

**Technical Notes for Guidance
on
Dossier Preparation
including preparation and evaluation of
study summaries
under Directive 98/8/EC
Concerning the Placing of
Biocidal Products on the Market**

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Short Title: TNsG on Preparation of Dossiers and Study Evaluation

**PART II
CA Reports Preparation and Presentation**

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The Technical Notes for Guidance on Dossier Preparation including preparation and evaluation of study summaries that were previously published as individual chapters on the ECB website were formatted and edited in three individual parts in pdf format.

Part II: Technical Notes for Guidance for the Preparation and Presentation of Reports by Competent Authorities Relating to the Decision on the Inclusion of Active Substances in Annex I, IA or IB of Directive 98/8/EC or for Authorisation or Registration of Biocidal Products

(CAs' Report Guidance)

Contents

1	General Introduction	3
1.1	Background	3
1.2	Objective of the CAs' report guidance	4
1.2.1	Whom the guidance is for	4
1.2.2	Standardisation of CAs' report preparation	4
1.3	Principles of guidance given	5
1.4	Reference documents to be consulted	5
2	Documentation Required for a CA's Report	6
2.1	Introduction	6
2.2	CA's report structure and content	7
3	Check for Completeness	9
3.1	Check for completeness of documentation	9
3.2	Check for completeness and quality of data	9
3.3	Literature search	10
3.4	Representative check of selected data	10
3.5	Outcome of completeness check	10
4	Document III - STUDY SUMMARIES	11
4.1	Purpose	11
4.2	All-in-one approach: use of applicant's study summaries by the rapporteur member state	11
4.2.1	Principles	11
4.2.2	Outcome	13
4.3	Confidential data and information	14
5	Document II - Risk Assessment	15
6	Document I - Evaluation Report	15
6.1	Subdocument I.1: Statement of subject matter and purpose	15
6.2	Subdocument I.2: Overall summary and conclusions	16
6.3	Subdocument I.3: Proposal for the decision	16
6.4	Listing of end points	17

7	Submission of CAs' Report to Commission, Member States and Applicant	18
8	Standard Units, Terms and Abbreviations	18
9	CAs' Report Relating to the Application for Authorisation of Biocidal Products	19

1 GENERAL INTRODUCTION

According to Article 11 of the BPD, the competent authority(ies) (CAs) receiving the application carry out an evaluation of the applicant's dossiers. This evaluation is called "CAs' report" in this document. The guidance given here primarily addresses the inclusion of active substances in Annex I, IA or IB of Directive 98/8/EC (BPD). For the documentation to be prepared by the CA with respect to applications for authorisation of biocidal products, see chapter 9. Due to the similar approaches for the structure of both the dossier and the CA's report, only specific aspects related to the CA's report are presented here. Parts already covered by the Dossier guidance in Part I of this document are referenced in order to avoid repetition.

This Technical Note for Guidance only refers to chemical substances and not to biocidally active fungi, micro-organisms and viruses (Annex IVA, IVB of BPD).

1.1 BACKGROUND

According to Article 11.1(a) of BPD, an applicant seeking the inclusion of an active substance in Annex I, IA or IB of BPD has to submit to the competent authority of one of the Member States:

- "a dossier for the active substance satisfying... the requirements of Annex IIA and, where specified, the relevant parts of Annex IIIA";
- "a dossier for at least one biocidal product containing the active substance satisfying the requirements of Article 8, with the exception of paragraph 3 thereof".

In accordance with Article 11 of BPD, the competent authority receiving the application, has to:

- verify the dossiers in terms of completeness with the requirements set out in Annexes IIA and IIB and, where relevant, in Annexes IIIA or IIIB of the BPD;

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- carry out an evaluation of the applicant's dossiers and prepare a report together with a recommendation for the inclusion, or otherwise, of the active substance in Annex I, IA or IB.

Article 11(3) states that the evaluation can be carried out by Member States other than the receiving one. The term 'Rapporteur Member State (RMS)' (or simply 'Rapporteur') used in this TNsG refers to the Member State evaluating the dossier.

