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TECHNICAL GUIDANCE DOCUMENT IN SUPPORT OF THE DIRECTIVE 98/8/EC CONCERNING THE PLACING OF BIOCIDAL PRODUCTS ON THE MARKET

GUIDANCE ON DATA REQUIREMENTS FOR ACTIVE SUBSTANCES AND BIOCIDAL PRODUCTS

ECB, February 2008

The Technical Notes for Guidance on Data Requirements that were previously published as individual chapters on the ECB website were formatted and edited in one single document in pdf format.

Chapter 2.5 of the previous version has been renamed to Part C of Chapter 2. No other changes have been made with respect to the content of the Guidance Document.

Foreword

The Biocidal Products Directive (Directive 98/8/EC of the European Parliament and of the Council)[1] lays down rules and procedures for authorisation of biocidal products in Member States.

The Directive foresees that the Commission shall draw up technical notes for guidance (TNsG) on the implementation of the authorisation procedures, the entry of active substances in the appropriate Annexes, the Annexes relating to data requirements and the Annex dealing with the common principles for evaluation of dossiers for biocidal products.

This TNsG (version 4.3.1) deals with the data requirements on active substances of biocidal products and on the biocidal products. It is the same as version 4.3 (of December 1999) except that editorial minor changes like deletion of double commas have taken place. This may have changed the line numbers.

The document has gone through a long process of writing and negotiations. Firstly, from February 1997 to December 1998 on the basis of a contract with the Commission the Finnish Environmental Institute made a draft proposal for a TNsG. Under the responsibility of the Commission (JRC-ECB) this draft was then discussed in a number of small expert groups in which Member States and Industry participated. Furthermore, the document has been discussed at two meetings of the Competent Authorities of Member States and at one technical meeting. All Member States, Industry and NGOs have been invited to these meetings. At each stage updated versions of the document have been circulated for all parties to comment upon.

At a meeting the 17-18 November 1999, Competent Authorities of Member States agreed in the coming years to use the document as the reference when setting specific data requirements for active substances and biocidal products. Consequently applicants should use the document when preparing complete dossiers according to Article 11 (inclusion of active substances into Annex I, IA or IB to the Directive) or according to Article 8 (approval of biocidal products).

It is recognised that the document still contain gaps, reflecting gaps in knowledge and the need to gain experience through the review programme in accordance with Article 16(2) to the Directive.

So far the main points to be addressed in future revisions are identified to be

- definition of and testing strategy on metabolites,
- refinement of testing requirements after the specification of detailed emission scenarios for each product type,
- adjustment after the borderlines with other Directives have been clarified, and
- adjustment to the guidance to be developed on risk assessment methodology for active substances.

The Scientific Committee on Toxicity, Ecotoxicity and the Environment has delivered its opinion on the TNsG on its 13th plenary meeting the 4 February 2000[2]. The section on waiving the mammalian toxicology data was refined in October 2000, and the CSTEE delivered its opinion regarding this on its 17th plenary meeting the 5th September 2000.

When further experience has been gained an updated TNsG on data requirement should be adopted in accordance with Article 33 of Directive 98/8/EC.

[1] OJ L 123, 24.4.1998, p. 1.

[2] The CSTEE opinion is available at http://www.europa.eu.int/comm/dg24/health/sc/sct/outcome_en.html.

This guidance document

- For guidance on the core data requirements, see Chapter 2, the Technical Notes for guidance on the common core data set for active substances and biocidal products.
- For guidance on additional data requirements, see part of Chapter 2.5 and Chapter 3, the Technical Notes for guidance on the product-type-specific data set for active substance and biocidal products.
- For guidance on the data requirements for substances of concern, see Chapter 4.
- For guidance on the data requirements for frame-formulations, low-risk biocidal products or basic substances, see Chapter 5.
- For guidance on good laboratory practice requirements, see Chapter 6.
- A list of abbreviations is compiled by the ECB and presented after the table of contents.

Guidance for reading the draft guidance document

- Text written in *italics* originates from the Biocidal Products Directive or its Annexes.
- Text after the ”bullet” symbol (•) is detailed guidance
- Numbering of the requirements differs from that given in Annexes II and III. Also the order of items may have been changed in some occasions. However, in order to facilitate comparison with the Annexes, the reference to the relevant Annex, Part and section is always given in brackets after the new number (e.g. [*Ann. IIA, VI, 6.1.2*]).
- Data requirement headings written in small letter size appear in Chapters two and three and are included as cross reference between the two chapters.

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List of Abbreviations

Standard term / Abbreviation	Explanation
ADME	Administration Distribution Metabolism and Excretion
AF	assessment factor
Ann.	Annex
ASTM	American Society for Testing and Materials
BBA	Biologische Bundesanstalt (German Federal Agency for Agriculture and forestry)
BCF	Bioconcentration factor
BIOEXPO	Project for risk reassessment of biocidal products for authorisation purposes *(Germany, January of 1998)*
BPD	Biocidal Products Directive
Bw, bw, b.w.	body weight
°C	degree(s) Celsius (centigrade)
CA	Chemical Abstract
CAS	Chemical Abstract (Service or System)
CEC	Commission of the European Communities
CEFIC	European Chemical Industry Council
CEN	European Committee for Normalisation
CEPE	European Committee for Paints and Inks
Ch.	Chapter
CIPAC	Collaborative International Pesticides Analytic Council Ltd.
CO_2	carbon dioxide
COST	European Co-operation in the field for Scientific and Technical Research
d	day(s)
DG	Directorate General
DIN (TTC,INT)	Deutsches Institut fuer Normung e.V. (*German Institute for Standardisation*)
DIS	Draft International Standard (*ISO*)
DRP	Detailed Review Paper (*from OECD)*
DT_{50}	period required for 50 percent dissipation (*define method of estimation*)
DT_{50lab}	period required for 50 percent dissipation under laboratory conditions (*define method of estimation*)
DT_{90}	period required for 90 percent dissipation (*define method of estimation*)
$DT_{90field}$	period required for 90 percent dissipation under field conditions (*define method of estimation*)
dw, d.wt.	dry weight
EC	European Communities or European Commission
EC_{50}	median effective concentration
ECB	European Chemicals Bureau *(Ispra (Va), Italy)*
ECCO	European Commission co-ordination
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of (New or Notified) Chemical Substances
EN	European Norm
EPA (DK, USA)	Environmental Protection Agency (of Denmark, or the United States of America)
EPAS	European Producers of Antimicrobacterial Substances
EPFP	European Producers of Formulated Preservatives
EPPO/OEPP	European and Mediterranean Plant Protection Organisation *(Paris, France)*
ESPE46/51	Evaluation System for Pesticides

EU	European Union
EUSES	European Union System for the Evaluation of Substances
EWPM	European Wood Preservation Manufactures
FELS	fish early-life stage
F_{mol}	fractional equivalent of the metabolite's molecular weight compared to the active substance [-]
f_{oc}	organic carbon factor (*compartment depending*)
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use (*European pesticide project for risk assessment)*
g	gram(s)
GEP	good experimental practice
GLP	good laboratory practice
gw	gram weight
h	hour(s)
ha	hectare(s)
HPLC	high (pressure or performance) liquid chromatography
IARC	International Agency for Research on Cancer
IC_{50}	median immobilisation concentration or median inhibitory concentration 1 (*explained by a footnote if necessary)*
INT	2-p-Iodophenyl-3-p-nitrophenyl-5-phenyltetrazoliumchloride testing method (*please refer to DIN)*
IOBC	International Organisation for Biological Control of Noxious Animals and Plants
IR	infrared
ISBN	international standard book number
ISO	International Standards Organisation
ISO (TC, SC, WG)	International Standards Organisation Technical Committee, Scientific Committee ,Working Group
IUPAC	International Union for Pure and Applied Chemistry
k	kilo- or rate constant for biodegradation
Ka	acid dissociation coefficient
Kb	base dissociation coefficient
Kd	dissorption coefficient
kg	kilogram(s)
K_{oc}	organic carbon adsorption coefficient
K_{om}	organic matter adsorption coefficient
K_{ow}	octanol-water partition coefficient
Kp	solid-water partitioning coefficient of suspended matter
kPa	kilopascals(s)
$L(E)C_{50}$	lethal concentration, median
l, L	litre(s)
log	*logarithm to the basis 10*
m	meter
µg	microgram(s)
mg	milligram(s)
MITI	Ministry of International Trade and Industry (*Japan)* *(inherent biodegradability tests)*
MMAD	mass median aerodynamic diameter
MOS	margin of safety
MT	material test
NMR	nuclear magnetic resonance
no**.,** n°	number
NOAEL	no observed adverse effect level

NOEC	no observed effect concentration
NOEL	no observed effect level
OECD	Organisation for Economic Co-operation and Development
OH	hydroxide
OJ	Official Journal
OPPTS	Office of Prevention, Pesticides, and Toxic Substances (*U.S.-EPA)*
Pa	Pascal unit(s)
PEC	predicted environmental concentration
pH	pH-value, potential hydrogen value, negative *logarithm* (*to the basis 10*) of the hydrogen ion concentration
pKa	negative *logarithm* (*to the basis 10*) of the acid dissociation constant
pKb	negative *logarithm* (*to the basis 10*) of the base dissociation constant
PNEC(s)	predicted no effect concentration(s)
$PNEC_{water}$	predicted no effect concentration in water
PT	product type
PT (CEN)	Project Team CEN
QA	Quality Assurance
QAU	Quality Assurance Unit
(Q)SAR	(Quantitative) structure activity relationship
RA	risk assessment
$Rate_{a.s.}$	use rate of active ingredient [kg /ha]
$Rate_{metabolite}$	application rate at which metabolite should be tested (kg/ha)
RENI	Registry Nomenclature Information System (*computerised database nomenclature and standardised diagnostic criteria for classifying tumours)*
RIVM	Netherlands National Institute of Public Health and Environmental Protection
RSD	relative standard deviation
S/L	short term to long term ratio
SCAS	semi-continuous activated sludge (*inherent biodegradability tests*)
SETAC	Society of Environmental Toxicology and Chemistry
SMEs	Small and Medium-sized Enterprises
STP	sewage treatment plant
TER	toxicity exposure ratio(s)
TG	Technical Guideline(s), Technical Group(s)
TGD	Technical Guidance Document
TNsG	Technical Notes for Guidance
TNO	Netherlands Organisation for Applied Scientific Research
TTC	2,3,5-Triphenyltetrazoliumchloride testing method (*please refer to DIN)*
UBA	Umweltbundsamt *(German Environmental Protection Agency)*
UV	ultraviolet
UVC	Unknown or Variable composition, Complex reaction products
UVCB	Undefined or Variable composition, Complex reaction products or Biological material
v/v	volume per volume ratio
VIS	visible
w/w	weight per weight ratio
WHO	World Health Organisation
WPRS	West Palearctic Regional Section
<	less than
≤	less than or equal to
>	greater than
≥	greater than or equal to

CHAPTER 1

INTRODUCTION TO AND GENERAL GUIDANCE ON DATA REQUIREMENTS FOR ACTIVE SUBSTANCES AND BIOCIDAL PRODUCTS

INTRODUCTION TO THE GUIDANCE ON DATA REQUIREMENTS

The Biocidal Products Directive (Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market) lays down rules and procedures for authorisation of biocidal products in Member States, and for approval of the active substances in biocidal products at the Community level. The aim of the Directive is to remove barriers to trade between Member States and at the same time to ensure a harmonised high level of protection for man and the environment with regard to biocidal products.

One essential element in the harmonised procedures is harmonised data requirements. The basic rule is that the studies and other data required for the inclusion of an active substance in Annex I (List of active substances with requirements agreed at the Community level for inclusion in biocidal products), IA (List of active substances with requirements agreed at the Community level for inclusion in low-risk biocidal products) or IB (List of basic substances with requirements agreed at the Community level) of the Directive and for the authorisation or registration of a biocidal product in a Member State are the same throughout the Community. This data must be the minimum necessary but it must be sufficient to conduct a proper risk assessment and make decisions.

The Directive itself gives rules on data requirements (especially in Article 8). In Annexes IIA and IIB detailed core data requirements common to all active substances and biocidal products, respectively, are specified. In addition, specific additional data requirements must be defined for each of the 23 product types and they are to be established on the basis of Annexes III A and IIIB. These two annexes contain indicative lists of tests for chemical active substances and biocidal products respectively. The specification of the additional data requirements is to take into account the characteristics of each product type. The common core data requirements in Annex II together with the specific data requirements in Annex III constitutes the complete set of data on the basis of which an overall and adequate risk assessment can be carried out.

Due to the wide scope of the Biocidal Products Directive and the extensive variation of exposure and risks of different biocidal products, the general rules given in the Directive and its Annexes have to be specified in order to ensure efficient and harmonised day-to-day implementation of the Directive. As written in Article 33, the Commission, in accordance with the procedure laid down in Article 28(2), shall draw up technical notes for guidance to facilitate the day-to-day implementation of this directive.

This Technical Notes for Guidance aims to give detailed and practical guidance on which studies and other data are required when applying for authorisation according to the Directive. It should be noted that only chemical biocidal products and substances are covered. Separate guidance on data requirements for substances of concern and on the data requirements in regard to the simplified procedures, i.e. those concerning frame-formulations, low-risk biocidal products and basic substances is also given (see Chapters 4 and 5).

Several EU and other documents have been used as a basis for the data requirements presented. The most important documents are listed in "Background documents" at the end of this Chapter.

This Technical Notes for Guidance is addressed primarily to the applicants whose obligation is to submit the data and to the competent authorities of the Member States whose task it is to assess the adequacy and relevance of the submitted data.

1.1 STRUCTURE OF THE GUIDANCE FOR DATA REQUIREMENTS

This Technical Note consists of several chapters. Chapter 1, the introduction, lays down the guiding principles for data submission. The actual data requirements detailed in this note is divided into two parts, into a **common core data set** (Chapter 2) required of all active substances and biocidal products regardless of the product type and an **additional data set** (Chapter 2.5 & Chapter 3) generated for each of the 23 different product types. Chapter 4 lays down basic data requirements for substances of concern and

Chapter 5 gives guidance on data requirements with regard to the simplified procedures. Chapter 6 contains detailed guidance on Good Laboratory Practice (GLP) requirements.

Chapter 2 concerns the common core data set for the 23 product types given in Annexes II A and II B of the Directive. References to the relevant test methods are given in this Chapter. It also clarifies the requirements set in Annex II of the Directive, for example by giving guidance on which test is the most suitable one on a specific occasion. It also lists certain generally accepted, scientifically or technically justified exemptions to the data requirements. When relevant, the product-type-specific data set (Chapter 3) is referred to.

Chapter 2.5 gives product type specific data set for active substances and biocidal product for the fate and behaviour in the environment and environmental effects. Based on the product type, for which an active substance will be used, additional data to those required for the core data set, might be necessary to be able to perform an initial risk assessment. Depending on the direct environmental exposure that the use of different product types gives rise to, specific additional data are always required for the different product types. These tests are mandatory and must be submitted. Chapter 2.5 will only summarise the tests; the general test specification will be given in Chapter 3.

Chapter 3 gives the product-type-specific data requirements defined for the 23 different product types. In addition, Chapter 3 may specify different requirements for different fields of use within the product types. In Chapter 3, the general headings of requirements listed in the common core data set (Chapter 2) are repeated in order to facilitate reading.

1.2 GUIDING PRINCIPLES WITH REGARD TO DATA REQUIREMENTS

The following guiding principles reflect the general guidance on data requirements presented given in the Directive:

1 **The common core data** forms the basis of the requirements. In general, the common core data set is regarded to be a **minimum set** required for all substances and product types. However, with respect to toxicological side some of the data requirements may on occasion be waived on the ground of, for example, limited exposure or other product-type-specific factors if sufficient and acceptable justification is provided. In addition, unloosened for assessment of ecotoxicological properties the inherent physical and chemical properties of the substances or the products may also justify waiving of some data requirements.

2 **The additional data requirements** set in this Technical Note for Guidance are triggered as a result of **the characteristics** of the active substances and on the product type and on the expected exposure of humans, animals and the environment**,** according to its use or application method, *taking into account both the proposed normal use and a possible realistic worst case situation* (Annex VI, para. 18).

3 Waiving of the data requirements outlined in these Technical Notes for Guidance is possible in certain cases. See Chapter 1.4 for specific guidance.

4 The data requirements have been specified in as much detail as possible. However, in certain cases **expert judgement** by the applicant and by the competent authority may be necessary in order to assess, for instance, whether an additional study is needed or on which organism or under which conditions a test should be performed. The applicant should propose the initial expert judgement, which is then examined by the competent authority and the European Commission. In making the decision as to whether additional testing is justified, the benefit for risk assessment, the compatibility with accepted risk assessment rationales, and the feasibility of the required test may have to be considered. When providing an expert judgement one must, when relevant, take into account both the proposed normal use and a

possible realistic worst case situation. Expert judgement decisions should be justified scientifically and be transparent. In certain cases the final decision on data requirements is made by the Standing Committee on Biocides. Where (at the time of writing of this guidance) there are endpoints of concern, but no clearly defined or standardised methods exist, care must be taken and the applicant must check-up where relevant methods take place. New test methods are continuously being developed and the applicant should be currently updated. Special care to check for test methods should be done for substances suspected to be endocrine disrupters, as several international programmes at the moment attempt to develop tests.

5 It is always the **applicant who is responsible** for the submission of the data. All data given in the application must always be supported by study reports or other data or letter of access. The data submitted by the applicant on both active substances and products and to a certain extent also on substances of concern must be sufficient for a proper risk assessment and decision making both at Community level and on the level of the individual Member States. The applicant should consult a Competent Authority on which data should be submitted to allow the proper risk management measures to be decided on if the active substance is likely to significantly fail the criteria for an Annex I listing.

