



EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate D - Food Safety: Production and distribution chain
Unit D.3 - Chemicals, contaminants and pesticides

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Guidance document on preparation of lists of studies relied upon with a view to Annex I – inclusion of existing active substances

This document has been conceived as a working document of the Commission Services, which was elaborated in co-operation with the Member States. It does not intend to produce legally binding effects and by its nature does not prejudice any measure taken by a Member State within the implementation prerogatives under Annex II, III and VI of Council Directive 91/414/EEC, nor any case law developed with regard to this provision. This document also does not preclude the possibility that the European Court of Justice may give one or another provision direct effect in Member States.

1. Introduction

In light of experience gained following the inclusion in Annex I of Directive 91/414/EEC of existing active substances reviewed as part of the first stage of the review programme; and in order to ensure the efficient administration of the re-registration process following the inclusion; this document provides guidance for the 2nd – 4th Stages of the review programme on:

- the preparation and updating of the list of Annex II and III data which during the re-evaluation process were considered as relied upon for the evaluation with a view to Annex I inclusion of a reviewed active substance
- the preparation of the list of Annex II data for which the main submitter has claimed protection and which during the re-evaluation process were considered as relied upon for the evaluation with a view to Annex I inclusion of a reviewed active substance
- the procedure for verification that listed studies are eligible for data protection
- the process for making the lists publicly available from an early stage in the procedure, updating them during the procedure and finalising them at the time of the decision on the active substance.

2. Responsibilities of the notifier during preparation of the dossier and if data are submitted subsequent to the dossier

When preparing the dossier the notifier, in accordance with the guidance document on the preparation of the dossier¹ should annotate the listing of individual test and study reports to indicate whether or not data protection is claimed in accordance with the requirements of Article 13(3) d of the Directive.

Subsequently if additional data are submitted notifiers should at the same time update the list of studies and send it to the RMS.

3. Responsibilities of the RMS during preparation of the DAR

The Commission regulations laying down the rules for the review programme for existing substances require that the rapporteur Member State include in the Draft Assessment Report (DAR):

- a reference to each test and study for each Annex point relied on for the assessment in the form of a list including the title, author(s), date of study, standard to which the study was conducted, holders name and, if any, the claim made for data protection.

¹ Guidelines and Criteria for the Preparation and Presentation of Complete Dossiers and of Summary Dossiers for the Inclusion of Active Substances in Annex I of Directive 91/414/EEC (Article 5.3 and 8.2). Document 1663/VI/94 Rev 8, 22 April 1998 (since 01 January 2005 replaced by OECD Dossier Guideline)

This is further elaborated in the guidance document for preparation of DARs² which requires two lists of tests and studies to be prepared:

- Annex A (Volume 2) is a list of all information, tests and studies submitted
- Annex B (Volume 3), at the end of each chapter, a list is required of information, tests and studies relied on together with any claims for data protection made by the notifier

It should also be noted that the structure for the DAR ensures that all confidential information is reported in the separate volume 4. It should be ensured that the study lists themselves do not contain confidential information such as names of impurities.

To ensure that these responsibilities are standardised as far as possible the following **criteria** should be used.

For the lists provided in Annex A.

Annex A should include all test and study reports and published papers submitted in support of the application and should include other relevant information available to, or brought to the attention of, the RMS. Detailed guidance is given at 4.5 of the guidance document for preparation of DARs.

For the lists provided in Annex B.

The lists provided in Annex B should be compiled having careful regard for the results of the evaluation and assessment(s) of the dossier submitted.

In order to ensure scientifically unacceptable studies are not included in the list of studies relied on it is expected that the RMS will conduct and present a summary, evaluation and assessment of each study. Detailed guidance is given at 4.6 of the guidance document for preparation of DARs.

In particular it is expected that for each study the evaluation presented in Annex B will contain a brief statement as to the acceptability of the study. In the case of it not being of acceptable quality, a concise statement of the rationale used in reaching that conclusion must be included, having regard to both information contained in the study report and information not so included.

The decision on the acceptability of studies should take into account:

- the applicability of GLP principles
- the acceptability of any justification provided for non-compliance with the principles of GLP, e. g. studies initiated before July 1993 or before 31 December 1997 for supervised trials or 31 December 1999 for studies on honey-bees and beneficial arthropods
- the suitability of the test method used, having regard to the justification provided for use of methods other than those specified in Annex II and Annex III of Directive 91/414/EEC

² Guidelines and Criteria for the Evaluation of Dossiers and for the Preparation of Reports to the European Commission by the Rapporteur Member States Relating to the Proposed Inclusion of Active Substances in Annex I of Directive 91/414/EEC. Document 1654/VI/94, rev 7, 22 April 1998 (in cases where the Dossier is submitted in OECD-format the DAR should be prepared following OECD-format too).