The term dossier may have been used both in singular and plural form in the TNsG, and may cover the submission of the information both for the active substance and products.

1.2 OBJECTIVE OF THE CAs' REPORT GUIDANCE

1.2.1 Whom the guidance is for

The CAs' Report Guidance is intended for use by the competent authorities of the Rapporteur Member State preparing a report of their evaluation of dossier submitted concerning:

- the application for the inclusion of a new active substance in Annex I, IA or IB to BPD;
- the application for the inclusion of an existing active substance in Annex I, IA or IB to BPD;
- the modification or removal of conditions or restrictions associated with the inclusion of an active substance already included in Annex I, IA or IB;
- the extension of use of an active substance into another product type;
- the special review of the inclusion of an active substance in Annex I, IA or IB, where indications exist suggesting that the conditions of inclusion are no longer satisfied;
- the routine review anticipating expiry of the period for which the active substance was included in Annex I, IA or IB.

1.2.2 Standardisation of CAs' report preparation

The CAs Report Guidance is intended to provide guidance on how the requirements for Annex I, IA or IB inclusion given by the BPD are accomplished by the RMS in a harmonised and, as far as possible, standardised procedure. Thus, the guidance aims at facilitating:

- a check for completeness;
- the evaluation of the applicant's dossier;
- decision making;
- the preparation of the complete documentation required for a report.

This standardisation should enhance the comprehensibility and effectiveness of the RMS's evaluation procedure. It is the responsibility of the evaluator to justify any deviation from the proposed schemes, where necessary.

1.3 PRINCIPLES OF GUIDANCE GIVEN

The CAs' Report Guidance document gives guidance on the following items:

- General structure and content of the documentation required in a CA's report;
- Structure, format and lay-out of the individual document types;
- Synergetic use of parts of the dossier for the preparation of corresponding parts of the report ("all-in-one approach").

The structure of the CA's report, the order of (sub)chapters and the formats to be used in the individual documents have been harmonised as far as possible with those used in the dossier. Hence, except for some specific items, the guidance given in the Dossier Preparation document also applies to the preparation of the CA's report.

1.4 REFERENCE DOCUMENTS TO BE CONSULTED

see Dossier Preparation document (Part I, chapter 1.4) in which other relevant guidance documents are listed.

2 DOCUMENTATION REQUIRED FOR A CA's REPORT

2.1 INTRODUCTION

The evaluation of a dossier commences with a check of the documentation submitted by the applicant. This is done by a formal check for completeness of documentation and data, as described in chapter 3.

After the dossier has been accepted, the evaluation can start. This takes place primarily at the level of the summaries of individual tests and studies, i.e. the STUDY SUMMARIES, and at the level of the preliminary RISK ASSESSMENT document submitted by the applicant.

For the preparation of the report, the Rapporteur Member State has to combine all information obtained from different applicants relating to the same active substance or biocidal product(s) containing the active substance, following the rules in Art. 12 of the Directive.

Comments submitted to the Rapporteur Member State by other Member States, any advisory committees, NGOs or the applicant should be considered. Consequently, Member States are encouraged to submit data which they have and which may not be publicly available.

Finally, an overall summary should be prepared by the Rapporteur Member State, which also includes a proposal to the Commission for decision. This document forms the EVALUATION REPORT and the basis for the decision-making by the Commission.

The evaluation of the applicant's dossiers by the Rapporteur Member State is facilitated by the fact that the documentation required for their report and its structure is more or less equivalent to that used for dossier preparation. For the principles to be followed in carrying out an evaluation, the other TNsGs and the other guidance documents listed in Dossier Preparation, Part I, chapter 1.4 should be consulted. In the following subchapters the purpose and format of the different

documents required for a CA's report are described or the corresponding subchapters of the Dossier Preparation are cross-referenced.