6 The data submitted by the applicant will be the basis for the classification and labelling of dangerous substances and preparations according to Council Directives 67/548/EEC and 88/379/EEC (amended as 99/45/EC), respectively. The substances may be classified for the first time or the data can be used to review a previous classification.

7 The ***data should suit individual circumstances*** and thus make it possible to assess the risks under differing conditions. The characteristics of the application technique, of the users (e.g. professional or non-professional users) as well as of the environment in which the product is intended to be used or into which the product may be released should be taken into account when preparing the application for authorisation.

8 *The **amount of animal testing**, especially on vertebrates, **shall be minimised**. This means that all unnecessary testing of substances and preparations must be avoided, and the data should be shared between applicants.* Concerning the latter, detailed rules are given in Article 13 of the Directive. The data generated and collected under other legislative regimes, especially under Council Directive 91/414/EEC, Council Directive 92/32/EEC and Council Regulation 793/93/EEC should be used, taking into account the rules on data protection and confidentiality.

9 In addition to the core and specific data required the applicant must submit **any additional available data**, which is relevant to the risk assessment. This requirement corresponds to the obligation of submission of new data after the authorisation has been granted (Article 14). For example, if several reports on similar studies are available they should all be submitted to allow a more sound risk assessment with, among others, assessment of inter-species variability. The additional data should be of an acceptable quality (see Chapter 1.4, point 2 and the detailed guidance on this subject in Part III). Guidance on data protection can be found in Part III.

10 *The Member State shall also take into consideration other relevant technical or scientific non-protected information which is reasonably available to them with regard to the properties of the biocidal product, its components, metabolites, or residues* (Annex VI, para. 7). This means that e.g. Member States and pressure groups should submit to the Member State making the risk assessment of the active substance also other relevant data reasonably available to them but which has not been available to the applicant. The applicant is not responsible for this additional information. The applicant, however, is responsible to search for data from all sources which he or she may reasonably be expected to have access to.

11 It is always possible to require additional information or studies if this is assessed to be

necessary for the proper risk assessment and decision making. The need for additional studies may be justified either by the properties of the chemical (i.e. hazard) or by the predicted exposure. According to Article 8(6) *when the evaluation of the dossier shows that further information, including data and results from further testing, is necessary to evaluate the risks of the biocidal product, the competent authority shall ask the applicant to submit such information.*

12 *Data may also be required on a **substance of concern** other than the active substance*. General rules and data requirements are laid down in Chapter 4 but the detailed requirements are left mainly to be judged on a case-by-case basis by the competent authorities after assessing the basic data submitted.

13 *During the process of evaluation and decision-making, Member States and applicants shall **co-operate** in order to resolve any questions on the data requirements quickly or to identify at an early stage any additional studies required, or to amend any proposed conditions for the use of the biocidal product to modify its nature or its composition in order to ensure full compliance with the requirements of The Common Principles or of this directive. The administrative burden, especially for small and medium-sized enterprises (SMEs), shall be kept to the minimum necessary without prejudicing the level of protection afforded to humans, animal and the environment* (Annex VI, para. 12). Specifically the SMEs need much advice from the competent authorities in order to be able to fulfil the obligations laid down in the Biocidal Products Directive.

1.3 GENERAL GUIDANCE ON GENERATING THE DATA

If new tests are performed in order to fulfil the data requirements, the following principles have to be followed:

1. According to Article 8(8), *as a general principle, tests must be conducted according to the **methods** described in Annex V of Council Directive 67/548/EEC,* according to the most recent adaptation to the technical progress. These are based on those recognised and recommended by international bodies in particular OECD. *In the event of a method being inappropriate or not described, other methods used should, whenever possible, be internationally recognised and must be justified*. Sources of recommended test methods are given in Chapter 1.6.

2. According to Article 8(8), *where appropriate, tests must be conducted in accordance with the provisions laid down in Council Directive 86/609/EEC of 24 November 1986 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes (OJ No L 358, 18.12.1986, p.1) and Council Directive 87/18/EEC of 18 December 1986 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of Good Laboratory Practice and the verification of their application for tests on chemical substances (OJ No L 15, 17.1.1987, p. 29).* Specific guidance on GLP requirements is given in Chapter 6.

3. In order to implement the three R's: Reduction, Replacement, Refinement minimising the use of and the number of animals used for laboratory and other scientific purposes, the following should be taken into account when planning new tests: If in the EC methods or OECD test guidelines for a given purpose, for example testing of acute oral toxicity, an established test method exists and in addition one or more alternative methods which may equivalently be used, the test method, which requires a lower number of test animals and/or causes less pain should be used. A number of alternative tests either not using test animals or reducing the number of test animals are under development and when endorsed, these tests are preferred when new tests have to be performed.

4. *Where test data exist that have been generated before the adoption of* the Biocidal Products Directive *by methods other than those laid down in Annex V to Council Directive 67/548/EEC, the adequacy of such data for the purposes of this Directive and the need to conduct new tests according to Annex V must be decided on a case-by-case basis, taking into account, amongst other factors, the need to minimise testing on vertebrate animals (Article 8(9)).* Such a decision should be first proposed by the applicant when collecting data for the application and then evaluated by the competent authority when checking the completeness of the application and approving the justification given for such a case. If a non-Annex V test has been performed, the nature of the differences must be indicated and justified (the same applies to deviations from the test protocol used). The test protocol should be provided in full unless there is sufficient detail in the test report. In certain cases, testing can be replaced by modelling using (Q)SAR, Quantitative Structure Activity Relation. The guidance document for risk assessment for new notified substances and existing substances contains further information on this.

5. As a general rule, tests on a active substance should be carried out on the substance as it is to be supplied for formulation of the product for which the approval is applied for, including any essential additives (stabilisers etc.) and impurities. The "Active substance as manufactured" should be understood to mean the active substance in the natural state or obtained by any production process, including any additive necessary to preserve the stability of the product(s) and any impurity deriving from the process used but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition. (cf. Directive 67/548/EC) A substance listed as an active substance in Annex I, IA or IB should be connected to what is active in the formulation. This means that a case-by-case decision must be taken by the competent authority on what to list e.g. simple ions or different molecular structures, precursor/activator, or unstable/breakdown active components, or multiple component products. A detailed description (specification) of the material used (i.e. a brief composition description for all batches used in tests), as provided for under paragraph A2.8 must be given. Where testing is done using an active substance the material used should be of the same specification as that which would be used in the manufacture of preparations to be authorised except where radio labelled material is used. All batches of a substance or a product used for testing should be representative of typical commercial material for which the approval is applied for and within the production concentration range. If for any test the composition of the substance or product is different from that quoted for commercial material, full details must be provided. Certain exceptions on this general rule are given in the Technical Note. When the long-term stability is in doubt, the composition should be measured before testing. Where appropriate, details of the stability of the substance in any vehicle used during testing should also be specified. For certain tests (e.g. some physico-chemical tests) there are specific requirements for purity of the active substance.

6. In addition, the specific guidance given in the relevant test guidelines should always be followed. For instance, guidance on when the testing of transformation products instead of the active substance is relevant may be found in the test guidelines concerned.

7. Some active substances may have characteristics that impede testing, or limits which methods can be used. Substances difficult to test need special attention. The difficulties may arise from the chemical nature of the substance (e.g. insoluble substances, metals, complex mixtures of chemicals, surface active or oxidising substances) or owing to the activity of the substance (e.g. the tests using rats as test animals are not suited for rodenticides). Where studies are conducted using an active substance produced in the laboratory or in a pilot plant production system, the studies must be repeated using the active substance as manufactured unless it can be justified that the test material used for the purposes of testing and assessment is essentially the same. In cases of uncertainty, appropriate bridging studies must be submitted to serve as a basis for a decision as to the possible need for repetition of the studies. Usually the test guidelines include guidance on the limitations of the method or give

detailed guidance on how the method should be modified when testing chemicals with specific characteristics. Separate guidance documents may be available for specific testing problems. For instance, guidance on testing volatile, or insoluble, or very reactive and only existing during the process substances is being drafted by the OECD[1]. Also the guidance given in the Technical Guidance Document concerning risk assessment of new and existing substances (ref. 3) should be followed when designing the testing strategy for substances difficult to test.

8. The test results must be reported properly and according to the guidelines used. The relevant basic or raw data should be included in the data forwarded to the competent authority. For example, individual data points should be provided in addition to mean values and calibration equations should be given to allow a suitable evaluation of the study by an assessor.

1.4 GUIDANCE ON NON-SUBMISSION OF DATA

The basic principle is that the applicant must address all the data specified in the common core data set and in the additional data requirements in accordance with the detailed guidance given in Chapter 2, Chapter 2.5 and Chapter 3. In certain cases, waiving of data requirements is possible, but the **applicant must always be able to justify the suggested exemptions from the data requirements.**

In certain cases it is even strongly recommended that in order to minimise testing on vertebrate animals or to avoid unnecessary suffering of experimental animals the data should not be generated; for example strong acids should not be tested for corrosivity. Detailed guidance may be given in the Technical Note for Guidance or in corresponding test guidelines. Also in these cases the applicant has to give justification for this waiving of data in the application.

According to Article 8(5) *information which is not necessary owing to the nature of the biocidal product or of its proposed uses need not be supplied. The same applies where it is not scientifically necessary or technically possible to supply the information. In such cases, a justification, acceptable to the competent authority must be submitted*. On the basis of the justification given by the applicant, the recipient competent authority shall decide whether the justification is acceptable. The justification must be acceptable to Member States. Arguments should be supported by reference to appropriate data and the original reports or a full list of the references cited should be provided. These should be summarised in sufficient detail for the Competent Authority to determine the validity of the arguments presented.

The acceptable justifications for waiving can be classified in four main groups and in several sub-groups:

1. The study is technically not possible to perform

In many cases the intrinsic physico-chemical or other properties of the substance or the product are such that not all tests can be performed: e.g. very volatile or unstable substances (e.g. oxidising or otherwise reactive substances) cannot be used in all test systems, mixing of the substance with water may cause danger of fire or explosion or the radio-labelling of the substance required in certain studies may not be possible. The guidance given in the test guidelines on the technical limitations of a specific method should always be respected.

[1] OECD (1999) Guidance Document on Aquatic Toxicity Testing of Difficult Substances. OECD Environmental Health and Safety Publication. Series on Testing and Assessment No XX. Draft June 1999.

2. Other existing data can be used instead of the required data:

a) existing data on one substance or product may be **read across** to fulfil the data requirement for another, similar substance or product. This is especially the case with frame formulations when general exemptions regarding the data requirements has been given (see Chapter 5) or with other very similar formulations with the same pattern of use.

b) *Information concerning the biocidal product may be **derived from existing data** where a justification acceptable to the competent authority is provided. In particular, the provisions of Council Directive 88/379/EEC* (amended as 1999/45/EC) *should be used wherever possible to minimise animal testing.* According to Council Directive 86/609/EEC, Article 7(2), an experiment shall not be performed if another scientifically satisfactory method of obtaining the result sought not entailing the use of an animal is reasonably and practically available. This means that the assessment of the hazards of a preparation may be carried out by using the appropriate **calculation method** (specified in Directive 88/379/EC and its amendment Directive 1999/45/EC), or by using a combination of the calculation method and testing. The scientific validity of the data to be produced by calculation method should be considered. The applicant must be able to show that there are no synergistic effects of toxicological or ecotoxicological significance and that using the calculation method is reasonable.

c) The data requirement can be fulfilled by an alternative study: e.g. a study is performed according to a test method not internationally recognised, but the applicant can prove, however, that the study is performed according to scientifically acceptable principles and is reliable enough for the purposes of the risk assessment. This if often the case with data on physical-chemical properties. Also studies published in the peer-reviewed literature can in some cases be used instead of conducting new tests. In those cases, however, specific attention must be paid to the substance used in the study and to the overall relevance and reliability of the study. The rules on data protection must also be respected in these cases. For example, a single original article published in public literature is considered to be in public domain and may be normally used when paying attention to the copyright but with review articles it should be checked that the possible data protection of the original study reports is respected. The applicant must be able to justify the acceptability of published data (e.g. where the composition is different from commercial material). More detailed guidance on the evaluation of the acceptability of the data and guidance on data protection is given in the technical note for guidance in support of annex VI.

3. The study is not scientifically necessary

In some cases it is not scientifically justified to perform a study due to the intrinsic properties of the chemical. In some cases the characteristics of the chemical are such that a study and a data requirement is simply not relevant. Also, the result may be predicted reliably from the intrinsic properties of the chemical or from other test results. For example, inorganic chemicals are not biologically degradable and thus their biodegradability cannot be tested. Owing to the activity of the substance, e.g. the irritation properties of a corrosive chemical must not be studied and e.g. the tests using rats as test animals are not suited for rodenticides.

4. The study is not necessary due to prerequisites fulfilled on limited exposure and toxicity profile

Without prejudice to Article 8.5 and taking into account that future developments in test strategies and protocols may influence the possibilities of waiving, waiving should be decided based on the potential exposure as well as on the toxicological profile of an active substance. The need for extensive toxicological testing should be dictated by a full consideration of the **level, frequency and duration of exposure**. No automatic waiving can be accepted and core data requirements can only be waived on a case-by-case basis with scientific justification. This is indicated in the preface and in the notes of Annex II A to directive 98/8/EC. The applicant must be able to demonstrate that, taking into account all relevant stages like processing, formulation, use and disposal of the active substance and the

product as well as of the treated material, exposure will be limited both under normal use and in the realistic worst case situations.
If waiving is possible, it is necessary to make reference to the exposure conditions in the Annex I listing of the active substance.
The environmental core data cannot be waived.

4.1 Considerations of Human Exposure :

There is an obvious need for good exposure data in order to decide under which use conditions one is able to waive toxicological tests. Requirements for data to assess exposures for biocides should be based upon consideration of use patterns, application methods, whether the biocidal products linked with the Annex I inclusion of the substance is expected to be applied by professionals or non-professionals, whether its use is indoor or outdoor, whether it has the potential for food/feed contact or not, etc. At least the following general exposure scenarios should be considered for the waiving decisions. The schemes for exposure data collection and exposure modelling distinguish between primary and secondary exposure. The following suggestion for the definition of these is based on the recommendations from the OECD workshop on human exposure assessment to wood preservatives (Ottawa, Canada 19-21 June 2000).

i. Primary exposure
   - is the exposure, which occurs to a person using biocidal products, and others involved in mixing & loading, application or post-application activities[2] (such as cleaning of equipment, maintenance of plant and handling of freshly treated items).

ii. Secondary exposure
   - is the exposure, which occurs post-application[3]. It may occur without the exposed person being aware of the fact. For example, it includes exposure via environment, relating to bystanders and consumers, including children, who may be exposed to biocidal products by inhalation, dermal contact or by ingestion, and have little or no control over this exposure. Secondary exposure through re-entry to treated premises may be residential and prolonged. Examples of populations that can be affected by secondary exposure include the general public, the immediate family of a professional user, the consumer, the maintenance engineer, the laundrer or the workplace colleague, who could be unwittingly exposed to biocidal products.

The primary and secondary exposure should be categorised based on thresholds with regard to the relevant level, frequency and duration of exposure before any decision on waiving can be made. The thresholds used to describe the level, frequency and duration are relative. Above thresholds the exposure will be of **full concern**, and in general no waiving will be possible. At or below the thresholds, the exposure will be of **lower concern**, i.e., waiving may be possible. The following are examples for the three terms.

[2] directly related to the application
[3] not directly related to the application

Level of exposure (How much?)**:**

Threshold for lower concern: a provisional safety margin of at least 1000 between the exposure and the overall NOAEL established from the set of toxicological studies that, in general, cannot be waived (see below, 4.2, Toxicological Considerations), i.e:

- 90-day, rodent
- two-generation, rat[4]
- teratogenicity, rabbit[4]
- subchronic toxicity study in the second species or chronic toxicity/carcinogenicity long-term toxicity studies in both species.

The level of exposure is NEGLIGIBLE, if specific exposure or use conditions will be linked to the Annex I listing of the active substance, e.g. automated application of a ready-to-use product in a completely closed industrial system.

Frequency of exposure (How often?)**:**

Threshold for lower concern: up to once per month (may be average per year, i.e., up to 12 exposures per year).

Duration of exposure (How long?)**:**

Threshold for lower concern: up to 3 months per year.
This 3 month period is primarily the threshold of lower concern with regard to long-term toxicity testing. For other toxicological endpoints (e.g. teratogenicity) the threshold of lower concern may be related to a much shorter duration.

The outcome of the application of these thresholds to primary exposure and secondary exposure will be among the determining factors in the waiving process with respect to toxicology data requirements.
If adequate "operational predictive good exposure models" can show that primary exposure only affects a working environment where exposure is controlled and that secondary exposure for the use patterns is only of low concern with regard to level, frequency and duration, then the toxicological based waiver (4.2) may be possible on a case-by-case basis if the following general prerequisites for secondary exposure can be assumed:

- The general public is not exposed above the threshold of concern (e.g. non-food exposure via environment).
- Residues affecting the human population are not expected (e.g. in food, feeding stuff or drinking water).