- where there are deviations from the test guidelines specified, or from other methods used, the suitability of the test method actually used, having regard to the justification provided for the deviations concerned
- where the identity of the test substance or material has not been adequately specified, or its stability in dosing vehicles or solvents used is questionable, the reliability or usefulness of the test or study concerned.

Only information, tests and studies regarded as being scientifically acceptable should be considered for inclusion in the lists provided in Annex B. Information, tests and studies included in the list are those without which it would not be possible to come to a decision on the inclusion of the active substance in Annex I of Directive 91/414/EEC having regard to:

- the criteria specified in Article 5 of Directive 91/414/EEC
- the extent that they are relevant, in the context of the supported representative uses, the evaluative and decision making criteria specified in Annex VI of Directive 91/414/EEC

The list would therefore include all appropriate Annex II and Annex III studies required for inclusion of the substance. It should be noted that:

- higher tier studies which have been provided to refine the risk assessment, for example mesocosm studies and operator biomonitoring studies, should be included. However specific care should be taken to attribute such data to the correct Annex (that is Annex II or Annex III).
- acceptable studies which, alone, do not address fully a particular requirement or concern identified in the context of inclusion in Annex I but together contribute to a weight of evidence approach (extent, quality and consistency of data available) should all be included.
- modelling data presented as study reports should be included.

The following should not appear in the list

- studies which are identified in the DAR as being of unacceptable quality.
- studies that are clearly not relevant to the assessment in the context of the supported representative uses in the dossier.
- studies that address a specific Member State's concern and are not a point of Annex II or III.

4. Procedure for finalising and making available the list of *information, tests and studies relied upon during the EFSA process*

- 4.1. The RMS should prepare the list of all references relied upon as a stand alone document and send it to EFSA at the same time as he submits the DAR. The list should be taken from Appendix B of the DAR and the following header added:

List of information, tests and studies which are considered as relied upon by the RMS for the evaluation with a view to Annex I inclusion

Version 1 –information, tests and studies relied upon by the RMS and identified in the Draft Assessment Report [date]

- 4.2. EFSA conducts a quality check on receipt of the DAR. In conducting this check EFSA might identify that the list of studies relied upon by the RMS is not of appropriate quality or has deficiencies or discrepancies which may necessitate revision or reconsideration of the list. However it should be noted that the quality check does not examine the DAR in depth and is not guaranteed to identify all problems with the study lists.
- 4.3. The list should be put on CIRCA by the EPCO-Team (BVL). This should be done at the same time as the DAR is circulated.
- 4.4. If, and when, additional information, tests and studies are evaluated then - if they are relied upon - these should be added to the list by the RMS, together with any claim for data protection, sent to EFSA and EPCO and updated on CIRCA via EPCO. This should be done at the same time as the addendum containing the additional evaluation is submitted.
- 4.5. If studies are added to or deleted from the list in accordance with the EFSA peer review, the RMS should send the revised version of the list to EFSA and EPCO to be updated on CIRCA by EPCO.

- 4.6. Additions, modifications or deletions should be indicated to facilitate traceability (e.g. track change)

- 4.7. With each addition or change to the list the header is updated:

List of information, tests and studies which are considered as relied upon for the evaluation with a view to Annex I inclusion

Version 2.X – information, tests and studies identified in the Draft Assessment Report [date] as relied upon and finalised during Peer Review [date]

- 4.8. EFSA will include the final version of this list in their conclusion to the Commission. It should be put on CIRCA by the ECCO-Team (BVL).

5. Procedure for finalising and making available the list of Annex II studies relied upon and for which data protection has been claimed by the main data submitter

- 5.1. Once the conclusion from EFSA has been received European Commission should via ECCO ask the RMS to amend the Version 2.X to delete all Annex II studies for which data protection has not been claimed by the main data submitter and to delete all Annex III studies and published references too.

The header is updated to:

***List of Annex II studies which were considered as relied upon for the evaluation with a view to Annex I inclusion and for which the main submitter has claimed data protection, Version 1 – [date]
(format see Appendix 1)***

- 5.2. Prior to Annex I inclusion the notifier will be asked by the RMS to check this list and make a declaration that in relation to the studies for which data protection has been claimed -

- None of the studies have been the basis of a decision on the initial authorisation, or to maintain a given authorisation, of a plant protection product in any Member State prior to their submission to support inclusion (i. e. the date of dossier submission), or to vary or maintain the inclusion, of the active substance in Annex I.
- None of the studies for which protection is claimed are simply re-interpretation of older studies e. g. re-interpretation in accordance with currently used evaluation and/or scoring systems (for example irritancy studies) or re-interpretation following re-examination of histopathological slides from the original study (for example carcinogenicity studies).