2.2 CA's REPORT STRUCTURE AND CONTENT

As described in the Dossier Preparation (Part I, chapter 2.2), the structure of the CA's report is in principle equivalent to the dossier structure. The following major differences exist with regard to the individual documents (see also Table 2-1):

- Document I is called EVALUATION REPORT instead of OVERALL SUMMARY AND ASSESSMENT to emphasize its official nature.
- Document I.1, called Statement of Subject Matter and Purpose, corresponds to the Application Form of the dossier.
- As with the dossier, there is no separate Appendix for the completeness check. As the CA's report will only usually be prepared if the dossier has been determined to be complete (as far as the completeness check allows such a determination to be made), such a listing shall not be included in the CA's report (see chapter 3).
- Dossier document IV is not applicable, as the original reports of tests and studies submitted by the applicant are not required to be included in the CA's report.
- The confidential data and information submitted by the applicant as Appendices of the dossier should form an Annex to the CA's report.

Guidance specific to the CA's report preparation is given in the following chapters in the order of preparation and not in the order appearing in Table 2-1.

Table 2-1. Detailed structure of CA's report documentation*)

Document type	Subdocument
DOCUMENT I EVALUATION REPORT	<u>Subdocuments</u> I.1. Statement of subject matter and purpose I.2. Overall summary and conclusions I.3. Proposal for the decision I.4. Demand for further information Appendices: - Listing of end points - List of terms and abbreviations
DOCUMENT II RISK ASSESSMENT	II-A Effects and exposure assessment - Active substance II-B Effects and exposure assessment - Biocidal product*) II-C Risk characterisation for the use of the active substance in biocidal product(s) Appendices: - Reference lists
DOCUMENT III STUDY SUMMARIES	III-A Study summaries - Active substance III-B Study summaries - Biocidal product(s)*) Appendices: - Reference lists
ANNEX CONFIDENTIAL DATA AND INFORMATION	

*) For the inclusion of a substance in Annex IB of the BPD, the B documents do not apply

3 COMPLETENESS CHECK

In accordance with Article 11.1(b) of the BPD, the receiving competent authority has to check:

- the completeness of the documentation submitted and
- the completeness and quality of the data submitted.

The receiving competent authority has to perform this check after receiving the dossier, based on the evaluation forms submitted by the applicant (see Dossier Preparation: Part I, chapter 4.6). During the review programme these checks must be carried out to the agreed deadlines. The following steps are involved:

3.1 CHECK FOR COMPLETENESS OF DOCUMENTATION

In the application form of the dossier the applicant has to confirm that all documents required are submitted with the application. The receiving competent authority should verify this and indicate the result in the respective official-use areas of the Application Form (see Dossier Preparation: Part I, chapter 6.2.1 and Appendix 6.1).

3.2 CHECK FOR COMPLETENESS AND QUALITY OF DATA

For each document type STUDY SUMMARIES (Doc. III-A and III-B), the applicant should submit a completeness check form confirming that the data requirements have been met (see Dossier Preparation: Part I, chapter 4.6.2). This form contains the following information for each possible end point:

- Information / test /study provided
- Justification
- Data protection
- Confidential data
- Reliability indicator

The receiving competent authority should scrutinize the STUDY SUMMARIES of the dossier and, using the "official use only" column of the forms for the completeness check, accept or correct the applicant's entries.

3.3 LITERATURE SEARCH

The Rapporteur Member State may conduct a literature search. Other Member States may wish to do a literature search, too. The search profile can be focused on specific aspects and should always take into account up-to-date papers. This can avoid duplication of work.

The Member States may also search for data not publicly available. The Member States may submit such data to the Rapporteur Member State.

3.4 REPRESENTATIVE CHECK OF SELECTED DATA

As a recommendation, in order to obtain an impression of the overall quality of data and its reporting, a limited number of individual standard formats should be selected for each of the main sections and examined in depth. The result of these checks should be documented.

3.5 OUTCOME OF COMPLETENESS CHECK

In case of significant deficiencies found by the Rapporteur Member State, the applicant will be given the opportunity to complete the dossier.

After the dossier have been accepted as complete, the Rapporteur Member State should:

- inform the applicant that the RMS has accepted the dossier and agrees that the applicant forwards a summary of the dossier to the Commission and the other Members States;
- forward a copy of the forms used for the check of completeness to the Commission;
- start the evaluation of the dossier.