4.2 Toxicological Considerations:

Without prejudice to Article 8.5 and considering that the following is a non-exhaustive list of possible scenarios, under the prerequisite that adequate data (according to chapter 2A, 6.12) have not indicated health risks in humans (e.g. if the substance is already in use for many years and supporting scientific data demonstrate that there is evidence of no adverse effect during many years of use) waiving of the following data requirements from the common core data set may be considered:

<u>Subchronic toxicity study (90-days) in the second animal species</u>

- if the subchronic studies in rodents are without indication of substance-related adverse effects at the limit dose level, or
- if there is a one year toxicity study in the second animal species (i.e. the non-rodent) available, or
- if the mechanism of the toxicity is known and it is justified that the toxicological effect is not

[4] If, in exceptional circumstances it is claimed that such testing is unnecessary, that claim must be fully justified (Text of footnote 5 from Annex IIA of the Directive 98/8/EC).

specific to the first species and mechanistic studies can show scientific evidence that the toxicological profile does not differ between the animal species.

- Waiving of this study is not possible in general, if long-term toxicity studies in both species are waived under the conditions described below.

Chronic toxicity studies in both species

- if the subchronic studies in rodents and non-rodents are without indication of substance-related adverse effects at the limit dose level.

Carcinogenicity studies in both species

- if no genotoxic potential for humans is identified in tests of genotoxicity (according to chapter 2A, 6.6) and
- if possible mechanisms of toxicological effects observed in subchronic toxicity studies are without any indications of non-genotoxic carcinogenicity and there are no structural alerts for carcinogenicity and
- if the subchronic studies in rodents and non-rodents are without indication of substance-related adverse effects at the limit dose level.

Teratogenicity study in the second species (normally in rats)

- if no developmental effects are observed in the first species and if no developmental or reproductive effects in the two-generation reproduction toxicity study (performed in the rat) are observed at the limit dose level.

Two-generation reproduction (fertility) toxicity study

In general, waiving on toxicological considerations is not possible, because no other studies can provide comparable information on the following issues relevant to the protection of sensitive population groups and life phases.

- male and female fertility
- specific sensitivity of neonates and offspring
- endocrine effects on reproductive functions
- specific sensitivity during the first part of pregnancy and lactation
- transgenerational exposure

4.3 Considerations of the human exposure as well as the toxicity profile

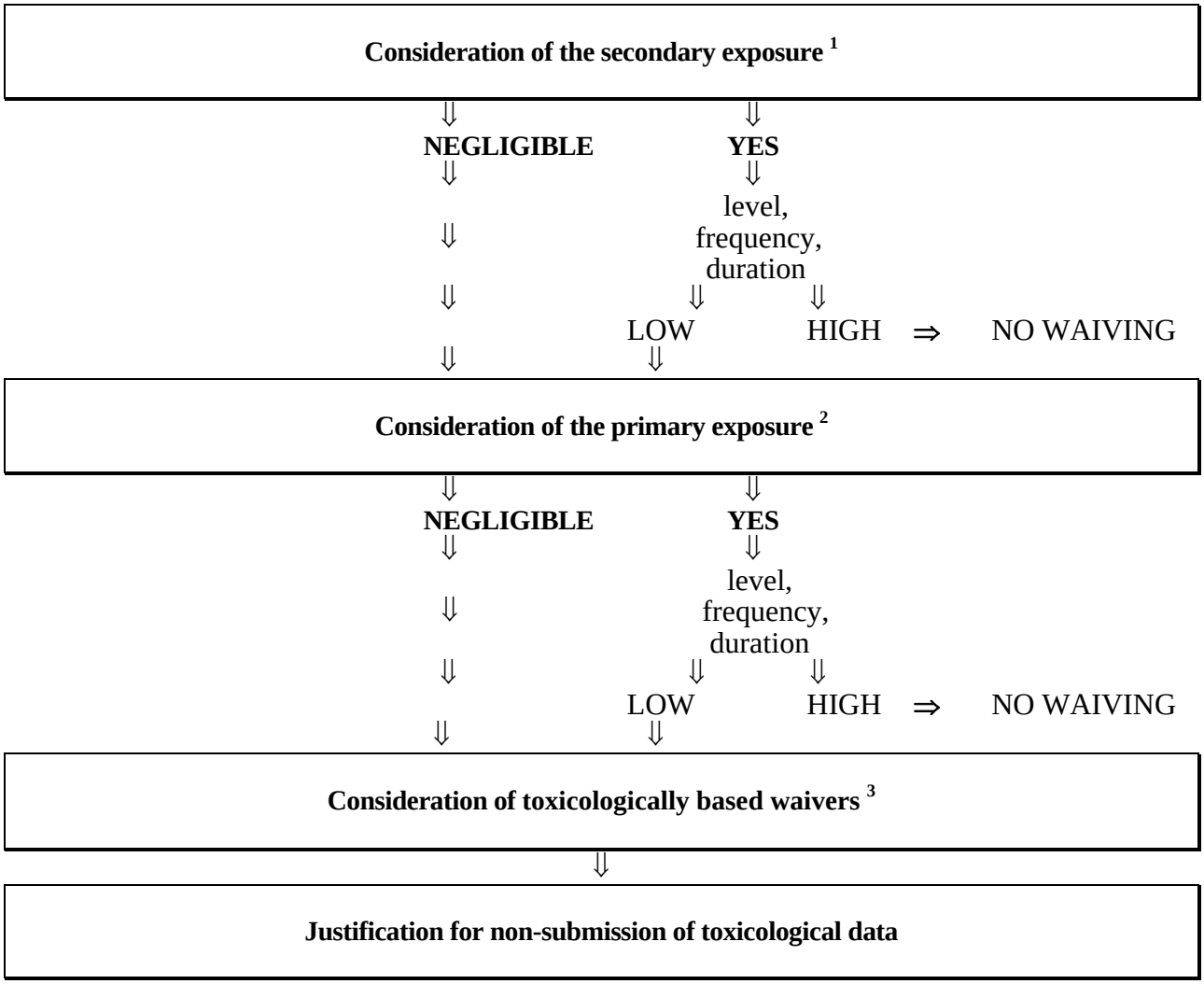
The decision for waiving of core data requirements may be possible on a case by case basis based on a consideration of both basic prerequisites:

- the general profile of exposure to the product (see 4.1) and
- the toxicity profile of the individual active substance (see 4.2).

In Figure 1.1 a decision making process based on exposure and toxicological aspects is proposed.

Figure 1.1: Scheme for a decision making process for exposure and toxicological aspects

HUMAN EXPOSURE to an active substance in a specific exposure scenario



- [1] **depending on** whether the proposed uses or applications of the active substance (with regard to Annex I inclusion) are indoor or outdoor, whether the uses have the potential for food/feed contact, etc.
- [2] **depending on** whether the active substance (with regard to Annex I inclusion) is expected to be applied by professionals or non-professionals, on the application methods, and the use pattern.
- [3] **depending on** whether the basic prerequisites on exposure and toxicity are fulfilled, waiving of common core toxicological data requirements may be possible on a case-by-case basis for the subchronic toxicity study in the second species or the chronic toxicity studies and carcinogenicity studies in both species; and the teratogenicity study in the second species.

1.5 TESTING OF METABOLITES AND TRANSFORMATION PRODUCTS

The current draft document for Directive 91/414/EC (February 1999) was not recommended for inclusion as it is, neither by the toxicology experts nor by the environment experts.

For the toxicology aspects of metabolites and transformation products consideration must be given to the possibility of the formation of metabolites not investigated by the usual testing, see Chapter 2A section 6.2, in mammals.

The environment group considered the draft guidance document on metabolites under Directive 91/414/EC (PPP) a good starting point. It is, however, still a draft for PPP and has certain aspects which are only relevant for PPP, and e.g. it would need a section on sewage treatment plants (STP) to be used for biocides. It would be a natural part of Chapter 3.

1.6 REFERENCES AND BACKGROUND DOCUMENTS

Publications

1. Development of data requirements and common principles for the evaluation and risk assessment of biocidal products. Danish Environmental Protection Agency, Pesticide Division. April 1994.
2. Doc. 1663/VI/94 rev. 8 of 22 April 1996: 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 Council Directive 91/414/EEC (Article 5.3 and 8.2). CEC DGVI.
3. Technical Guidance Documents in support of the Commission Directive 93/67/EEC on risk assessment for new notified substances and the Commission Regulation (EC) 1488/94 on risk assessment for existing substances. April 1996.
4. Decision-making scheme for the environmental risk assessment of plant protection products. Council of Europe & European and Mediterranean Plant Protection Organisation (EPPO). 97/6077.
5. Procedures for assessing the environmental fate and ecotoxicity of pesticides. Ed. M. Lynch. Society of Environmental Toxicology and Chemistry, SETAC - Europe, Brussels. March 1995. ISBN 90-5607-002-9.
6. van Dokkum, H.P., Scholten, M.C.Th., & Bakker, D.J. Development of a concept for the environmental risk assessment of biocidal products for authorisation purposes (BIOEXPO). Part 1: Framework and data requirements for environmental compartments. Part 2: Release estimation for 23 biocidal product types. UBA Research Project No. 106 01065, Final Report UBA IV 1.4, Umweltbundesamt, Germany. January 1998.
7. Preliminary results from the survey on the regulation of biocides in OECD Member Countries.
8. European Directive on biocidal products. Comments and proposals concerning efficacy data requirements. CEFIC, EPAS/EPFP Working Group. Brussels, September 1996.
9. Environmental hazard classification - Data collection and interpretation Chapter. 2nd ed. Nordic Council of Ministers. TemaNord, Environment.1995:581.
10. Classification and labelling of chemical substances for terrestrial effects: Development of classification criteria for the soil compartment. Nordic project group for ”Criteria for classification of substances dangerous for the environment: soil/terrestrial environment”. Draft proposal to OECD 1996.03.01 by A. Lundgren, I. Petterson & L. Torstensson.
11. Soil quality. Guidance on the ecotoxicological characterization of soils and soil materials. Prepared by F. Riepert & B.M. Wilke. Draft guideline, ISO/TC 190/SC 7/WG 3. 4th draft February 1997. Doc ISO/TC 190/SC 7/WG 3/N1.
12. Detailed Review Paper on Aquatic Testing Methods for Pesticides and Industrial Chemicals (Part 1: Report, Part II: Annexes). OECD Test Guidelines Programme. 1998. Final draft.
13. Guidance Paper for Aquatic Ecotoxicology developed in ECCO 38 -Guidance Document Meeting. Draft. Braunschweig. March 3-4.
14. Guidance note to those completing summary notification dossier of a new chemical substance. In accordance with Council Directive 92/32/EEC, article 7 or 8 (ref.: O.J. L 154, 5 June 1992). Draft. 22 March 1995.

15. Notification of new substances. Guidance to Notifiers - Data Collection in SNIF Format for Level 1 and 2 Toxicity and Ecotoxicity Studies. CEC DGXI. Brussels. 20 November 1996.
16. Doc. XI/584/93 (rev. 3 Final). Guidance on testing polymers. In: Guidance Document NOTIF/20/97. CEC DGXI. Brussels
17. Guidelines for the evaluation of wood protection products. Council of Europe. Partial agreement in the social and public health field. Council of Europe Publications Section, Strasbourg 1987. ISBN 92-871-1070-0.
18. Guidelines for the evaluation of antifouling paints. Council of Europe. Health protection of consumers. Council of Europe Press, 1994. ISBN 92-871-2457-4.
19. Guidelines for the evaluation of slimicides. Council of Europe. Health protection for the consumer. Council of Europe Publishing, Strasbourg 1996. ISBN 92-871-3116-3.
20. Environmental aspects related to disinfectants. Council of Europe. Health protection for the consumer. Council of Europe Publishing, Strasbourg 1996. ISBN 92-871-3169-4.
21. Guidelines for the evaluation of pesticides used for the control of public hygiene pests. Council of Europe. Health protection for the consumer. Council of Europe Press, 1994. ISBN 92-871-2356-X.
22. Miljöfarligheten hos mikrobiocider i kylvatten. M. Hedenmark, Rapport från kemikalieinspektionen 6/91. Stockholm, 1991.

Directives

1. Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances.
2. Council Directive of 88/379/EEC 7 June 1988 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous preparations (The Directive is amended by directive 99/45/EC of 31 May 1999).
3. Council Regulation 793/93/EEC of 23 March 1993 on the evaluation and control of the risks of existing substances.
4. Council Directive 92/32/EEC of 30 April 1992 amending for the seventh time Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances.
5. Council Directive 87/18/EEC of 18 December 1986 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances. Amended by Directive 99/11/EC of 8 March 1999.
6. Council Directive 86/609/EEC of 24 November 1986 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes.
7. Council Directive 80/778/EEC of 15 July 1980 relating to the quality of water intended for human consumption
8. Council Directive 80/68/EEC of 17 December 1979 on the protection of groundwater against pollution caused by certain dangerous substances
9. Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market: Annexes II and III
10. Commission Directive 93/71/EEC of 27 July 1993 amending Council Directive 91/414/EEC concerning the placing of plant protection products on the market
11. Commission Directive 94/37/EC of 22 July 1994 amending Council Directive 91/414/EEC concerning the placing of plant protection products on the market
12. Commission Directive 94/79/EC of 21 December 1994 amending Council Directive 91/414/EEC concerning the placing of plant protection products on the market
13. Commission Directive 95/36/EC of 14 July 1995 amending Council Directive 91/414/EEC concerning the placing of plant protection products on the market
14. Commission Directive 96/12/EC of 8 March 1996 amending Council Directive 91/414/EEC concerning the placing of plant protection products on the market
15. Commission Directive 96/46/EC of 16 July 1996 amending Council Directive 91/414/EEC concerning the placing of plant protection products on the market

16. Commission Directive 96/68/EC of 21 October 1996 amending Council Directive 91/414/EEC concerning the placing of plant protection products on the market

1.7 SOURCES OF PUBLICATIONS

The EC methods are published in the Official Journal of the European Communities. The testing methods are described in Annex V to Council Directive 67/548/EC. They are adapted to the technical progress regularly. An actualised list of available methods and the references to the directives that lay them down is available for downloading at the European Chemicals Bureau website (ECB, http://ecb.ei.jrc.it/testing-methods/index.htm). The services of the European Commission published in January 1997 an informal compilation of methods that covers methods in force until 1996: Classification, packaging and labelling of dangerous substances in the European Union. Part II – Testing Methods (ISBN 92-828-0076-8, available at the OPOCE). However, it is recommended to consult the ECB website for new and revised methods introduced into Annex V after that date.

The EUSES model, the European Union System for the Evaluation of Substances is available from the European Chemicals Bureau (EC/ECB), Ispra, Italy.

The USES 2.0 model is available from RIVM, NL.

The OECD test methods can be obtained through a national book sales agent of OECD. List of the agents can be obtained from the OECD, Paris, France, or directly via their internet address.

ASTM Standards may be obtained from the American Society of Testing Methods, West Conshohocken, Pennsylvania, USA.

The BBA test methods of the Federal Biological Research Centre for Agriculture and Forestry (BBA), Braunschweig, Germany, can be obtained from its distributor of publications: the Saphir Verlag, Ribbesbüttel, Germany.

Availability of European Committee for Standardisation, CEN Standards: The text of European Standards, transposed as national standards, can be purchased from CEN National Members and Affiliates. Contact information for CEN National Members and also draft European Standards may be obtained from the CEN Central Secretariat, Brussels, Belgium.

DIN Standards may be obtained from the Beuth Verlag, Berlin, Germany, which is the subsidiary of DIN, the German Institute for Standardisation.

EPPO Guidelines may be obtained from the Secretary of the European and Mediterranean Plant Protection Organisation, Paris, France.

Orders for ISO International Standards should be addressed to the ISO member bodies (non-USA users, if subscribing to Internet from a USA-based provider, should consult the ISO member list for ordering ISO standards in their country) which are normally the primary ISO sales agents, or for customers in countries where there is no member body, to the ISO Central Secretariat, Geneva, Switzerland.

The SETAC guidance document can be obtained from the Society of Environmental Toxicology and Chemistry (SETAC - Europe), Brussels, Belgium.

The US EPA Office of Prevention, Pesticides, and Toxic Substances Test Guidelines can be obtained from the Environmental Protection Agency electronically at their world wide website or in paper or disks from the US Government Printing Office, Washington, USA

CHAPTER 2

COMMON CORE DATA SET FOR ACTIVE SUBSTANCES AND BIOCIDAL PRODUCTS

PART A:

COMMON CORE DATA SET FOR ACTIVE (CHEMICAL) SUBSTANCES:

DOSSIER REQUIREMENTS

1 APPLICANT *[Ann IIA, I.]*

1.1 Name and address, etc. *[Ann IIA, I. 1.1]*

- Names, address, telephone and fax numbers, e-mail, and other contact information of the applicant.
- The applicant shall be required to have a permanent office with a legally responsible representative within the European Community.

1.2 Active substance manufacturer *[Ann IIA, I. 1.2.]*

- *Name, address* and *location of* manufacturing *plant.*

2 IDENTITY *[Ann IIA, II.]*

- The information must be sufficient to identify the active substance, to define it on terms of its specification and to characterise it as to its nature. Chapter One gives the definition of "active substance as manufactured".

2.1 Common name *proposed or accepted by ISO and synonyms*

- The name of the active substance must be given as registered in the list in Annex I to Directive 67/548/EEC or, if the name is not included therein, as given in EINECS or in ELINCS and the ISO common name of the substance, if available.
- Generally known names, trade names, abbreviations, etc. must be included.

2.2 Chemical name *[Ann IIA, II. 2.2.]*

- The chemical name must be given according to *IUPAC nomenclature* and CAS-name, if different.
- For substances that may exist as isomers each isomer, if available, should be given correct designation.
- For substances of undefined or variable composition (UVCB), identity and proportion of compounds in reaction mixture should be given.