When contacting the main data submitter the RMS can draw to their attention any claims for protection which they consider to be doubtful, for example for very old studies or studies which are known, or suspected, to have been used for national authorisations.

- 5.3. At the time of Annex I inclusion the header of the table is updated to:

List of Annex II studies which were considered as relied upon for the evaluation with a view to Annex I inclusion and for which the main data submitter has claimed data protection, Version 2 – final [date]

(format see Appendix 1).

5.4. The finalised list is put on CIRCA by the ECCO-Team (BVL) and Commission website is updated with the final list being provided alongside the finalised Review Report.

Appendix 1

ACTIVE SUBSTANCE

List of **Annex II studies** which were considered
as relied upon for the evaluation with a view to Annex I inclusion
and for which the main submitter has claimed data protection

Version x - (date)

B.1 Identity, B.2 Physical and chemical properties, B.3 Data on application and further information, B.4 Proposals for classification and labelling, B.5 Methods of analysis

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not	Reports ³ on previous use in granting national authorizations

B.6 Toxicology and metabolism

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not	Reports on previous use in granting national authorizations

B.7 Residue data

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not	Reports on previous use in granting national authorizations

³ Entries are based on information received from the main data submitter and in certain cases Member States. Neither the Commission nor the Member States are responsible for the completeness or validity of this information received.

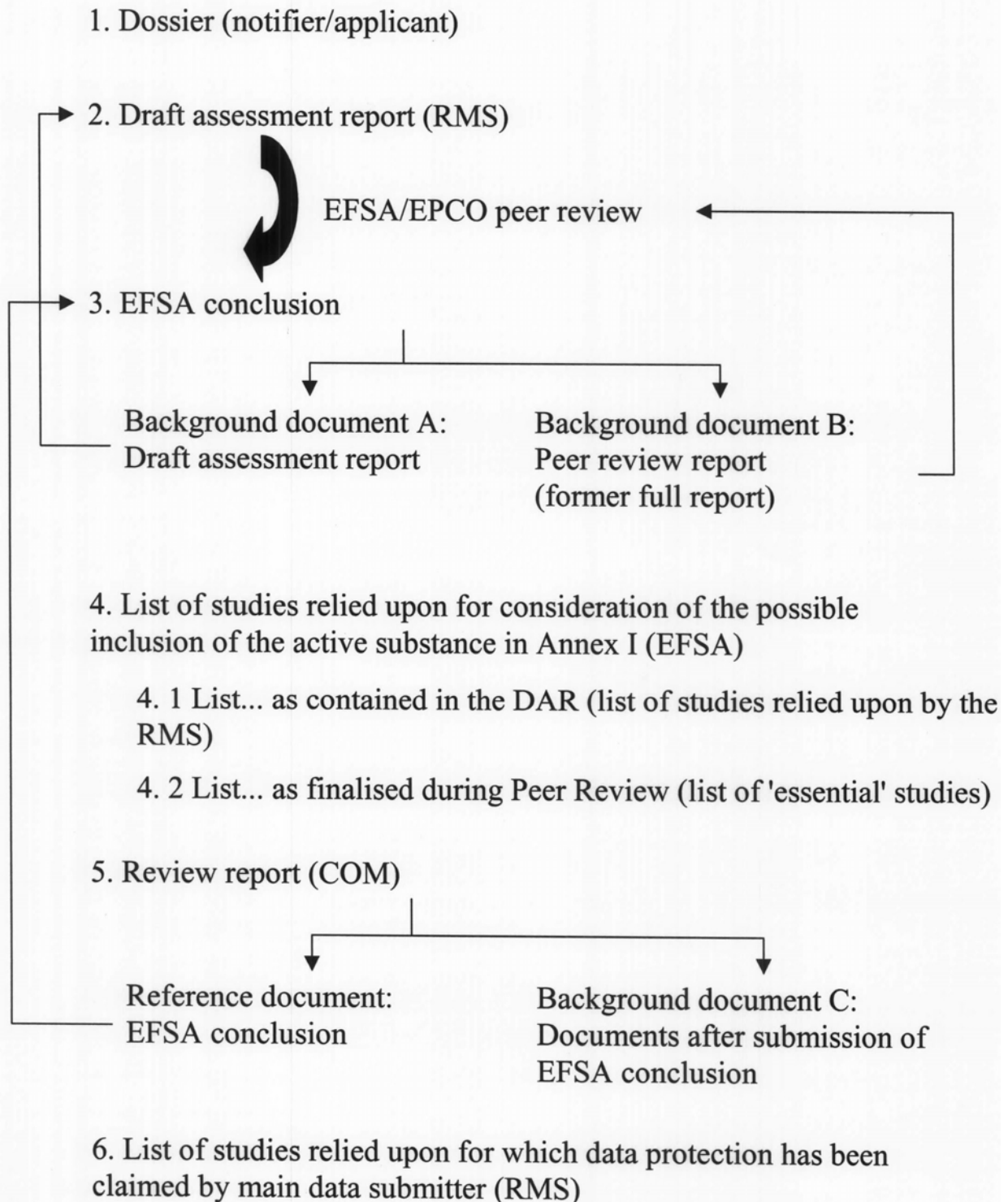
B.8 Environmental fate and behaviour

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not	Reports on previous use in granting national authorizations