If, on request of the RMS, the applicant does not complete the dossier within a given time period, the application will be rejected. In case of an existing active substance appropriate measures should be taken in accordance with Article 16(2) of the BPD.

The check for completeness forms are not part of the CA's report.

4 DOCUMENT III - STUDY SUMMARIES

4.1 PURPOSE

With regard to the CA's Report, the objective of document type STUDY SUMMARIES is:

- to evaluate the data provided by the applicant as to their validity, i.e. acceptability of the quality, compliance with standard test guidelines and, where relevant, GLP or, in the case of tests not conducted according to accepted guidelines, the suitability of test methods;
- to provide evaluated data summaries based on the key study concept to be used for the risk assessment.

4.2 ALL-IN-ONE APPROACH: USE OF APPLICANT'S STUDY SUMMARIES BY THE RAPPORTEUR MEMBER STATE

4.2.1 Principles

The STUDY SUMMARIES submitted by the applicant provide the general basis to the RMS (and other Member States) for their critical evaluation and assessment of the dossier. The standard formats given in **Part III** of the TNsG on Dossier Preparation and Study Evaluation have been designed in such a way that allows the RMS (and other Member States) to:

- annotate on the applicant's version and/or to amend and change applicant's entries;
- mark and comment on any deficiencies of tests and studies or of their reporting;
- comment on the applicant's summary and conclusion;
- include comments on the evaluation of the individual tests and studies submitted to the Rapporteur Member State by other Member States.

Separate space is reserved for the RMS' entries in the form of:

- a separate comment area (shaded column); where the RMS can mark fields, e.g. with an X, in the case of reporting errors, study deficiencies for any other reason;

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- a separate part "Evaluation by Competent Authorities", in which the RMS can enter a revised version of the applicant's summary and conclusion after considering the marked text in the evaluation box. In the fields "Guidelines and Quality Assurance", "Materials and methods" and "Results and discussion" the RMS can indicate any errors found in the applicant's study summaries or discuss relevant discrepancies and deficiencies referring to the corresponding (sub)heading number(s) in a similar manner. An example is given in Fig. 4-1.

This so-called all-in-one approach is intended to minimize the duplication of work, as the RMS has to annotate only in the case of discrepancies with the applicant's entries. The lay-out of these standard formats guarantees a high transparency of the comments and evaluation carried out by the Rapporteur Member State and should facilitate the harmonisation process between the Member States.

Fig. 4-1 Example of annotations on applicant's study summary by Competent Authorities

	3 MATERIALS AND METHODS	
3.1.2 Specification	Deviating from specification given in section 2 as follows:	X
3.1.2.1 Description		
3.1.2.2 Purity	93,6%	X
Evaluation by Competent Authorities		
EVALUATION BY RAPPORTEUR MEMBER STATE		
Date	14 Feb. 2000	
Materials and Methods	In accordance with method OECD 408, groups of 10 male and 10 female Wistar rats were administered XXXX (purity 93.6 %) at levels of 0, 11, 111 or 611 ppm in their diet over a period of 90 days. Additional recovery groups	
	Comments: The purity of the test substance (see 3.1.2.2) is much lower than that given in section 2. No further specification is given in 3.1.2. However, a check of the original study report revealed that the impurities are not substances of concern.	
Results and discussion	Reversible findings in the high-dose group include a depressed general condition and an ungroomed coat, retarded body weight gains (not fully reversible), transiently lower thrombocyte counts (THRO), elevated	
Conclusion	NO(A)EL: 11 ppm, equivalent to: 1.1 mg/kg bw/day (males), 1.1 mg/kg bw/day (females), based on histopathological findings in the liver at 111 ppm	
Reliability	1	

4.2.2 Outcome

The evaluation of the applicant's STUDY SUMMARIES by the RMS results in:

- the original dossier STUDY SUMMARIES (where applicable combined with the data submitted by other notifiers) with
- annotations as to deficiencies and inadequacies in the tests and studies and their impact on the risk assessment;
- the corrected version of each summary and conclusion and the evaluation of each test and study, to be included in the "evaluation box". This concise summary including tabular overviews of the findings can be transferred to the RISK ASSESSMENT document where appropriate.