2.3 Manufacturer's development code number(s) *[Ann IIA, II .2.3.]*

- Company(ies) code number(s) or internal name(s).

2.4 CAS- and EC-numbers *[Ann IIA, II. 2.4.]*

- The CAS-number, EC number (EINECS, ELINCS or No Longer Polymer List) and other numbers (e.g. CIPAC-number) must be given, if available.
- For mixture of isomers the CAS- and/or EC-numbers of the mixture and individual isomers should be given, if available.

2.5 Molecular and structural formula, molecular mass *[Ann IIA, II. 2.5.]*

- The molecular formula should be given according to the traditional Hill system and, where different, to the CAS-system.
- *Full details of any isomeric composition must be included.*
- An empirical formula should be determined for substances of undefined or variable composition, if possible.
- For polymers the number average molecular weight and the molecular weight distribution are required.
- OECD test guideline 118.

2.6 Method of manufacture of the active substance *[Ann IIA, II. 2.6.]*

- A description of *the synthesis pathway in brief terms*; the chemical reactions taking place, initial products and substances generated in the synthesis etc. must be presented.
- The method of extraction should be provided, where relevant.
- When relevant, where the data refers to a pilot plant production system, the information required must be re-submitted when the industrial scale production plant comes on stream and production procedures have stabilised.
- Chemical engineering data is not required as a rule, but submission may be required, where necessary.

2.7 Specification of purity of the active substance, as appropriate *[Ann IIA, II. 2.7.]*

- Give typical concentration and upper and lower limits for typical commercial batches of the active substance *in g/kg, g/l* or % w/w (v/v).
- For substances of undefined or variable composition the purity is 100% minus unreacted starting materials.
- When relevant, where the data refers to a pilot plant production system, the information required must be re-submitted when the industrial scale production plant comes on stream and production procedures have stabilised and if production changes result in a changed specification and purity.

2.8 Identity of impurities and additives, as appropriate *[Ann IIA, II.2.8.]*

- The following information on impurities and additives, including by-products of synthesis, optical isomers, degradation products (if the substance is unstable), unreacted and endgroups etc. of polymers and unreacted starting materials of UVC-substances, must be provided, where possible:
  - common name and chemical name in conformity with 2.1. and 2.2.,
  - CAS- and EC-numbers, if available,
  - molecular and *structural formula*, molecular mass,
  - the typical concentration and *the range* of concentrations *expressed as g/kg, g/l* or % w/w (v/v),
  - the maximum content of active isomer and the ratio of the content isomer/ diastereoisomers, where relevant.
- An indication of the functions of the components added to the active ingredient (additives) prior to the formulation of the biocidal product (e.g. stabiliser, antifreeze, antifoaming agent, dispersing agent, and inhibitors) must be given.
- When relevant, where the data refers to a pilot plant production system, the information required must be re-submitted when the industrial scale production plant comes on stream and production procedures have stabilised and if production changes result in changed specification and purity. Substances present in quantities 1 g/kg or higher must be stated. Furthermore, quantities of

substances below the concentration limit 1 g/kg, specified in Directive 67/548/EEC, Annex I, or which may be of toxicological or ecotoxicological significance (i.e. substances of concern) must be stated.

2.9 The origin of the natural active substance or the precursor(s) of the active substance *[Ann IIA, II.2.9.*]

- *E.g. an extract of a flower*.
- The scientific name of species, common name and strain, and polymer starting material should be given, if relevant.

2.10 Exposure data in conformity with Annex VIIA to Council Directive 92/32/EEC (OJ No L 154, 5.6.1992, p.1) amending Council Directive 67/548/EEC *[Ann IIA, II.2.10.]*

- Information should be sufficient to allow an approximate but realistic estimation of human (occupational and consumer) and environmental exposure associated with the production process, the proposed/expected uses and disposal of an active substance. Precise details of the production process, particularly those of a commercially sensitive nature, are not required. Substances manufactured outside the EU do not need a description of the manufacturing process for exposure estimation purposes. The prediction of the exposure levels should also describe a reasonable worst case situation, excluding accidental exposure and abuse. Exposure levels or concentrations need to be derived based on available measured data and/or modelling. A starting point is the report 'Assessment of human exposures to biocides', see reference EC 1998.

3 PHYSICAL AND CHEMICAL PROPERTIES *[Ann IIA, III.]*

- The information provides direct input parameters for assessing physical, chemical and technical hazards, as well as prerequisites for performing and guidance information for optimising other tests.
- Ideally, one batch of substance of stated specification should be used for all tests. If for any test the composition of the substance is different from that quoted in sections 2.7. -2.8. then full details must be provided.

3.1 Melting point, boiling point, relative density *[Ann IIA, III. 3.1.]*

- *These data must be studied for a purified active substance of stated specification.*
- If the melting point or boiling point cannot be determined, the sublimation or decomposition temperature should be given.
- Measurements of the melting point and boiling point should be taken up to 360 °C.
- The boiling point should be measured at normal atmospheric pressure unless decomposition occurs, in which case reduced pressure can be used.
- Usually the freezing point of liquid substances should be determined if above –20 °C. An indication that no freezing has occurred during preliminary tests is also acceptable. For viscous liquids the pour point is an acceptable alternative.
- The density of gas should be calculated from its molecular weight and the Ideal Gas Laws. Polymer density should be determined by buoyancy methods, where appropriate.
- EC methods A.1 (Melting/freezing temperature), A.2 (Boiling temperature) and A.3 (relative density) based on OECD guidelines 102, 103 and 109.

3.2 Vapour pressure *[Ann IIA, III. 3.2.]*

- Vapour pressure at two temperatures (at 20 ^{o}C and 25 ^{o}C) or as a vapour pressure curve must *be studied for the purified substance of stated specification.* The unit is the Pascal (Pa).
- Where the vapour pressure is less than 10^{-5} Pa, the vapour pressure at 20 °C and 25°C may be estimated by a vapour pressure curve.
- The vapour pressure needs not to be measured, if calculations indicate that the value is significantly less than 10^{-5} Pa.
- The study needs not to be conducted (unless there are minor volatile impurities or degradation products etc. in the substance) if the melting point is above 300 °C. A limit value based on measurement or a recognised calculation method is sufficient where the melting point is between 300 °C and 200 °C.
- EC method A.4 based on OECD guideline 104.
- The Henry's law constant must be always stated for solids and liquids if it can be calculated. The Henry's law constant depends on the water solubility and vapour pressure of a substance, and expresses the tendency of a substance to evaporate from aqueous solutions. The unit should be stated as Pa x m^3 x mol^{-1}.

3.3 Appearance *[Ann IIA, III. 3.3.]*

- *Physical state, colour* and odour at 20 °C and 101,3 kPa.
- *These data must be submitted both for a* purified *active substance of a stated specification* and the active substance as manufactured, if different.
- A description of the odour associated with the active substance as manufactured and of a purified active substance as noted during the handling of the materials in laboratories or production plants, must be reported.

3.4 Absorption spectra (UV/VIS, IR, NMR), and a mass spectrum, molar extinction at relevant wavelengths, where relevant *[Ann IIA, III. 3.4.]*

- *These data must be submitted for a purified active substance of stated specification.*
- Absorption spectra and mass spectrum must be determined and reported for the identification of impurities of concern, where necessary.

3.5 Solubility in water *[Ann IIA, III. 3.5.]*

- These data must be submitted for a purified active substance of stated specification.
- *The studies must include the effect of pH (5 to 9) and temperature on solubility.*
- Should be studied at or near 20 °C and for a substance the solubility of which is temperature dependent solubility at 10 ^{o}C and 30 ^{o}C should be reported, if relevant
- *Must be studied when relevant*. Water solubility should be measured unless the substance is hydrolytically unstable. Phrases such as "insoluble in water" are not sufficient; instead a limit test should be performed so that a positive statement can be made (e.g. until analytical limit). For complex mixtures, a mass balance may be the only practical method. However, the extract should be compared (e.g. HPLC) with the mixture to check for differential solubilities of components.
- Where the stability of the active ingredient in aqueous media is such that the water solubility cannot be determined, a justification based on test data must be submitted.
- Colloid and micelle formation and other possible observations must also be reported.

- EC method A.6 or the corresponding OECD guideline 105.

3.6 An additional data requirement. See Chapter 3, part A.
3.7 An additional data requirement. See Chapter 3, part A.
3.8 An additional data requirement. See Chapter 3, part A.

3.9 Partition coefficient n-octanol/water including effect of pH (5 to 9) and temperature *[Ann IIA, III. 3.6.]*

- *These data must be submitted for the purified substance of stated specification.*
- Where the stability of the active ingredient in aqueous media is such that the partition coefficient cannot be determined a justification based on test data must be submitted.
- For those substances which are extremely soluble in one of the phases a limit value should be provided. If necessary it can be based on the individual solubilities in n-octanol and water.
- If the test cannot be performed a calculated value should be provided, if relevant.
- EC method A.8. corresponding partly to OECD guideline number 107 and is partly similar to OECD guideline 117.
- A draft OECD guideline (pH metric) is planned to be finalised during spring 2000.

3.10 Thermal stability, identity of relevant breakdown products *[Ann IIA, III. 3.7.]*

- Data on thermal stability to the point of melting, sublimation or decomposition is to be identified.
- If possible, the thermal breakdown compounds are to be evaluated and the possibility of formation of dangerous substances is to be considered.
- OECD guideline 113.

3.11 Flammability including auto-flammability and identity of combustion products *[Ann IIA, III. 3.8.]*

- The flammability of active substances which are solids, gases or substances which evolve highly flammable gases must be determined and reported according to EC methods A.10 (solids), A.11. (gases) and A.12 (contact in water) and pyrophoric properties according to EC method A.13. (solids and liquids)
- Substances with very low melting point (<50 ^{o}C) should be tested according to method A15 (Auto-ignition temperature, liquids and gases) and the test can be terminated at 400^{o}C.
- Test A12/A13 can be omitted if experience in use indicates that negative results would be obtained or if a substance is expected to react violently under the test conditions.
- The auto-flammability of the active ingredient must be determined and reported according to EC methods A.15 (liquids and gases) and A.16 (solids). A9 can be used for substances with a melting point below 100 °C.
- Considerations on further testing of substances with melting point less than 100 ^{o}C should be done on a case-by-case basis (UN transport classification methods are available).

3.12 Flash-point *[Ann IIA, III. 3.9.]*

- The flash-point must be provided for liquids whose vapours can be ignited.
- The closed cup method is the only acceptable procedure in general. If an open cup method has been used and the flash-point is above 70 ^{o}C, it may be acceptable.
- EC method A.9.

3.13 Surface tension *[Ann IIA, III. 3.10.]*

- The surface tension should be measured using an aqueous solution of sufficient concentration such that any surface activity potential is expressed; i.e. at 90% of saturation (the concentration must be quoted) to maximum concentration of 1 g/l (where viscosity permits). Inconsistencies between the water solubility result and the solubility reported should be fully addressed.
- EC method A.5 based on OECD guideline 115.

3.14 An additional data requirement. See Chapter 3, part A

3.15 Explosive properties *[Ann IIA, III. 3.11.]*

- The test can be exempted when available thermodynamic information (heat of formation/decomposition) or absence of certain reactive groups in the structural formula or its "oxygen balance" establishes beyond reasonable doubt that the substance is incapable of decomposing, forming gases or releasing heat very rapidly.
- EC method A.14.

3.16 Oxidising properties *[Ann IIA, III. 3.12.]*

- In cases where an examination of structural formula establishes beyond reasonable doubt that the active ingredient is incapable of reacting exothermically with combustible material, it is acceptable to provide such information as justification for the non-determining of oxidising properties.
- EC method A.17. (solids)

3.17 Reactivity towards container material *[Ann IIA, III. 3.13.]*

- Suitable container materials which are resistant against corrosion and do no react with the substance in question, and/or container materials that cannot be used with the substance, must be specified taking into consideration the properties of the chemicals (e.g. pH and impurities) and storage conditions (e.g. pressure and temperature).
- The information can be obtained from experience in use and the chemical structure.

4 ANALYTICAL METHODS FOR DETECTION AND IDENTIFICATION

- Information on analytical methods is required for assessing compliance with conditions for issuing authorisation for a biocidal product according to Article 5(1c) of the Directive. This information is also required for the post-authorisation control and monitoring purposes, and for the assessment of justifications which should be provided for the methods used for the generation of data as required in accordance with this Directive.
- For substances which are difficult to analyse a description of the problems should be given.

4.1 Analytical methods for the determination of pure active substances and, where appropriate, for relevant degradation products, isomers and impurities of active substances and their additives (e.g. stabilisers) *[Ann. IIA, IV.4.1.]*

- Information on analytical methods is required concerning degradation products,

isomers and impurities of the active substance and additives (e.g. stabilisers) which are of toxicological or ecotoxicological concern (i.e. which are relevant for risk assessment) or which are present in quantities ≥ 1 g/kg in the active substance as manufactured.

- The description of the method used should include necessary preliminary treatments, details of the equipment and materials used as well as of other conditions, and a recovery rate, interference by other substances and other information on the specificity of the method, and linearity, a limit of determination, intra-laboratory repeatability and where possible inter-laboratory reproducibility in order to allow an assessment of the accuracy and precision of the analysis of the natural active substance used in the different study reports submitted.
- Recovery rates should be determined at the level of the measurement(s). This means that for the determination of the active ingredient in a formulation or an impurity at a constant level, one recovery rate (measured at the stated composition) is sufficient. In case of the determination of residues or impurities of varying levels the recovery rates should be determined at least at two concentration levels: one near the limit of determination and one at a higher level (usually 2-3 orders of magnitude higher, within the range of the calibration curve).
- An explanation must be provided for any interference occurring which contributes more than ± 3 % to the total quantity determined.
- For the determination of a pure active substance, the calibration range must extend (by at least 20 %) the highest and lowest nominal content of the analyte in relevant analytical solutions. Duplicate calibration determinations must be made at three or more concentrations. Alternatively, five concentrations, each as single measurements, are acceptable. Reports submitted must include the equation of the calibration line and the correlation coefficient and representative and properly labelled documentation from the analysis, e.g. chromatograms.
- For the repeatability in the determination of the pure active substance, in principle a minimum of five determinations must be made. The relative standard deviation (% RSD) must be reported. Outliers identified through an appropriate method (e.g. Dixon's or Grubb's test) may be discarded. Where outliers have been discarded, that fact must be clearly indicated. An explanation as to the reason for the occurrence of individual outliers must be attempted.

4.2 Analytical methods in all relevant environmental media including recovery rates and the limits of determination for the active substance, and for residues thereof, and where relevant in/on the following *[Ann. IIA, IV.4.2.]*:

(a) Soil

- The proposed limit of determination must not exceed a concentration which is of concern with regard to the exposure of non-target organisms. Normally the proposed limit of determination should not exceed 0.05 mg/kg.

(b) Air

- This needs to be submitted e.g. if the substance is volatile (i.e. if the vapour pressure ≥0.01 Pa) or sprayed, or occurrence in air is otherwise probable.
- The proposed limit of determination must take into account relevant health based limit values or relevant exposure levels.

(c) Water

- *The applicant should confirm that the substance itself and any of its degradation products which fall within the definition of pesticides given for parameter 55 in Annex I to Council Directive 80/778/EEC of 15 July 1980 relating to the quality of water intended for human consumption (OJ No L 229, 30.8.1980, p. 11). This Directive as last amended by Directive 91/692/EEC, OJ No L 377, 31.12.1991, p. 48; and amended by directive 98/83/EC) can be estimated with adequate reliability at the MAC specified in that Directive for individual pesticides.*
- Directive 75/440/EC (concerning the quality required of surface water intended for the abstraction of drinking water in the Member States).
- Detection and analytical method(s) for natural water and natural sediment (the natural environment).

(d) Animal and human body fluids and tissues

- Where an active substance is classified as toxic or highly toxic, analytical methods must be submitted which allow determination of the active substance at the no adverse effect concentration.

The following guidance applies to the data requirements a to d:

- Methods for the analysis for parent compounds and/or metabolites of concern must be submitted.
- For each method and for each relevant representative matrix, the specificity, precision, recovery, and limit of determination must be experimentally determined and reported.
- In principle, residue methods proposed should be multi-residue methods; a standard multi-residue method must be assessed and reported as to its suitability for residue determination. Where residue methods proposed are not multi-residue methods, or are not compatible with such methods, an alternative method must be proposed. Where this requirement results in an excessive number of methods for individual compounds, a "common moiety method" may be acceptable.

5 EFFECTIVENESS AGAINST TARGET ORGANISMS AND INTENDED USES

- Information on the effectiveness and intended uses of the active substance must be sufficient to permit an evaluation of the product, including the nature and benefits that accrue following use of the substance in comparison to suitable reference substances or damage thresholds, and to define its conditions of use. Actual

efficacy studies are required in Section B5, data set for the biocidal product.

5.1 Function, for example fungicide, rodenticide, insecticide, bactericide *[Ann. IIA, V.5.1.]*

5.2 Organism(s) to be controlled and products, organisms or objects to be protected. *[Ann. IIA, V.5.2.]*

- For an organism to be controlled give both the common name and the scientific name when possible and also the sex, strain and stadia where relevant and appropriate. Where complexes of organisms are involved, generic names, representative of the diversity of the complex must be indicated. Where human and/or animal pathogens are involved, the specific name(s) must be given.
- Indicate in which parts of the Community the organisms to be controlled exist.