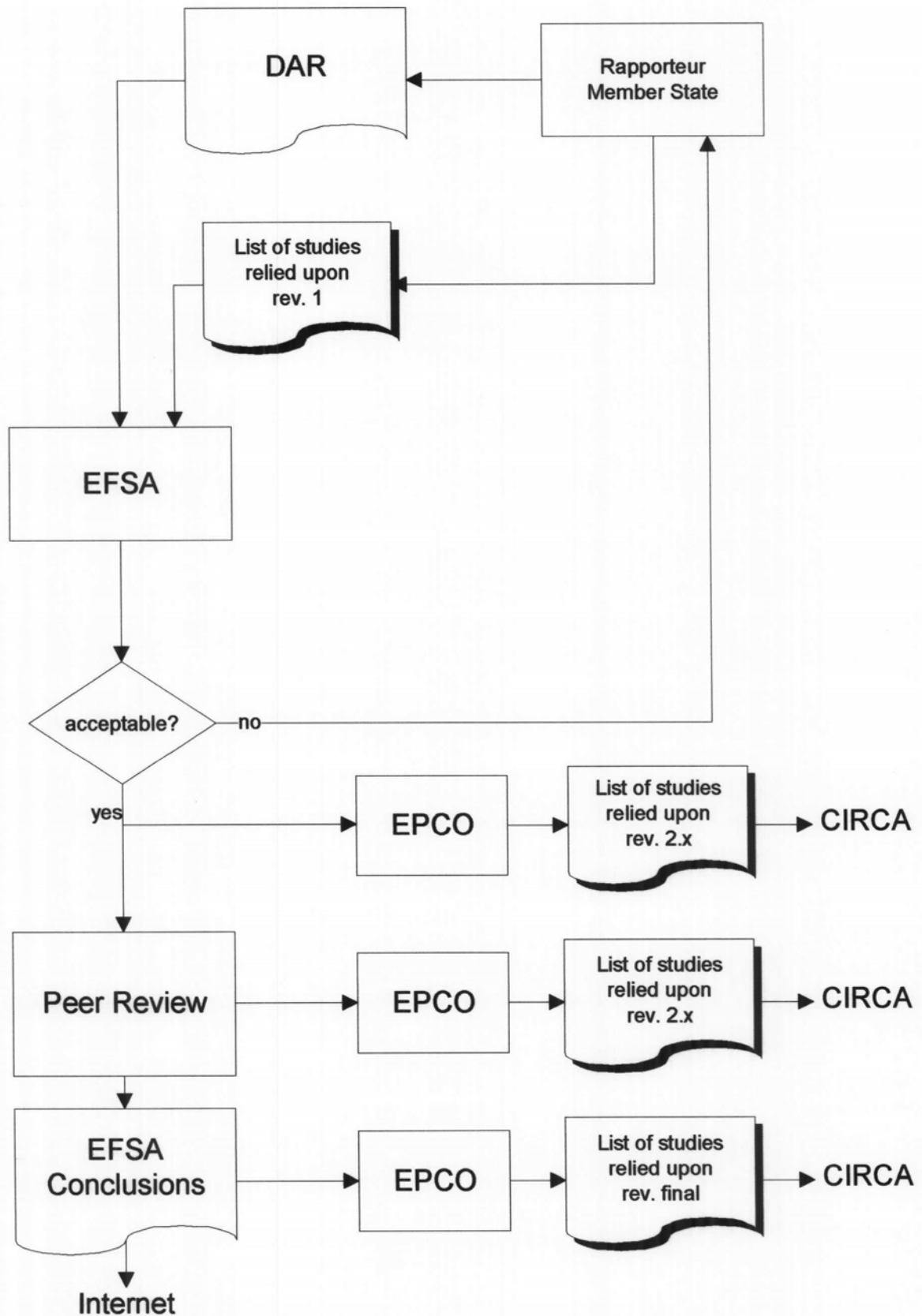
B.9 Ecotoxicology

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not	Reports on previous use in granting national authorizations

Documentation for 2nd stage active substances



Procedure for finalising and making available the list of studies relied upon during the EFSA process



**Procedure for finalising and making available
the list of Annex II studies relied upon and
for which data protection has been claimed by the main data submitter**

