dangers of chemicals used in personal care products. May also support the implementation of prevention measures.
9 CONCLUSIONS

This report outlines the particular vulnerability of certain population groups in the population, such as the foetus, children, pregnant women, elderly, occupational groups and disadvantaged communities, to chemical exposure. Whether the impacts of exposures are visible at birth or later in life, consensus is broad that such vulnerable groups need to be provided with a high level of protection in respect of their exposure to chemicals, as stated in the 7th EAP. Yet, despite the policy and legislative measures and other activities put in place, significant improvement opportunities exist to augment the protection of children and vulnerable groups from harmful chemical exposure.

Chemicals and their impact on health is a matter that affects a multitude of regulatory areas. Numerous pieces of EU legislation thus incorporate measures with the objective of (also) protecting children or other vulnerable groups from toxic exposure. However, provisions referring to vulnerable groups are often lacking or inconsistent between similar types of legislation. In particular, the study highlighted that where relevant, the EU legislation should include provisions defining any vulnerable population groups where special protection should be ensured. Other areas that could be considered in EU legislation are the specific windows of vulnerability that exist for certain groups, as well as ensuring a consistent reference to vulnerable groups within specific groups of legislation that offer a certain type of protection (e.g. at the workplace, or in relation to food). In addition, the study shows that certain EU legislation, such as the Drinking Water Directive and Food Contact Materials Framework Regulation, are not updated with the most relevant scientific evidence and lack specific measures which can strengthen the protection of vulnerable groups.

Challenges also exist with respect to chemical risk assessment for vulnerable groups. In particular, current risk assessments typically focus on single substances and do not consider the risks to children and other vulnerable groups from combined exposure to toxic chemicals. Therefore, a regulatory approach for cumulative risk assessment needs to be developed. The ‘early exposure – late effect’ pattern linked to, for example, endocrine-disrupting substances, poses specific difficulties for risk assessors. Bioaccumulation effects cannot yet be properly measured and assessed, and thus adult onset effects resulting from early life exposures (latency period) are unknown. The risks of chemical mixtures, new substances such as nanomaterials, and environmentally induced epigenetic toxicity are areas that need further attention. Despite the value of HBM, current methods are unable to differentiate exposures from different sources and they therefore only represent a snapshot of exposure for a specific time. These data are also subject to significant variation and may not show past exposure for short-lived substances.

While a wealth of information and evidence on the impacts of chemicals on specific vulnerable populations has been collected in recent decades, significant knowledge gaps remain. The scientific community has had the tendency to consistently focus on the same substances (e.g. copper, lead, zinc, cadmium, iron, nickel, chromium, etc.) when studying the harmful effects of chemicals, and there is a need to further extend this scope and study new areas, such as the non-intentionally added substances, nanomaterials, as well as on the potentially harmful effects of certain neurotoxicants on brain development. During sensitive early life stages, exposure to EDCs and neurotoxins - such as lead, arsenic, mercury, PCBs, pesticides, and solvents - can cause lifelong damages, and therefore further research on the impact of chemicals on the brain is of paramount importance.

Finally, the study shows the need to develop communication strategies targeting the general public and specific vulnerable groups on how to reduce exposure from certain toxic compounds (i.e. household dust) and classes of chemicals (EDCs and neurotoxicants), as well as on how to avoid certain harmful behaviours (i.e. hand to mouth). Improving labelling and packaging of consumer products would also help to increase knowledge on the potential harmful effects of exposure to certain ingredients or compounds.
REFERENCES

LITERATURE AND WEBPAGES


(accessed November 2016).


Bearer C.F., 1995, ‘How are children different from adults?’, Environ Health Perspect, 103:7-12.


at: http://doi.org/10.3390/ijerph13050495


January 2017)


### ACTS & OFFICIAL DOCUMENTS FROM INTERNATIONAL AND EUROPEAN INSTITUTIONS


LEGISLATION RELEVANT TO CHEMICALS AND VULNERABLE GROUPS


OTHER LEGISLATION CONSIDERED


Europe Direct is a service to help you find answers to your questions about the European Union.

Freephone number (*):

00 800 6 7 8 9 10 11

(*) The information given is free, as are most calls (though some operators, phone boxes or hotels may charge you).

LEGAL NOTICE
This document has been prepared for the European Commission however it reflects the views only of the authors, and the Commission cannot be held responsible for any use which may be made of the information contained therein.


ISBN [number]
doi:[number]

© European Union, 2014

Printed in [Country]

PRINTED ON ELEMENTAL CHLORINE-FREE BLEACHED PAPER (ECF)
PRINTED ON TOTALLY CHLORINE-FREE BLEACHED PAPER (TCF)
PRINTED ON RECYCLED PAPER
PRINTED ON PROCESS CHLORINE-FREE RECYCLED PAPER (PCF)

Image(s) © [artist's name + image #], Year. Source: [Fotolia.com] (unless otherwise specified)
How to Obtain EU Publications

**Free publications:**
- one copy:
  via EU Bookshop (http://bookshop.europa.eu);
- more than one copy or posters/maps:
  from the European Union’s representations (http://ec.europa.eu/represent_en.htm);
  from the delegations in non-EU countries (http://eeas.europa.eu/delegations/index_en.htm);
  by contacting the Europe Direct service (http://europa.eu/europedirect/index_en.htm) or calling 00 800 6 7 8 9 10 11 (freephone number from anywhere in the EU) (*).

(*) The information given is free, as are most calls (though some operators, phone boxes or hotels may charge you).

**Priced publications:**

**Priced subscriptions:**