5.3 Effects on target organisms, and likely concentration at which the active substance will be used *[Ann. IIA, V.5.3.]*

5.3.1 Effects on target organisms *[Ann. IIA, V.5.3.]*

- The effects on the target organisms required for the claimed efficacy should be described and specified if possible for each use and method of application if these have different effects.
- The dependence of the effect on the concentration of the active substance should be indicated.
- The possible existence of a threshold concentration for the desired effect should be stated. This is the case if the dependence of the desired effect on the concentration of the active substance is not found (or is much weaker) below a certain concentration, the threshold concentration.

5.3.2 Likely concentration(s) at which the active substance will be used *[Ann. IIA, V.5.3.]*

- The likely use concentrations in the target should be stated for each use and method of application. Indicate if the use concentrations should be different in different parts of the European Community.
- Justification for the selection of the use concentrations should be given. The likely use concentration should ideally be the minimum effective concentration, taking into account all relevant parameters that impact on efficacy.

5.4 Mode of action (including time delay) *[Ann. IIA, V.5.4.]*

- The mode of action in terms, where relevant, of the biochemical and physiological mechanism(s) and biochemical pathways involved should be stated. Where available, the results of experimental studies must be reported.
- Where it is known that in order to exert its intended effect the active substance must be converted into a metabolite or degradation product following application or use of a preparation containing it, justification should be submitted for why this metabolite or degradation product is not considered to be the active substance. In addition, available information relating to the formation of reactive metabolites or reaction products must be provided. This information must include:
  - the chemical name, empirical and structural formula, molecular mass, and CAS and EC (EINECS, ELINCS or No Longer Polymers list) numbers if available;
  - the processes, mechanisms and reactions involved;

- kinetic and other data concerning the rate of conversion and if known the rate limiting step; and
- environmental and other factors effecting the rate and extent of conversion.

- Indicate also if the actual active substance is the result of a combined action of different products (i.e. when such a combination is necessary to achieve the intended effect).

5.5 Field of use envisaged *[Ann. IIA, V.5.5.]*

- State in which of the product type(s) (given in the Directive, Annex V) that the active substance is intended to be included. Indicated also the fields of use specified in the Directive. In addition, give a detailed description of the overall use patterns. Information on the fields of use envisaged should be sufficient to allow for an approximate but realistic estimation of human and environmental exposure to the active substance.

5.6 User: industrial, professional, general public (non-professional) *[Ann. IIA, V.5.6.]*

- Definitions:
  a) industrial user, i.e. manufacturer of products (manufacture: all operations of purchase of starting materials and packaging materials, production, quality control release, storage, distribution of products and the related controls; where production can be defined as: all operations involved in the preparation of a product, from receipt of materials, through processing and packaging, to its completion as a finished product);
  b) professional user, including also other professional user than manufacturer; and
  c) non-professional user (the general public) at work-place and/or at home.
- Indicate user with the help of the categories given above, including also 'other professional user than industrial' where relevant.
- The following are examples of the use(r) categories: vacuum impregnation of timber and addition of in-can preservatives are industrial use, preservatives for liquid-cooling and processing systems are used by professionals, avicides and piscicides are used by other professional user than industrial, and disinfectants for water beds are mainly used by non-professionals.

5.7 Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies *[Ann. IIA, V.5.7.]*

- Including also cross-resistance. Where such information is not directly relevant to the uses for which authorisation is sought or to be renewed (e.g. different species of harmful organism), it must nevertheless be submitted as it may provide an indication of the likelihood of resistance development in the target population.
- Where there is evidence or information to suggest that in commercial experimental use the development of resistance is likely, evidence must be generated and submitted as to the sensitivity to the substance on the part of the populations of the harmful organism concerned. In such cases a management strategy designed to minimise the likelihood of resistance or cross-resistance developing in target species must be provided. This is addressed in the draft technical note for guidance in support of annex VI.

5.8 Likely tonnage to be placed on the market per year *[Ann. IIA, V.5.8.]*

- An estimate of the quantity of the active substance placed or to be placed on the EU market (i.e. imported or produced). The quantities for biocidal use and in which product type(s), and the quantities for use other than as a biocide should be indicated, if available. For new substances not previously marketed, production plans covering the next few years after authorisation should be provided.

6 TOXICOLOGICAL AND METABOLIC STUDIES *[Ann IIA, VI.]*

6.1 Acute Toxicity *[Ann IIA, VI. 6.1.]*

For studies 6.1.1 to 6.1.3, substances other than gases shall be administered via at least two routes, one of which should be the oral route. The choice of the second route will depend upon the nature of the substance and the likely route of human exposure. Gases and volatile liquids should be administered by the inhalation route.

- The acute toxicity tests provide an indication of possible adverse effects of the active substance. Administration via different routes makes possible an overall assessment of relatively acute hazard of exposure in different exposure routes. Furthermore, acute toxicity testing serves as an initial step in planning dosage levels for subsequent testing. Acute toxicity testing may provide valuable information for accidental situations.
- Any other acute toxicity studies conducted using other than oral, dermal or inhalation administration routes, must be referred to in accordance with Chapter 3, A.6.11.

6.1.1 Oral *[Ann IIA, VI. 6.1.1]*

- For substances with low acute oral toxicity a limit test with 2000 mg/kg b.w. may be sufficient. However, need for testing of higher dose could be decided on a case-by-case basis.
- When planning new tests, the EC methods B.1.bis, B.1.tris (or the corresponding OECD guideline 420 and 423) and the OECD Guideline 425 are recommended. EC method B.1 (or the corresponding OECD Guideline 401) should not be used. Existing results based on EC method B.1 (or OECD method 401) are accepted.

6.1.2 Dermal *[Ann IIA, VI. 6.1.2.]*

- Dermal toxicity must be reported in an active substance except for gases.
- For substances with low acute dermal toxicity a limit test with 2000 mg/kg b.w. may be sufficient.
- EC method B.3 or the corresponding OECD guideline 402.

6.1.3 Inhalation *[Ann IIA, VI. 6.1.3.]*

- Inhalation toxicity must be reported where the active substance is:
  - a volatile substance (vapour pressure > 1 x 10^{-2} Pa at 20 ^{o}C),
  - a powder containing a significant proportion (e.g. >1% on a weight basis) of particles with particle size MMAD <50 micrometers or

- to be included in preparations which are powders or are to be applied in a manner which generates aerosols, particles or droplets in the inhalable size range (MMAD < 50 micrometers).

- Substances classified as corrosive in skin must not be studied.
- The full study using three dose levels may not be necessary if a substance at an exposure concentration to the limit concentrations of the test guideline (limit test) or at the maximum attainable concentration produces no compound-related mortalities.
- EC method B.2. or the corresponding OECD guideline 403.

6.1.4 Skin and eye irritation *[Ann IIA, VI. 6.1.3.]*

- The tests will provide information on the degree and nature of skin, eye and associated mucous membrane irritation, especially with regard to the reversibility of responses.
- These tests need not be carried out if the active substance is a strong acid or base (pH below 2 or above 11.5) and *where the active substance has shown to have potential corrosive properties,* or is a severe skin irritant, *eye irritation test shall not be necessary.*
- It may be possible to accept positive findings from *in vitro* test methods which are close to validation by recognised organisations
- EC methods B.4 (skin irritation) and B.5 (eye irritation) or the corresponding OECD guidelines 404 and 405.

6.1.5 Skin sensitisation *[Ann IIA, VI. 6.1.5.]*

- The test will provide sufficient information to assess the potential of the active substance to cause skin sensitisation reactions.
- While the guinea-pig Maximisation test is considered to be the preferred adjuvant technique in certain cases there may be good reasons for choosing the Buehler test or the Local Lymph Node Assay (LLNA). However, scientific justification may be given when either of the two latter mentioned is used.
- The test is not needed if the active substance is classified as a sensitiser according to Directive 67/548/EEC or is otherwise known to be a sensitiser (e.g. see human data in paragraph A6.12.6).
- EC method B.6 or the corresponding OECD guideline 406.

6.2 Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study *[Ann IIA, VI. 6.2.]*

- The test(s) should provide basic data about rate and extent of absorption, the tissue distribution and the relevant metabolic pathway including the degree of metabolism, the routes and rate of excretion and the relevant metabolites.
- Usually a single application test with two different doses (low and high doses) and a repeated dose toxicokinetic study in one appropriate species, usually the rat, by the oral route is required. In some cases it may be necessary to perform additional tests on other species and using other exposure routes. However, these requirements depend on e.g. the results obtained in physico-chemical and toxicological studies of the test substance. An expert judgement is required for detailed additional data requirements (see Chapter 1.2, point 4).
- An appropriate dermal absorption assessment is needed. A sequential approach should be applied for the decision if biological testing is needed (TNO 1999). If testing is necessary to decide whether this test should be performed *in vivo* or *in vitro*, the present development of the OECD test Guidelines Programme for

Guidelines on Percutaneous Absorption/Penetration has to be taken in account.

- E.g. Method B.36 or the corresponding OECD guideline 417.

For the following studies, 6.3 (where necessary), 6.4, 6.5, 6.7 and 6.8, the required route of administration is the oral route unless it can be justified that an alternative route is more appropriate.

- The primary required route is the oral route.
- Justification to replace the oral route by another significant route, or to require testing in addition to the oral route includes: proposed or potential applications of the substance/products, route of exposure, the results of the acute toxicity tests and on physico-chemical properties of substance (for highly volatile (liquids) substances and gases an inhalation study could be appropriate; aerosols should be treated case by case). The dermal route could be relevant if dermal penetration studies demonstrate significant dermal penetration.
- Repeated dose toxicity testing provides information on adverse effects as a result of prolonged exposure. The repeated toxicity studies must be sufficient to establish or identify:
  - the dose-response relationship
  - the no-observed-adverse-effect-level (NOAEL)
  - target organs and effects in target organs
  - mode of toxic action, where possible
  - the cumulative effects of the substance
  - toxic effects after the different routes of exposure.
- The results in short-term toxicity studies will help in selecting dose levels for long-term toxicity testing and to assess the need for further studies (e.g. mechanistic studies. See Chapter 3, A-6.10). Planning of the long-term studies should be made on the basis of the results in the short-term toxicity studies and studies on toxicokinetics.
- Possible neurotoxic effects, immunological effects and endocrine disrupting effects should be taken into consideration. If some evidence of neurotoxicity or possible effects on immune or endocrine systems is provided, further in-depth investigation may be required. An expert judgement is required for deciding on supplementary studies (see Chapter 1.2, point 4).

6.3 Short term repeated dose toxicity (28 days) *[Ann IIA, VI. 6.3.]*

- These tests are used as a range-finding test and *are not required when an* adequate *sub-chronic toxicity study is available in a rodent.* These tests must be submitted if they have been conducted.
- For substances with low toxicity, a limit test administered by oral routes with 1000 mg/kg b.w. may be sufficient.

6.3.1 Repeated dose toxicity (oral)

- EC method B.7 or the corresponding OECD guideline 407.

6.3.2 Repeated dose toxicity (dermal)

- A percutaneous study is required, where the potential dermal exposure is significant and route-to-route extrapolation is not possible.
- However, a percutaneous study may be necessary where it is justified that dermal route is more appropriate or specific effects of concern are different from the effects seen in the studies in other routes.

- EC method B.9 or the corresponding OECD guideline 410.

6.3.3 Repeated dose toxicity (inhalation)

- For volatile substances (vapour pressure >1x 10^{-2} Pa) or in cases where the potential inhalation exposure is significant, an inhalation study is required instead of the oral study.
- In some cases (e.g. aerosols and dusts/particulate matter) studies by the inhalation route should be required in addition to studies by the oral route.
- EC method B.8 or the corresponding OECD guideline 412.

6.4 Subchronic toxicity [*Ann IIA, VI. 6.4.]*

- Should usually be studied in *two species, one rodent and one non-rodent*.
- For substances with low toxicity, a limit test administered by oral routes with 1000 mg/kg b.w. may be sufficient.
- Where testing in two species is required the testing may be waived only if it is scientifically justified; in case residues are found in the food chain waiving is not possible.

6.4.1 Subchronic oral toxicity test

- Usually rat is the preferred rodent species and dog as the non-rodent species. If there is evidence from the 90-day studies that the dog is significantly more sensitive and where such data is likely to be useful in extrapolating results to man, in addition to the 90-day study a 12 month toxicity study in dogs may need to be conducted and reported. It is possible to replace a 90-day study in dog by a one-year study in a dog. An expert judgement is required to determine whether the one-year test is needed (see Chapter 1.2, point 4).
- EC methods B.26 (90-day repeated oral dose study using rodent species) and B.27 (90-day repeated oral dose study using non-rodent species) or the corresponding OECD guidelines 408 or 409.

6.4.2 Subchronic dermal toxicity test

- A percutaneous study in the rat is preferred, where the potential dermal exposure is significant and route to route extrapolation is not possible.
- However a percutaneous study may be necessary where it is justified that dermal route is more appropriate or specific effects of concern are different from the effects seen in the studies in other routes.
- The test should not be required for substances with low dermal toxicity, e.g. substances which have shown no toxic effects in the 28 day study at limit-dose.
- EC method B.28 or the corresponding OECD guideline 411.

6.4.3 Subchronic inhalation toxicity test

- For volatile substances and gases (vapour pressure > 1x 10^{-2} Pa)
- In cases where inhalation exposure is significant, an inhalation study is required instead of the oral study.
- EC method B.29 or the corresponding OECD guideline 413.

6.5 Chronic toxicity *[Ann IIA, VI. 6.5.]* The test is required for one rodent and one other mammalian species. It is recommended to study the rat first, and based on this result more testing in another mammalian species may be necessary
A test should be performed in a *rodent*, the rat being the preferred species.

The long-term-toxicity of an active substance may not be required where a full justification demonstrates that these tests are not necessary based on the sub-chronic toxicity test (and demonstrated reversibility) in the same species.

- Any new long-term toxicity study and the carcinogenicity study (A6.7) should be combined. The recommended species is the rat.
- EC methods B.30 or the corresponding OECD guidelines 451, 453.

6.6 Genotoxicity studies **(**, *[Ann IIA, VI. 6.6.])*

- The testing of genotoxicity is a screening program to identify substances which might cause permanent transmissible changes in the amount or structure of a single gene or gene segments, a block of genes or chromosomes. Genotoxicity studies may provide pre-screening information on the genotoxic carcinogenic potential of a substance.
- At least one *in vitro* test for gene mutations, one test for clastogenicity in mammalian cells and one test for gene mutation in mammalian cells are required. Additional tests, which may become necessary upon positive results of the initial screening tests or for other reasons, should be selected on a case-by case basis taking into consideration genetic end-points, mechanistic aspects, cell-specific aspects, physico-chemical, toxicokinetic and toxicodynamic properties and relevant information on the chemical analogues of the substance. An expert judgement is required to decide on additional studies (see Chapter 1.2, point 4).
- EC methods B.10-B25 or the corresponding on OECD guidelines 471-485.

6.6.1 *In vitro* gene mutation study in bacteria *[Ann IIA, VI. 6.6.1.]*

- E.g. EC method B.14 (Salmonella typhimurium-reverse mutation assay) or the corresponding OECD guideline 471.

6.6.2 *In vitro* cytogenicity study in mammalian cells *[Ann IIA, VI. 6.6.2.]*

- E.g. EC method B.10 (*In vitro* mammalian cytogenetic test) or the corresponding OECD guideline 473.

6.6.3 *In vitro* gene mutation assay in mammalian cells *[Ann IIA, VI. 6.6.3.]*

- E.g. EC method B.17 (*In vitro* mammalian cell gene mutation test) or the corresponding OECD guideline 476.

6.6.4 If positive in 6.6.1, 6.6.2 or 6.6.3, then an *in vivo* genotoxicity study will be required (bone marrow assay for chromosomal damage or a micronucleus test) *[Ann IIA, VI. 6.6.4.]*

- EC methods B.11 (*In vivo* mammalian bone-marrow cytogenetic test, chromosomal analysis), B.12 (Micronucleus test) or the corresponding OECD guidelines 474, 475 are preferred testing methods. Tests performed accordingly EC methods B.24 (Mouse spot test) or the corresponding OECD guideline 484, B.39 (in vivo UDS assay) or the corresponding OECD guideline 486 and other tests may give supplementary information on genotoxicity.

6.6.5 If negative in 6.6.4 but positive in some of *in vitro* tests then undertake a second *in vivo* study to examine whether mutagenicity or evidence of DNA damage can be demonstrated in tissue other than bone marrow. *[Ann IIA, VI. 6.6.5.]*

- Methods: See point 6.6.4.

6.6.6 If positive in 6.6.4 then a test to assess possible germ cell effects may be required.

[Ann IIA, VI. 6.6.6.]

- EC method B 22 (Rodent dominant lethal test) and B23 (*In vivo* mammalian germ cell cytogenetics) or the corresponding OECD guidelines 478 and 483.