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- comments on the Rapporteur Member State's evaluation from other Member States, any advisory committee or, if considered relevant, from the applicant.

4.3 CONFIDENTIAL DATA AND INFORMATION

Accounting for the details stated in Article 19 of the BPD, an applicant may indicate certain information as being confidential. This information is submitted to the Rapporteur Member State as Appendix to the dossier Document III (cf. Dossier Preparation: **Part I**, chapter 2.2.1).

The receiving competent authority should examine the justifications provided by the applicant for each confidentiality claim and decide:

- whether such claims should be rejected, in which case (i) the document and subsection numbers of the CA's report where this information is included should be indicated and (ii) the rationale for the rejection should be given;
- whether such claims can be accepted, in which case the rationale used should be given.

According to Article 19 of the BPD, some information cannot be claimed as confidential, and this includes "a summary of results of the tests required ... to establish the substance's or the product's efficacy and effects on humans, animals and the environment, and where applicable, its ability to promote resistance". This implies that such information has to be summarised by the applicant in the STUDY SUMMARIES (Doc. III) and RISK ASSESSMENT (Doc. II) documents.

The receiving competent authority should use the list of the completeness check (see chapter 3.2) to keep track of the confidential information.

All information being accepted as confidential is to be kept as an Annex to the CA's Report. This Annex is to be treated as confidential by all other competent authorities of the Member States and the Commission. However, by including cross-references to particular items of confidential information in the appropriate parts of the CA's report it should be indicated that further information is available to the competent authorities.

5 DOCUMENT II - RISK ASSESSMENT

The guidance given in the TNsG on Dossier Preparation (see **Part I**, chapter 5) also applies to the RISK ASSESSMENT documents to be prepared by the competent authorities of the Rapporteur Member State.

An all-in-one approach as with the STUDY SUMMARIES is not appropriate on this DOCUMENT II level. This is because the Rapporteur Member States have to carry out a risk assessment on their own, based on the critically evaluated STUDY SUMMARIES and the risk assessment submitted by the applicant as well as based on any other relevant technical and scientific information available to the RMS. However, this does not on principle exclude the adoption or adaptation of parts of the corresponding dossier documents where appropriate.

6 DOCUMENT I - EVALUATION REPORT

Document I including its subdocuments should provide:

- a concise but comprehensive overview of the context in which the dossier was submitted and evaluated, and
- an overall summary and assessment including the conclusions derived from the evaluation of the dossier data.
- a proposal for the decision on the Annex I, IA or IB inclusion, or otherwise of the active substance

The guidance given in the Dossier Preparation , i.e. OVERALL SUMMARY (see Guidance Dossier: **Part I**, chapter 6) also applies to the corresponding EVALUATION REPORT. Specific items are as follows:

6.1 SUBDOCUMENT I.1: STATEMENT OF SUBJECT MATTER AND PURPOSE

This subdocument corresponds to the application form of the dossier and indicates the purpose for which the CA's report has been prepared. In addition, it contains information characterising the substance in question and the biocidal product(s) containing the active substance with regard to the identity, physico-chemical properties, intended uses, effectiveness, and classification and labelling requirements (cf. Dossier Preparation: **Part I**, chapter 6.2.1).

6.2 SUBDOCUMENT I.2: OVERALL SUMMARY AND CONCLUSIONS

Depending on the subject matter and purpose, the OVERALL SUMMARY AND CONCLUSIONS should establish the rationale for the conclusions which the competent authorities of the Rapporteur Member State have drawn on the basis of the dossier data or other data and information available to them. Thus, this document summarises the relevant aspects derived from the risk assessments for the use of the active substance in biocidal product(s).

6.3 SUBDOCUMENT I.3: PROPOSAL FOR THE DECISION

This subdocument should be structured into:

- **3.1 Background to the proposed decision**

In this subchapter the rationale used in making the proposal should be outlined concisely describing the relevant conclusions as to the items covered by the overall summary and assessment. The description should be in text form with no further subsections being required.