6.6.7 If the results are negative for the three tests 6.6.1, 6.6.2 and 6.6.3, then further testing is normally only required if metabolites of concern are formed in mammals, and in Chapter 1.4 further guidance is given on the non-submission of data. (See also the Technical Guidance Document for the Risk Assessment New and Existing Chemicals)

6.7 Carcinogenicity study *[Ann IIA, VI. 6.7]*

- The carcinogenicity study identifies the carcinogenicity potential of the substance in laboratory animals in order to facilitate the extrapolation of potential risks to humans. The studies must be sufficient to establish the species specificity and organ specificity of tumours induced, to establish the dose-response relationship and for non-genotoxic carcinogens to identify doses eliciting no adverse effects (threshold dose).
- *One rodent and one other mammalian species* should be tested. *New studies should be combined with those in A6.5*. The rat and the mouse are usually the species used for testing carcinogenic potential, while the rat is used for a combined chronic toxicity/ carcinogenicity testing.
- *The carcinogenicity of an active substance may not be required where a full justification demonstrates that these tests are not necessary.*
- On the basis of positive results in carcinogenicity studies, indicating non-genotoxicity effects additional mechanistic studies or considerations may be needed (especially if a non-genotoxic mechanism is indicated) (See Chapter 3, A6.10).
- While the standard reference points for the treatment responses are concurrent control data, historical control data may be helpful in the interpretation of particular carcinogenicity studies. Where submitted, historical control data should be from the same species and strain, maintained under similar conditions and should be from contemporaneous studies. The information on historical control data provided must include:

- -identification of species and strain, name of supplier, and specific colony identification, if the supplier has more than one geographical location,
- -name of the laboratory and the dates when the study was performed,
- -description of the general conditions under which animals were maintained, including the type or brand of diet and, where possible, the amount consumed,
- -approximate age, in days, of control animals at the beginning of the study and the time of killing or death,
- -description of the control group mortality pattern observed during or at the end of the study, and other pertinent observations (e.g. diseases, infections),
- -name of the laboratory and the examining scientists responsible for gathering and interpreting the pathological data from the study, and
- -a statement of the nature of the tumours that may have been combined to produce any of the incidence data.

- The doses tested, including the highest dose tested, must be selected on the basis of the results of short-term testing and where available at the time of planning the studies concerned, on the basis of metabolism and toxicokinetic data. The highest dose level in the carcinogenicity study should elicit signs of minimal toxicity such as slight depression in body-weight gain (less than 10 %), without causing tissue

necrosis or metabolic saturation and without substantially altering normal life-span due to effects other than tumours. If the long-term toxicity study is carried out separately, the highest dose level should elicit definite signs of toxicity without causing excessive lethality. Higher doses, causing excessive toxicity are not considered relevant to evaluations to be made.

- In the collection of data and compilation of reports, incidence of benign and malignant tumours must not be combined, unless there is clear evidence of benign tumours becoming malignant with time. Similarly, dissimilar, unassociated tumours, whether benign or malignant, occurring in the same organ, must not be combined, for reporting purposes.
- In the interest of avoiding confusion, harmonised terminology and diagnostic criteria such as that developed by the Hannover Tumour Registry (RENI) and published by WHO/IARC series should be used in the nomenclature and reporting of tumours. If an alternative nomenclature is applied, the diagnostic criteria must be given in the report.
- EC methods B.32 (Carcinogenicity test), B.33 (Combined chronic toxicity/carcinogenicity test) or the corresponding OECD guidelines 451, 453.

6.8 Reproductive toxicity *[Ann IIA, VI. 6.8.]*

- These tests provide information on adverse effects on male and female fertility and embryonic and foetal development including possible adverse effects on the offspring during lactation and on the maternal animals. The tests will give additional information on any enhancement of general toxic effects on pregnant animals.
- *If, in exceptional circumstances, it is claimed that such testing is unnecessary, this claim must be fully justified.*
- A scientific expert judgement is required to decide on supplementary studies (see Chapter 1.2, point 4).

6.8.1 Teratogenicity test *[Ann IIA, VI. 6.8.1*

- The tests should normally be performed in *the rabbit and one rodent species*
- In case that one study is performed the preferred species is the rabbit.
- For substances with low toxicity a limit test with 1000 mg/kg b.w. may be sufficient
- While the standard reference point for treatment responses are concurrent control data, historical control data may be helpful in the interpretation of the particular teratogenicity studies. The historical control data provided must include the same principles as reported (see Chapt.2, point 6.7). A computerised database as reference for these data may be useful.
- A glossary or detailed description of terminology and diagnostic principles for malformations and variations must be given in the report.
- EC method B.31 or the corresponding OECD guideline 414.

6.8.2 Two-generations reproduction study *[Ann IIA, VI. 6.8.2.]*

- This should be conducted using *two generations, in one species* (the rat),
- The investigation should carefully be performed both with male and female animals.
- EC method B.35 or the corresponding OECD guideline 416.

(6.9 An additional data requirement. See Chapter 3, part A.)
(6.10 An additional data requirement. See Chapter 3, part A.)

(6.11 An additional data requirement. See Chapter 3, part A.)

6.12 Medical data in anonymous form *[Ann IIA, VI. 6.9.]*

- Data and information on the effects of human exposure, if available, may provide valuable information for confirming the validity of extrapolations made and conclusions reached from animal data and for identifying unexpected adverse effects which are specific to humans.
- Data and information following accidental or occupational exposure have to be submitted where available and of adequate quality. Practical data and information relevant to the recognition of the symptoms of poisoning, on the effectiveness of first aid and therapeutic measures must be included.
- It is usually not possible to require this data for new active substances.

6.12.1 Medical surveillance data on manufacturing plant personnel if available *[Ann IIA, VI. 6.9.1.]*

- The reports should include detailed information on the design of the programme and exposure to the active substance and to other chemicals. Data relevant to the mechanism of the action of substance should also be included where feasible. The data may consist of published articles or unpublished medical surveys.

6.12.2 Direct observation, e.g. clinical cases, poisoning incidents if available *[Ann IIA, VI. 6.9.2.]*

- The reports should include a complete description of the exposure situation, clinical symptoms observed and therapeutic measures. Reports of any follow-up studies should be enclosed.

6.12.3 Health records, both from industry and any other available sources *[Ann IA, VI.6.9.3.]*

6.12.4 Epidemiological studies on the general population, if available *[Ann IIA, VI. 6.9.4.]*

- Information related to occupational exposure or other exposure, consist of three main sources: case reports, descriptive epidemiological studies and analytical epidemiological studies, case-control or cohort studies. Where available, data should be supported with data on levels and duration of exposure.

6.12.5 Diagnosis of poisoning including specific signs of poisoning and clinical tests, if available *[Ann IIA, VI. 6.9.5.]*

- A detailed description of clinical signs and details of clinical tests useful for diagnostic purposes (bio-monitoring). Symptoms of poisoning including full details of the time courses involved to all exposure routes must be described.

6.12.6 Sensitisation/allergenicity observations, if available *[Ann IIA, VI. 6.9.6.]*

- Information on the sensitisation/allergenicity of workers and others exposed must be provided and included, and where relevant, any incidence of hypersensitivity.
- Reports should include details of frequency, level, duration, symptoms observed, and other relevant data.
- Evidence that the substance can induce specific respiratory hypersensitivity will usually be based on human experience data. The clinical history data including both medical and occupational history, and reports from appropriate lung functions tests related to exposure to the substance should be submitted, if available. Reports of other supportive evidence must also be submitted, e.g.

- a chemical structure related to substances known to cause respiratory hypersensitivity
- *in vivo* immunological tests
- *in vitro* immunological tests
- studies indicating other specific but non-immunological mechanisms of action
- data from a positive bronchial challenge test.

6.12.7 Specific treatment in case of an accident or poisoning: first aid measures, antidotes and medical treatment, if known *[Ann IIA, VI. 6.9.7.]*

- First aid measures in the event of poisoning and eye contamination must be provided.
- Therapeutic regimes and the use of antidotes must be described. Information based on practical experience, where it exists and is available, or in other cases information based on theoretical grounds, as to effectiveness of alternative treatment regimes, where relevant must be provided. Contraindications associated with particular regimes, particularly those relating to ”general medical problems” and conditions, must be described.

6.12.8 Prognosis following poisoning *[Ann IIA, VI. 6.9.8.]*

- The expected effects and the duration of these effects following poisoning must be described.

(6.13 An additional data requirement. See Chapter 3, part A.)
(6.14 An additional data requirement. See Chapter 3, part A.)
(6.15 An additional data requirement. See Chapter 3, part, A.)
(6.16 An additional data requirement. See Chapter 3, part A.)

6.17 Summary of mammalian toxicology and conclusions

- Each study submitted should be summarised and, for old studies, and the quality and relevance should be evaluated and the information should be stated at the relevant sub-chapters.
- An overview of the results of the studies and any additional toxicological information should be given here. This is the initial mammalian hazard assessment.
- A reporting format is under development.

7 ECOTOXICOLOGICAL PROFILE INCLUDING ENVIRONMENTAL FATE AND BEHAVIOUR

- The information provided must be sufficient to classify the active substance as to hazard (according to the Directive 67/548/EEC) and to permit an assessment of the fate and behaviour of the active substance in the environment, and of the impact on non-target species (flora and fauna), likely to be at risk from exposure to the active substance, its metabolites, degradation and reaction products, where they are of environmental significance.
- It may be necessary to conduct separate studies for metabolites, degradation or reaction products where these products can constitute a relevant risk to non-target organisms or to the quality of water and where their effects cannot be evaluated by the available results relating to the active substance. Before such studies are performed, the information from sections A6 ‘Toxicological and metabolic studies’ and A7 ‘Ecotoxicological profile’ has to be taken into account.

- Where relevant, tests should be designed and data analysed using appropriate statistical methods. Full details of the statistical analysis should be reported (e.g. all point estimates should be given with confidence intervals, exact probability values should be given rather than stating significant/non significant).

Fate and Behaviour in the Environment

- Information related to the fate and behaviour of the active substance and its degradation products in the environment is needed in order to be able to assess the exposure of the environment, for example, by the approximate estimation of the likely concentrations of the substance in the different compartments of the environment.
- The data and information provided should be sufficient to:
  - identify the relative importance of the types of processes involved (balance between chemical and biological degradation),
  - where possible, identify the individual components present,
  - establish the relative proportions of the components present and their distribution as between water, including suspended particles, and sediment, and
  - permit the residue of concern and to which non-target species are or may be exposed, to be defined.
- Where radio-labelled test material is used, radio-labels should be positioned at sites (one or more as necessary), to facilitate the elucidation of metabolic and degradative pathways and to facilitate investigation of the distribution of the active substance and of its metabolites, reaction and degradation products in the environment.

7.1 Fate and Behaviour in Water

7.1.1 Degradation, initial studies

7.1.1.1 Abiotic *[Ann. IIA, VII.7.6.2.]*

7.1.1.1.1 Hydrolysis as a function of pH and identification of breakdown products *[Ann.IIA, VII.7.6.2.1.]*

- Must be examined at least at three different pH-values. For substances with a low hydrolysis rate, just the preliminary test carried out at 50 °C for five days may be sufficient. A substance of which less than 10% hydrolyses in 5 days at 50°C (i.e. is considered hydrolytically stable) need not to be further tested for hydrolysis.
- Identification is required for breakdown products that at any sampling time account for more than 10% of the active substance added. *Annex to Chapter 1 on metabolites currently drafted for plant protection products could be re-written to cover metabolites for biocides as well).*
- Test according to EC method C.7. or the corresponding OECD guideline 111 (Hydrolysis as a function of pH).

7.1.1.1.2 Phototransformation in water including identity of the products of transformation *[Ann.IIA, VII.7.6.2.2.]*

- Test according to the SETAC procedures (SETAC 1995) or e.g. US-EPA guideline OPPTS 835.2210 (US-EPA, 1998). [**Note:** There is an OECD draft guideline available.]
- *The data must be submitted for a purified active substance of stated specification.*
- Identification is required for transformation products that at any sampling time account for more than 10% of the active substance added.

- The results submitted should correspond to the light intensities and spectral distribution from northern to southern European regions, for example, in 40 and 65 degrees (proposed average 50 degrees) northern latitude during spring and autumn. This may be presented e.g. by extrapolation.
- Further guidance for conducting the study may be found in an OECD Guidance Document (OECD 1997).

7.1.1.2 Biotic *[Ann.IIA, VII.7.6.1.]*

7.1.1.2.1 Ready biodegradability *[Ann.IIA, VII.7.6.1.1.]*

- At least a screening test on ready biodegradation is always required of organic compounds, unless a simulation test is required. (More details are given in Chapter 3, 7.0.2 testing strategy on biodegradation of biocidal active substances and testing methods).
- Test according to any of the EC methods C.4-A-F or the corresponding OECD guideline 301 A-F taking especially notice of the Annex to these methods concerning the evaluation of the biodegradability of chemicals suspected to be toxic to the inoculum.
- See Chapter 3 for guidance on further studies.

7.1.1.2.2 Inherent biodegradability, where appropriate *[Ann.IIA, VII.7.6.1.2.]*

- May be performed if the compound is not readily degradable unless a simulation test is performed. Simulation tests are preferred instead of new tests on inherent biodegradability. The testing strategy to follow is described in Chapter 3, 7.0.2.2.2.
- EC method C.12 and EC.C.9 or the corresponding guidelines OECD 302 A-B and OECD 302 C.

(7.1.2 An additional data requirement on rate and route of degradation in aquatic systems; guidance is given in Chapter 3).

7.1.3 Adsorption/desorption screening test *[Ann.IIA, VII.7.7.]*

- A screening test is always required according to, for example, to the new EC method C.18 or the corresponding OECD guideline 106 tier 2 (Adsorption/de-sorption) The adsorption is studied in five different soil types by means of adsorption kinetics at a single concentration and determination of distribution coefficients Kd and Koc. Although not explicitly mentioned in the guideline the handling procedure can also be applied to sediments.
- An alternative method is the estimation of adsorption with HPLC, OECD guidelines 121 (draft, will soon be adopted as new EC method). The method provides an estimate of a chemical's partitioning behaviour between aqueous phases and organic surfaces of soils, sediments and sludge (Koc). This estimate is normally sufficient for a preliminary exposure assessment of substances (e.g. feed in fugacity type models). It should be noted however, that for some substances the HPLC-technique is not yet fully validated.
- *Where the results of this test indicate the need to do so, the* additional *test described in the Chapter 3, in paragraph A7.1.4 (data set for the active substance) shall be required, and/or the* additional *test described in paragraph A7.2.3.* A more detailed testing strategy is described in Chapter 3.

(7.1.4-7.3 Additional data requirements, see Chapter 3, part A.)

Ecotoxicological studies

- The ability of the active substance or its degradation product(s) to damage the function and structure of biotic systems is to be clarified with a selection of ecotoxicity tests. Effects in the ecologically functional groups of producers, consumers and decomposers in relevant media (water, soil, and air) are addressed in these tests.
- There is a need to report all potentially adverse effects found during routine eco-toxicological investigations and to undertake and report, where required by the competent authorities, such additional studies which may be necessary to investigate the probable mechanisms involved and to assess the significance of these effects. All available biological data and information which is relevant to the assessment of the ecotoxicological profile of the active substance must be reported.
- The species tested should be relevant to the environments likely to be affected due to the manner of use or disposal of the substance. Seawater species should be used if the substance is likely to influence directly or indirectly only estuarine or marine environments. If a marine or brackish water environment is affected but it is not the only aquatic target environment, then a toxicity test in a marine or in a brackish water species, respectively is required in addition to the fresh water tests (see Chapter 2.5).
- The information on fate and behaviour in the environment, generated and submitted in accordance with paragraphs A7.1 to A7.3, data set for the active substance, together with information on the nature of the preparation and its manner of use; this defines the nature and extent of potential exposure. The toxicokinetic and toxicological studies and information submitted in accordance with section A6 provide essential information as to toxicity to vertebrate species and the mechanisms involved.
- In the case of studies in which dosing extends over a period, dosing should preferably be done using a single batch of active substance if stability permits. Whenever a study implies the use of different doses, the relationship between dose and adverse effect must be reported.
- In order to facilitate the assessment of the significance of test results obtained, including the estimation of intrinsic toxicity and the factors affecting toxicity, the same strain (or recorded origin) of each relevant species should, where possible, be used in the various toxicity tests specified.
- As required by EC test methods, concentrations of the test substance should be measured at least at the beginning as well as at the end of the test. Normally, however, it will be necessary to monitor the concentrations more frequently. The LC_{50}'s, EC_{50}'s and NOEC’s should be calculated based on the measured concentrations. However, where the measured concentrations are close to the nominal concentrations (i.e. > 80% of nominal), it is acceptable to calculate the LC_{50}'s, EC_{50}'s and NOEC’s based on nominal concentrations of the tested substance. In other cases, the geometric average measured concentrations should be used.

7.4 Effects on Aquatic Organisms

7.4.1 Aquatic toxicity, initial tests

- The tests should provide the acute toxicity values related to mortality, immobilisation or growth and growth rate, NOEC values, and details of observed effects.

- When carrying out toxicity tests on aquatic organisms, it is useful to test information on the solubility and stability of the substance in the test medium, as it may differ from the result obtained under the water solubility test (paragraph A3.5, data set for the active substance).

7.4.1.1 Acute toxicity to fish *[Ann. IIA, VII.7.1.]*

- Should be studied with one species and a fresh water species is preferred or, if different aquatic environments are exposed, with two species (cf. Chapter 2.5). The two species selected should represent fresh water and marine environments. *Cyprinodon variegatus* may be used as marine species.
- Test according to the EC method C.1 or the corresponding OECD guideline 203 (where test with *Cyprinodon variegatus* is also possible), or for a marine species e.g. US-EPA guideline OPPTS 850.1075 (US-EPA 1996a).

7.4.1.2 Acute toxicity to invertebrates *[Ann. IIA, VII.7.2.]*

- Test according to the EC method C.2 on freshwater crustacea (*Daphnia*) or the corresponding OECD guideline 202.
- Test on marine/brackish crustacea according to, for instance, the ISO standard ISO/DIS 14669 (still a draft) with marine/brackish crustacea may be appropriate or e.g. the US-EPA guidelines OPPTS 850.1035 (marine mysids) and 850.1045 (marine paneid shrimps) may be used. OPPTS 850.1035 may also be conducted in brackish water, if relevant.
- Tests on marine/brackish molluscs e.g. short-term tests on embryos of e.g. *Mytilus edilus* according to ASTM E724 can be performed. Tests can also be conducted with the brackish water mollusc *Macoma baltica* (Bryant et al. 1985 as quoted in OECD DRP on Aquatic Testing Methods for Pesticides and Industrial Chemicals, 1998).

7.4.1.3 Growth inhibition test on algae *[Ann. IIA, VII.7.3.]*

- Should be studied with one species and a fresh water species is preferred or, if different aquatic environments are exposed, with two species. For instance, in addition to a test in a fresh water species a test in a salt or brackish water species (e.g. the marine diatom, *Skeletonema costatum*, or the blue-green algae - or cyanobacterium, *Anabaena flos-aquae*, suitable both for fresh and brackish water) should be submitted if relevant, see Chapter 2.5.
- Test according to EC method C.3 or the corresponding OECD guideline 201, or for a marine species a test according to for instance the ISO standard ISO 10253 (ISO 1995). For a marine or brackish water species e.g. the US-EPA guideline OPPTS 850.5400 (US-EPA 1996d) may be used.
- For certain product types industry may have efficacy data relating to the effects on algae.

7.4.1.4 Inhibition to microbiological activity *[Ann. IIA, VII.7.4. and Ann. IIIA, VII.3]*

- For example, test according to the EC method C.11. or the corresponding OECD guideline 209 (Activated sludge, respiration inhibition test).
- Relevant efficacy data may be available from industry.

7.4.2 Bioconcentration *[Ann. IIA, VII.7.5.]*

- An estimation of the intrinsic potential for bioconcentration in aquatic organisms on the basis of physical and chemical properties (e.g. partition coefficient n-octanol/ water) and especially in the case of surface active (surface tension lower

than 50 mN/m) dissociating or inorganic substances such as metals, on the basis of toxicokinetic studies (including metabolism), residue studies or monitoring data on aquatic organisms (e.g. data on residues in tissues of aquatic organisms and on concentrations in the environment) or a relevant study available should be submitted. Specific bioconcentration studies may be required as additional data for which guidance is given in Chapter 3. For estimation of BCF, see the Technical Guidance Document (for risk assessment of new and existing substances) Chapter 3 p. 349.

- The evaluation of aquatic bioconcentration should include an estimate of the bio-concentration factor related to an aquatic food chain, freshwater and/or marine, with an aquatic species and a fish eating bird/predator.

7.5 (Additional data requirement guidance is given in Chapter 3, Part A).

7.6 Summary of ecotoxicological effects and fate and behaviour in the environment *[Ann. IIA, VII.7.8.]*

- A summary of all studies and data on environmental fate and effects (both those in the core data set and additional studies, and including mammalian studies submitted for the human risk assessment in Section A6, data set for the active substance, and relevant also for the environment) should always be attached to the application. As a minimum the following information should be presented regarding every study:
  - indication of the quality assurance of the test (e.g. a performance according to GLP); and
  - An overview of the results of the studies (the results from the ecotoxicological tests and fate and behaviour in the environment, together with relevant additional data from Chapter 2.5 should be given here). This is the initial environmental hazard assessment.
  - A reporting format is under development.

8 MEASURES NECESSARY TO PROTECT MAN, ANIMALS AND THE ENVIRONMENT

- Reference can be made to the corresponding data submitted for the product when it is also applicable to the active substance.

8.1 Recommended methods and precautions concerning handling, use, storage, transport or fire *[Ann IIA, VIII. 8.1.]*

- The guidance given for the corresponding data requirement for the product (paragraph B8.1) also applies here.

8.2 In case of fire, nature of reaction products, combustion gases, etc. *[Ann IIA, VIII. 8.2.]*

- The guidance given for the corresponding data requirement for the product (paragraph B8.4) also applies here.

8.3 Emergency measures in case of an accident *[Ann IIA, VIII. 8.3.]*

- The guidance given for the corresponding data requirement for the product (paragraph B8.2) also applies here.

8.4 Possibility of destruction or decontamination following release in or on the follow ing: (a) air (b) water, including drinking water (c) soil *[Ann. IIA, VIII.8.4.]*

- The guidance given for the corresponding data requirement for the product (paragraph B8.6) also applies here.

8.5 Procedures for waste management of the active substance for industry or professional users *[Ann. IIA, VIII.8.5.]*

- Information necessary for safe disposal including treated material must be given. If preliminary treatment of the waste is necessary, information about this must also be given. If the waste from the substance is classified as hazardous waste (e.g. according to Council Decision 94/904/EC[1]), this has to be mentioned separately and appropriate handling according to the related legislation indicated.
- More information is given in Part B section 8.5 (product specific guidance).

8.5.1 Possibility of re-use or recycling *[Ann. IIA, VIII.8.5.1.]*

- The possibility of recovery or recycling should be given for both normal uses of the substance and quantities involved in spills.

8.5.2 Possibility of neutralisation of effects *[Ann. IIA, VIII.8.5.2.]*

- Neutralisation procedures (e.g. by reaction with an alkali to form less toxic compounds) for use, for instance, in the event of accidental spillage must be described where they are feasible. Details to be given: proposed procedures for small and large quantities, evaluation of products of neutralisation (in small and large quantities), procedures for disposal of neutralised waste (in small and large quantities).

8.5.3 Conditions for controlled discharge including leachate qualities on disposal *[Ann. IIA, VIII.8.5.3.]*

- E.g. controlled landfill or extensive dilution (to be specified) before discharge to surface water.
- If a controlled landfill is recommended for use as a disposal sight, information about the necessary preliminary treatment, the fate of the waste in the landfill, the release of active substances or breakdown products from the waste etc. must be given.

8.5.4 Conditions for controlled incineration *[Ann. IIA, VIII.8.5.4.]*

- If the waste disposal method suggested is incineration, the compounds generated by burning (e.g. whether polychlorinated dioxins and furans or other halogen compounds can be formed), recommended burning conditions (temperature, reaction time and oxygen content) and other information needed for the safe incineration of the waste must be given.

8.6 Observations on undesirable or unintended side-effects, for example, on beneficial and other non-target organisms *[Ann. IIA, VIII.8.6.]*

- The guidance given for the corresponding data requirement for the product (paragraph B8.7) applies also here.

1 Council Decision of 22 December 1994 establishing the list of hazardous waste pursuant to Article 1(4) of Council Directive 91/619/EEC on hazardous waste. OJ No L 356/14. 31.12.1994.

8.7 Identification of any substances falling within the scope of List I or List II of the Annex to Directive 80/68/EEC on the protection of ground water against pollution caused by certain dangerous substances (OJ No L 20, 26.1.1980, p. 43.) *[Ann. IIIA, VIII.1.]*

- All biocides and their derivatives are classed in either List I or II. In addition other substances (additives, impurities) in the active substance as manufactured may fall within the scope of the Lists. Specify which substances are classed in List I and which in List II.

9 CLASSIFICATION AND LABELLING [*Ann IIA, IX.]*

Proposals including justification for the proposals for the classification and labelling of the active substance according to Directive 67/548/EEC.

- The classification comprises a description of the category/categories of danger and qualifying risk phrases for all dangerous properties.
- On the basis of classification, give a proposal for labelling including the hazard symbol(s) and indications of danger, risk phrases and safety phrases.
- State the existing classification and labelling if given in Annex I of the Directive 67/548/EEC.

10 SUMMARY AND EVALUATION OF SECTIONS 2 TO 9

- This section is the hazard and effects assessment of the active substances. Guidance will be given in the documents for risk assessment of the active substance and the product, and the guidance for inclusion into annex I (under preparation).
- Each sub-Chapter from 2 to 9 should contain a short summary of the main results and conclusions of the studies. These sub-conclusions are the basis for further risk assessment.
- *A risk assessment on the active substance shall* be submitted. *If there are, in addition, any* degradation products, impurities or additives that are considered to be [*substances*] *of concern then* a proposal for *a risk assessment* should be submitted *for each of these. The risk assessment shall cover the proposed normal use of the* active substance *together with a realistic worst-case scenario including any relevant production and disposal issue either of the biocidal product or any material treated with it.*
- The risk assessment should be conducted according to the principles given in the existing technical guidelines for new and existing chemicals and should include the work with developing relevant exposure scenarios and a full justification for the risk indicators presented (e.g. human exposure levels, NOAELs, NOELS, MOS, PECs, PNECs).
- *In each of the areas where risk assessments* should be *carried out, i.e. effects on man, animals, and the environment, the results for the active substance together with the results for any substance of concern* should be combined in order *to produce an overall assessment for the* active substance. *This should take account of any likely synergistic effects of the active substance(s) and its* degradation products that are considered to be *substances of concern.*
- *A summary should also be made on the* effectiveness against target organisms *and*

of the unacceptable effects.

- A proposal for the entry conditions to Annex I of the Directive should be submitted on the basis of the overall assessment of the active substance (see para. 10.2 of the Directive).
- A reporting format is under development.

PART B:

COMMON CORE DATA SET FOR (CHEMICAL) BIOCIDAL PRODUCTS

DOSSIER REQUIREMENTS

- In many cases data derived during the development stage of the product may be used to fulfil the data requirements described in Part B when the data is of sufficient quality.

1 APPLICANT *[Ann IIB, I.]*

1.1 Name and address, etc. *[Ann IIB, I. 1.1.]*

- Name, address, telephones and faxes numbers, e-mail and other contact information of the applicant.
- Applicant shall be required to have a permanent office with a legally responsible representative within the European Community.

1.2 Manufacturer*/formulator* of the biocidal product and the active substance(s) *[Ann IIB, I. 1.2.]*

- *Name*, *address*, telephone number including *location of* formulating *plant(s).*
- Contact information of formulator if other than the manufacturer.

2 IDENTITY *[Ann IIB, I.]*

- The information must be sufficient to identify each substance, to define it on terms of its specification and to characterise it as to its nature. The definition of "active substance as manufactured" is given in Chapter 1.

2.1 Trade name or proposed trade name, and manufacturer's development code number of the preparation, if appropriate *[Ann IIB, I. 2.1.]*

- If different trade names are used in different Member States, all of those have to be cited.

2.2 Detailed quantitative and qualitative information on the composition of the biocidal product e.g. active substance(s), impurities, adjuvants, and inert components. *[Ann IIB, I. 2.2.]* The following information must be given:

- The information on individual ingredients before mixing and the final composition of product shall be given. If a non-active ingredient is a preparation, full quantitative and qualitative specification of this preparation has to be given.
- The chemical name of each ingredient according to IUPAC or CA and their content in the product (g/kg). Trade names shall also be mentioned.
- CAS number and EC number (EINECS, ELINCS or No Longer Polymer List number).
- Structure or structural formula.

- Functions of the ingredients must be given (e.g. solvent, stabiliser).
- Classification of components according to Directive 67/548/EEC for the components or classification of preparations according to Directive 88/379/EEC amended by 1999/45/EC, as appropriate.

2.3 Physical state and nature of the biocidal product *[Ann IIB, I. 2.3.]*

- *E.g. emulsifiable concentrate, wettable powder, solution.*

3 PHYSICAL, CHEMICAL AND TECHNICAL PROPERTIES *[Ann IIB, III.]*

- The information shall provide direct input parameters for assessing physical, chemical and technical hazards, prerequisites for performing and guidance information for optimising other tests.

3.1 Appearance *[Ann IIB, III. 3.1.]*

- *Physical state, colour* and description of odour.
- For substances with intense odour or taste in water, a description of the substance(s) in question must be given, together with a threshold concentration for air or water, if available.

3.2 Explosive properties [*Ann IIB, III. 3.2.]*

- An acceptable justification for non-performance of a test for explosive properties is where none of the components are classified as explosive and where available thermodynamic information establishes beyond reasonable doubt that the product is incapable of exothermic reaction.
- EC method A.14.

3.3 Oxidising properties [*Ann IIB, III. 3.3.]*

- Oxidising properties do not have to be determined if it can be shown without reasonable doubt on the basis of thermodynamic information that the preparation is incapable of reacting exothermically with combustible materials.
- An acceptable justification for non-performance of a test for oxidising properties is where none of the components are classified as oxidising and where available thermodynamic information establishes beyond reasonable doubt that the product is incapable of exothermic reaction.
- EC method A.17.

3.4 Flash-point and other indications of flammability or spontaneous ignition *[Ann IIB, III. 3.4]*

- An acceptable justification for non-performance of a test for flammability properties is where none of the components are classified as flammable and where available thermodynamic information establishes beyond reasonable doubt that the product is incapable of exothermic reaction.
- The flash-point of liquids must be determined and reported according to EC method A.9 and the flammable properties of solids and gases according to EC methods A.10 (solids), A.11 (gases), and A.12 (contact with water), as appropriate. The auto-flammability of preparations must be determined and reported according to A.15 (liquids and gases) or A.16 (solids), as appropriate.

3.5 Acidity/alkalinity and, if necessary, pH value (1 % in water) *[Ann IIB, III. 3.5.]*

- The product pH should be determined and if found to be acidic or alkaline, the quoted test method used.
- In cases where preparations are acidic (pH<4), the acidity and pH must be determined and reported e.g. according to CIPAC method MT31 (MT is Material Test) and where preparations are alkaline (pH>10) the alkalinity must be determined and reported e.g. according to CIPAC method MT 75. The pH of a 1% aqueous dilution, emulsion or dispersion of preparation must be determined e.g. according to CIPAC method MT 75, where relevant.

3.6 Relative density *[Ann IIB, III. 3.6.]*

- The relative density of liquid materials must be determined and reported according to EC method A.3. Preparations which are powders or granules must be determined e.g. according to CIPAC methods MT 33, MT 159, or MT 169, as appropriate.

3.7 Storage stability - stability and shelf-life *[Ann IIB, III. 3.7.]*

- *Effects of light, temperature and humidity on technical characteristics of the biocidal product; reactivity towards container material.*
- E.g. CIPAC methods MT 46, MT 39, MT 48, MT 51, or MT 54, as appropriate.

3.8 Technical characteristics of the biocidal product, e.g. wettability, persistent foaming, flowability, pourability and dustability *[Ann IIB, III. 3.8.]*

- The wettability of solid preparations which are diluted for use must be determined and reported e.g. according to CIPAC method MT 53.3.
- The persistence of foaming of preparations to be diluted with water must be determined and reported e.g. according to CIPAC method MT 47.
- The flowability of granular preparations must be determined and reported e.g. according to CIPAC method MT 172.
- The pourability of suspensions must be determined and reported e.g. according to CIPAC method MT 148.
- The dustability of dustable powders must be determined and reported e.g. according to CIPAC method MT 34.

3.9 Physical and chemical compatibility with other products including other biocidal products with which its use is to be authorised *[Ann IIB, III. 3.9.]*

- Those products and active ingredients with which the product will be used. Possible incompatibility with any products or active ingredients should be mentioned.

3.10 An additional data requirement. See Chapter 3, part B.

3.11 An additional data requirement. See Chapter 3, part B.

4 METHODS OF IDENTIFICATION AND ANALYSIS

- Information on analytical methods is required for assessing compliance with conditions for issuing authorisation for a biocidal product according to Article 5(1c) of the Directive. This information is also required for post-authorisation control and monitoring purposes, and for the assessment of justifications which should be provided for the methods used for generation of data as required for this Directive.
- For products which are difficult to analyse a description of the problems should be given.

4.1 Analytical method for determining the concentrations of the active substance(s) in the biocidal product *[Ann. IIB, IV.4.1.]*

- A quantitative and, if possible, also a qualitative method for defining the active substance in the product must always be stated.
- In the case of a preparation containing more than one active substance, a method capable of determining each, in the presence of the other, should be provided. If a combined method is not submitted, the technical reasons must be stated.

4.2.1 In so far as not covered by paragraph A4.2 (data set for the active substance), analytical methods including recovery rates and the limits of determination for toxicologically and ecotoxicologically relevant components of the biocidal product and/or residues thereof, where relevant in or on the following *[Ann. IIB, IV.4.2]*. Product-type-specific guidance is given here:

(a) Soil

- May be required, for example, for product types 2, 3, 8, 10, 11 (preservatives used in cooling towers), 12 (not required for paper mill preservatives) and 21.

(b) Air

- Required, for instance when the substance is volatile, or sprayed or occurrence in air is otherwise probable.
- May be required, for example, for product types 8, 11 (preservatives used in cooling towers), 12, 13, 18 and 21.

(c) Water (including drinking water)

- Required for all product types if contamination of water cannot be excluded.

(d) Animal and human body fluids and tissues

- May be required, for example, for product types 3, 4, 5, 14, 19 and 20.

(e) Treated food or feeding stuffs

- Required for product types 3, 4 and 20.

5 INTENDED USES AND EFFICACY

- Information on effectiveness and intended uses of the product, together with its active substances, must be sufficient to permit an evaluation of the product, including the nature and benefits that accrue following use of the product in comparison to suitable reference products or damage thresholds, and to define its conditions of use.

5.1 Product type and field of use envisaged *[Ann. IIB, V.5.1.]*

- The intended and potential use and product type(s) given in the Directive, Annex V should be indicated together with the fields of use. In addition, a detailed description of the overall use patterns of the product should be given. This information on the use envisaged should be sufficient to allow an approximate but realistic estimation of human and environmental exposure to the product.
- Any relations which give case to exposure e.g. relevant product types should always involve further studies/estimation of human and environmental exposure.
- For material preservatives of product types 6, 7, 9, and 10, the different use areas in which the material treated with the product is intended to be used should be indicated for these preservatives (e.g. indoors or outdoors, in cattle sheds, or in drinking water or food storage or processing or their facilities.
- For product type 8, the hazard classes, as defined in the standard EN 335-1 (CEN 1992), in which wood treated with the product is intended to be used should be indicated for wood preservatives. For uses not described in this standard, such as curative or anti-sapstain products, see also guidance document by the European Wood Preservation Manufacturers' Group (EWPM 1996) describing also these other use sectors.
- For product type 21, in addition to the fields of use, specify also if the product is intended to be used in marine environments, in brackish water and/or in fresh waters. The uses should also distinguish between for example, aqua-culture, buoys and other small static objects, sluice doors, harbour constructions, oil rigs, inlet pipes of cooling water systems, marine sensors, ships' hulls (e.g. deep sea, coastal, inland waterway vessels), etc.