- **3.2 Proposed decision regarding the inclusion, or otherwise, in Annex I, IA or IB**

In this subchapter the proposed decision should be outlined, including any conditions or restrictions to be associated with the inclusion in Annex I, IA or IB.

- **3.3 Justification for the restriction(s) regarding the planned inclusion in Annex I, IA or IB**

The reasons for any restrictions should be given.

- **3.4 Demand for further information**

In this subdocument the RMS should indicate further Annex II or Annex III tests and studies required and the dates at which these data have to be submitted, if:

- a decision as to the inclusion, or otherwise, of an active substance in Annex I, IA or IB is postponed because reasons can be given that further data are required;
- any conditions or restrictions are associated with the proposed inclusion in Annex I, but are thought to be removable if a further data base is provided.

6.4 LISTING OF END POINTS

The critical end points which are used in or relevant to the decision proposal should be summarised in a draft listing of end points and appended to Doc. I. This listing is intended to provide a quick profile of the active substance and should reflect the RMS's assessment of the data.

The listing provided by the applicant (cf. Dossier Preparation: **Part I**, chapter 6.2.4 and Appendices 4.2 / 4.3) can be used and modified, if necessary, to reflect the evaluation carried out by the RMS.

7 SUBMISSION OF CA'S REPORT TO COMMISSION, MEMBER STATES AND APPLICANT

After the Rapporteur Member State has carried out the evaluation of the dossier, it should submit a copy of the CA's report, together with a recommendation for the inclusion, or otherwise, of the active substance in Annex I, IA or IB to:

- the Commission,
- the other Member States and
- the applicant.

It is recommended to forward the CA's report both as hard copies and in electronic form.

8 STANDARD UNITS, TERMS AND ABBREVIATIONS

See TNsG on Dossier Preparation and Study Evaluation, Part I, chapter 7

9 CAS' REPORT RELATING TO THE APPLICATION FOR AUTHORISATION OF BIOCIDAL PRODUCTS

According to Article 8(10) of the BPD, the competent authorities of a Member State receiving an application for authorisation of a biocidal product have to ensure that a file is compiled on each application. Each file should contain at least:

- a copy of the application;
- a record of the administrative decisions taken by the Member State concerning the application and the dossier submitted, together with
- a summary of the application and dossier submitted.

Taking into account the common principles laid down in Annex VI of the BPD, the Member State has to evaluate the dossier submitted and, if applicable, other dossiers for which letters of access are provided and to conduct a risk and efficacy assessment for the biocidal product concerned.

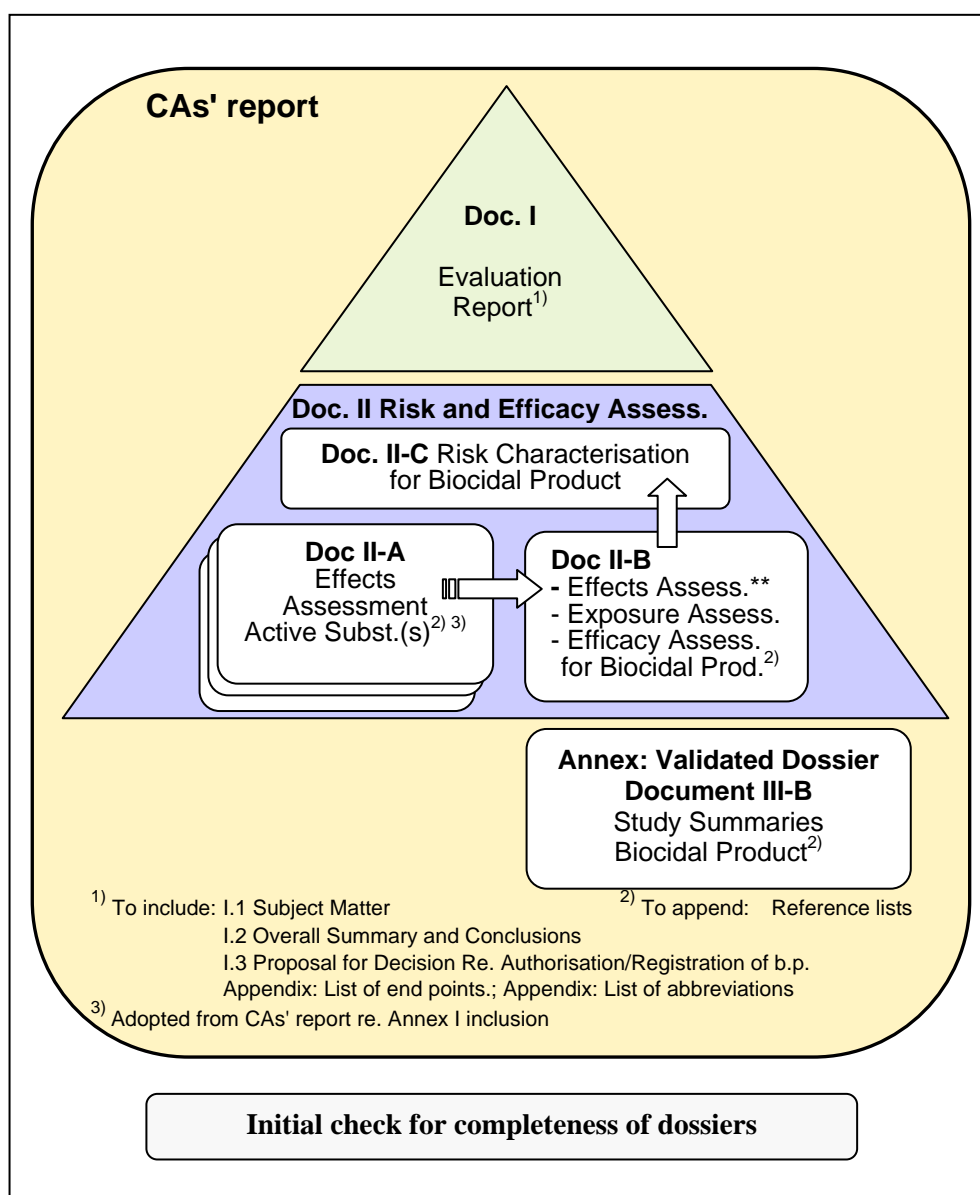
In principle, the documentation required to support the administrative decision could follow the format proposed for the CAs' report to be prepared in the context of applications for Annex I inclusions. Some modification to the CAs' Report structure is required as outlined in the following.

Since no reassessment of the human health and environmental effects should be carried out for active substances already included in Annex I or IA of the BPD, the CA's reports prepared for active substances should be directly referred to. The structure of the CAs' documentation could follow the scheme shown in Fig. 9-1 and outlined as follows:

- A biocidal product can contain more than one active substance, for which CAs' evaluations must be available from the Annex I inclusion.
- The human health and environmental effects assessment for the product is mainly based on the effects assessment for the active substance(s) and substances of concern contained in that product.

-
- Hence, the documents on effects assessment for active substance (Doc. II-A) are adopted from the previous evaluations carried out by the CAs in the context of the Annex I inclusion.
 - After validating the applicant's study summaries on the biocidal product, the relevant data and information are summarised and evaluated in Doc. II-B.
 - A risk assessment is carried out based on the Doc. II-A and Doc. II-B. Relevant parts from the risk assessment document pertaining to the Annex I inclusion of active substances can be adapted, if possible.
 - In addition to the risk assessment, an efficacy assessment is to be carried out, based on the data and assessment submitted by the applicant.
 - An overall summary and assessment document should be prepared, similar to the approach described for the Annex I inclusion of the active substance. Where relevant, this document should also include conditions of use and risk management options.

Fig. 9-1. Structure of the CAs' report documentation required for the evaluation of applications for the authorisation or registration of a biocidal products



** In the case of applications for registration of low-risk products, the effects assessment is confined to data on the active substance(s) only. In general, the data required for the product are, except for efficacy data, limited.