5.2 Method of application including description of system used *[Ann. IIB, V.5.2.]*

- The method of addition for the product in different uses. If the product is to be diluted, the substance used for dilution and concentration as a percentage of the active substance in the solution must be stated. A description of the application technique (e.g. dipping, spreading, spraying, automatic/manual dosing etc.) should be included. The substances that may have to be added to the solution and their dosages must also be given.
- If certain technical device will be used together with product, a description of this device should be provided. (from 3.1)

5.3 Application rate and if appropriate, the final concentration of the biocidal product and active substance in the system in which the preparation is to be used, for example cooling water, surface water, water used for heating purposes *[Ann. IIB, V.5.3.]*

- The recommended dose of the product and the active substance per object (e.g. per surface area of the material to be protected or as a concentration in a water system).

- For product type 21, the final concentrations of each biocidal component in the antifouling coating layer of the antifouling product and in addition the thickness of the film should also be given.

5.4 Number and timing of applications, and where relevant, any particular information relating to geographical variations, climatic variations, or necessary waiting periods to protect man and animals *[Ann. IIB, V.5.4.]*

- Describe, where relevant, how the applications should differ in different parts of the Community.
- Indicate the recommended duration of application and possible re-applications.
- For disinfectants of Main Group 1, potential information on effects of temperature and humidity on the frequency of application must be supplied where relevant. For veterinary hygiene products (product type 3) to be used in animal husbandry, and products in product type 4 and 20, the waiting periods necessary to prevent the dislodging of unacceptable residues from treated equipment in food or feed products should be given.
- For material preservatives of product types 6 to 10, instructions on the minimum drying time or time to reach resistance to leaching (fixation) of the product in the material treated. Information on the effects of e.g. temperature and humidity on drying or fixation has to be given, i.e. when the treated material is dry enough for safe exposure of humans and the environment. Furthermore, when possible, a qualitative or quantitative method should be stated for determining that the proper drying or resistance to leaching has been achieved.
- For product types 11 and 12, when used in an open system with process water, information on the minimum dilution or treatment time for the active substance in waste water should be given in order to assure a sufficient degree of degradation or dilution before it is released to a water course to protect aquatic organisms from harmful effects.
- For pest control products of Main Group 3 and product type 23, for products used in e.g. fumigation, clearance times sufficient to protect bystanders etc. should be given.
- For molluscicides (product type 16) and piscicides (product type 17), necessary waiting periods should be given to prevent harm or dislodging of unacceptable residues from treated tanks or basins for e.g. the subsequent batch of aquaculture.
- For product type 21, instructions on the minimum drying time of the coating and information on the effects of for instance, temperature and humidity on drying have to be given, i.e. it should be indicated when the coating is dry enough to be ready for launching and whether the coating should be washed before launching in order to reduce the primary release into the aquatic environment. Furthermore, a method for ensuring that a proper coating has been achieved should be given.
- Furthermore for product type 21, instructions on how to determine the mean biocide release rate and thereby the timing of the next application of the antifouling coating (i.e. the dry-docking or slipping interval) should be given with details on the effects of mean water temperature, vessel speed, salinity, etc. on the release rate and length of the service period of the coating.

5.5 Function, for example fungicide, rodenticide, insecticide, bactericide *[Ann. IIB, V.5.5.]*

5.6 Pest organism(s) to be controlled and products, organisms or objects to be protected *[Ann. IIB, V.5.6.]*

- For an organism to be controlled, both the common name and the scientific name, and also the sex, strain and stadia where relevant and appropriate must be given. Where complexes of organisms are involved, the organisms must be specifically mentioned.

5.7 Effects on target organisms *[Ann. IIB, V.5.7.]*

5.8 Mode of action (including time delay) in so far as not covered by paragraph A5.4 (data set for the active substance) *[Ann. IIB, V.5.8.]*

5.9 User: industrial, other professional, general public (non-professional) *[Ann. IIB, V.5.9.]*

- For the definitions, see paragraph A5.6, data set for the active substance.

Efficacy Data

5.10 The proposed label claims for the product and efficacy data to support these claims including any available standard protocols used, laboratory tests, or field trials, where appropriate *[Ann. IIB, V.5.10.]*. Product type specific guidance is given here.

- The guidance on product evaluation in support of Annex VI of the Directive provides further amplification in this area. Although at the time of writing detailed product type specific guidance is not yet available for all product types and use patterns, details for those product types currently outstanding are now in preparation.
- The applicant must demonstrate that the biocidal product is effective and suitable for its intended use when applied according to its instructions for use. This can be confirmed by provision of data that may include laboratory studies, pilot plant or field test data or other relevant study data, the test conditions of which are comparable with the purpose applied for and which are comparable with the environmental characteristics relevant for the intended use. Further product-type-specific guidance is given in the guidance document on product evaluation in support of Annex VI of the Directive.
- For field studies conducted outside the territory of the Member State in which the authorisation is being sought, a justification of the relevance of such data must be made. The extent of the information required will vary depending on the product type and proposed use pattern and upon the similarity of the conditions in the two countries. Justification may include, as relevant and appropriate, information on the harmful organism (e.g. comparison of genera/species and its relevance to the Member State in which authorisation is sought), meteorological parameters (e.g. mean temperatures and rainfall) and location details.
- The test method should measure a response and, as appropriate, an end-point relevant to the label claims. The method should employ a reference product for comparison, if possible, and an untreated control. The efficacy test reports should contain dose response data for dose rates lower than the recommended rate. However, this may not be always possible for field studies.
- Where earlier formulations of the product or other products containing the same active substance(s) are cited as supporting evidence, all relevant formulation

details must be given and the relevance of this evidence to the current formulation must be fully justified.

- The tests (and data generated) should be based on sound scientific principles and practices. Compliance with quality standards such as GEP (Good Experimental Practice) and ISO 9000 is highly recommended. More detailed guidance on appropriate test methods is given in paragraph 52 of Annex VI in the Directive and in the associated guidance document. A guidance document on use of efficacy methods is being developed by OECD (Overview of Efficacy testing methods for biocides. Draft 1999.)
- For product types 1 and 2, the European standard efficacy method tests of the CEN for disinfectants and antiseptics (e.g. CEN standards 1040, 1275, 1276, 1499 and 1500; several others are in preparation) are highly recommended.
- For product types 3, 4 and 5 the European standard efficacy testing methods of the CEN are highly recommended; several of these are in preparation.
- National guidance on efficacy testing with disinfectants is available. Further product specific guidance document on product types encompassed within Main Group I (Disinfectants) can be found in the guidance document on product evaluation in support of Annex VI of the Directive.
- For product type 8, the European standard efficacy tests of CEN are highly recommended for wood preservatives. These standards are not suitable to all wood preservatives. Modifications to them or development of new ones may be necessary. See specific guidance in the guidance document for product evaluation in support of annex VI.
- For product type 10, see specific guidance in the guidance for product evaluation.
- For product type 14, EPPO guidelines for efficacy testing are highly recommended (e.g. EPPO guidelines 97, 113, 114, 169 and 198 for rodenticides). Further product specific guidance document on product type 14 can be found in the guidance document on product evaluation in support of Annex VI of the Directive.
- For product type 16, EPPO guidelines for efficacy testing are highly recommended (e.g. EPPO guidelines 95 for molluscicides in terrestrial environment).
- For product type 18, see specific guidance in the guidance document for product evaluation.
- For product type 19, EPPO guidelines 199 and 200 are available for efficacy testing of rodent repellents intended for plant protection. These might be modified for biocidal use.
- For product type 21, the standard test protocols of CEPE (1993) and ASTM (1987) for conducting efficacy tests are recommended for antifouling products. The latter is an internationally recognised draft test method. Further product specific guidance document on product type 21 can be found in the guidance document on product evaluation in support of Annex VI of the Directive.

5.11 Any other known limitations on efficacy including resistance *[Ann. IIB, V.5.11.]*

- Possible restrictions or recommendations concerning the use product in specific environmental or other conditions. State possible factors that can reduce the efficacy, for instance hot, cold or humid environments or the presence of other substances, in addition to the grounds for these. Possible recommendations concerning the avoidance of the continuous use of the product in order to prevent the development of resistant strains and the grounds for these. State if the product cannot be mixed with, for example, other biocidal products or if the use of the

product with other biocidal products is recommended.

- The guidance given on resistance for the corresponding data requirement of the active substance (paragraph A5.7) also applies here.
- For product type 14 and 15, residue data in target organisms concerning the active substance and including toxicologically relevant metabolites would be needed in order to assess the risks towards predators. (cf. Chapter 2.5 part B)

6 TOXICOLOGICAL STUDIES *[Ann IIB, VI]*

Information may be derived from existing data where a justification acceptable to the competent authority is provided. In particular, the provisions of directive 88/379/EEC (amended as 1999/45/EC) *should be used whenever possible to minimise animal testing.*

6.1 Acute toxicity *[Ann IIB, VI. 6.1.]*

For studies 6.1.1. to 6.1.3. biocidal products other than gases shall be administered via at least two routes, one of which should be the oral route. The choice of the second route will depend upon the nature of the product and the likely route of human exposure. Gases and volatile liquids should be administered by the inhalation route.

- In some cases it may be necessary to study acute toxicity in all three routes.
- The acute toxicity tests are to provide an indication of possible adverse effects of the toxicity of the biocidal product. Administration via different routes makes possible an overall assessment of the relative hazard of different exposure pathways. Acute toxicity testing may provide valuable information for accidental situations.

6.1.1 Oral *[Ann IIB, VI. 6.1.1.]*

- For preparations with low acute oral toxicity, a limit test at 2000 mg/kg b.w. may be sufficient.
- When planning new tests, the EC methods B.1.bis, B.1.tris (or the corresponding OECD TGs 420 and 423) and the OECD TG 425 are recommended) EC method B.1 (or OECD TG 401) should not be used. Existing results based on EC method B.1 (or OECD TG 401) are accepted.

6.1.2 Dermal *[Ann IIB, VI. 6.1.2]*

- Dermal toxicity must be reported except for gases.
- For preparations with low acute dermal toxicity a limit test at 2000 mg/kg b.w. may be sufficient.
- Preparations which are classified as corrosive must not be studied.
- EC method B.3 or the corresponding OECD guideline 402.

6.1.3 Inhalation *[Ann IIB, VI. 6.1.3.]*

- Inhalation toxicity must be reported, if the preparation is
  - volatile (vapour pressure > 1 x 10^{-2} Pa at 20 ^{o}C) or
  - a powder containing a significant portion (e.g. > 1% on a weight basis) of particles with particle size MMAD < 50 micrometers or
  - to be applied in a manner which generates aerosols, particles, or droplets in an inhalable size range (MMAD < 50 micrometers).
- Preparations classified as corrosive must not be studied.
- A full study using three dose levels may not be necessary if a preparation at an

exposure concentration to the limit concentrations of the test guideline (limit test) or at the maximum attainable concentration produces no compound related mortalities.

- EC method B.2 or the corresponding OECD guideline 403.

6.1.4 For biocidal products that are intended to be authorised for use with other biocidal products, the mixture of products, where possible, shall be tested for acute dermal toxicity and skin and eye irritation, as appropriate *[Ann IIB, VI. 6.1.4.]*

- These tests will be required where a product is used together with other product (e.g. to increase efficacy of certain product) and where exposure to the mixture can not be excluded.

6.2 Skin and eye irritation *[Ann IIB, VI. 6.2.]*

- The tests will provide information on degree and nature of skin, eye and associated mucous membrane irritation, especially with regard to reversibility of responses.
- If the active substance is a strong acid or base (pH value below 2 or above 11.5) the test does not need to be carried out.
- It may be possible to accept positive findings from *in vitro* test methods which are close to validation by recognised organisations.
- If the materials have been shown to have potential corrosive or severe irritant properties the test should not be carried out.
- However, if the formulation of the product gives reasons to believe and accept that the product should be classified and labelled as an irritant then the tests not may be carried out.
- EC methods B.4 (dermal irritation) and B.5 (eye irritation) or the corresponding OECD guidelines 404 and 405.

6.3 Skin sensitisation *[Ann IIB, VI. 6.3.]*

- The test will provide information to assess the potential of the product to cause a skin sensitisation reaction.
- This is not needed where the preparation contains a substance(s) which is/are classified as a sensitiser(s) according to Directive 67/548/EC or is otherwise known be a sensitiser(s), e.g. on the basis of epidemiological data.
- While the guinea pig Maximisation test is considered to be the preferred adjuvant technique in certain cases there may be good reasons for choosing the Buehler test or the Local Lymph Node Assay (LLNA). However, scientific justification may be given when either of the two latter mentioned is used.
- E.g. EC method B.6 or the corresponding OECD guideline 406.

6.4 Information on dermal absorption *[Ann IIB, VI. 6.4.]*

- Estimation of effects of solvents and additives to the dermal absorption of active substance(s) should be given.
- A dermal absorption test at an appropriate dose level could be performed if there is dermal exposure.
- An appropriate dermal absorption assessment is needed. A sequential approach should be applied for the decision if biological testing is needed (TNO 1999). If testing is necessary to decide whether this test should be performed *in vivo* or *in vitro*, the present development of the OECD test Guidelines Programme for Guidelines on percutaneous Absorption/Penetration has to be taken in account.
- EC method B.36 or OECD guideline 417

6.5 Available toxicological data relating to toxicologically relevant non-active substances
(i.e. substances of concern) *[Ann IIB, VI. 6.5.]*

- A short evaluation of the toxicological properties of the other substances in the preparation must be attached. The source(s) of information (scientific literature, regulatory reviews, etc.) must be stated and a summary must be given in the evaluation. Copies of any literature cited must also be included in the data submission.
- Detailed guidance on submitting this data is given in Chapter 4.

6.6 Information related to the exposure of the biocidal product *[Ann IIB, VI. 6.6]*

- Sufficient information on exposure to the biocidal product likely to occur during the proposed conditions of use must be submitted. The information should include all relevant stages of formulation and of use (Chapter 2 part A 2.10) and all possible exposure routes. Actual exposure data and/or calculations using validated models are acceptable. Test reports of any studies conducted related to the exposure of the biocidal product on humans must be submitted. An expert judgement is needed to decide if any other studies are required (see Chapter 1.2, point 4). A starting point is the report 'Assessment of human exposures to biocides', see reference.

Where necessary, the test(s) described in Part A (core data set for the active substance), *shall be required for the toxicologically relevant non-active substances of the preparation* (see Chapter 4).

7 ECOTOXICOLOGICAL DATA FOR THE BIOCIDAL PRODUCT

Information may be derived from existing data where a justification acceptable to the competent authority is provided. In particular, the provisions of directive 88/379/EEC (amended as 1999/45/EC) *should be used whenever possible to minimise animal testing.*

- Where appropriate, the general guidance given on the information to be provided on the ecotoxicological profile of the active substance (section A7) applies also here.
- The information provided for the product, together with other relevant information, and that provided for the active substance, should be sufficient to:
  - specify the hazard symbols, the indications of danger, and relevant risk and safety phrases for the protection of the environment which are to be included on packaging (containers),
  - predict the distribution, fate, and behaviour in the environment as well as the time involved (e.g. when equilibrium has been reached, whether exposure is short or long-term),
  - identify non-target species and populations for which concern arise because of potential exposure, and
  - identify measures necessary to minimise contamination of the environment and the impact on non-target species. Justified estimates must be made of the predicted environmental concentrations (PEC) of the active substance and relevant metabolites, degradation and reaction products, in soil, groundwater, surface water (including marine, if relevant) and air following use as proposed

or already occurring. In addition a realistic worst-case estimation must be made. More detailed guidance on environmental exposure assessment, including model calculations, may be found in the Technical Notes for guidance in support of annex VI of the Directive.

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Information on how the active substance or a substance of concern due to handling it or from a waste water treatment plant, etc., to which compartment of the environment (soil, sediment, water, air) can be released into the environment, and an estimation on how large the amounts released are.
- Sources of environmental exposure: for example production, distribution, storage, mixing and loading, uses and disposal or recovery should be described. The measured or estimated extent of release: frequency and intensity (e.g. dose and duration) should be indicated. The descriptions should cover the most significant routes of exposure.
- Define aquatic recipients in detail: for instance surface water, ground water, estuaries or marine environment. Assess possible ways of transformation and distribution.
- Information on representative measured concentrations or monitoring data, for example, in wastewater or in the environment or on concentrations based on model calculations, and which can be used as predicted environmental concentrations in the relevant environmental compartments.
- Product type specific guidance on this issue is given in Chapter 2.5.

7.2 Information on the ecotoxicology of the active substance in the product, where this cannot be extrapolated from the information on the active substance itself *[Ann. IIB, VII.7.2.]*

- Required, for example, if the composition (formulation) of or the application technique for the product is suspected to influence the degradation and transformation, mobility and adsorption properties or effects on aquatic or terrestrial organisms in a way that may considerably alter the conclusions of the risk characterisation. For instance, assessment by an expert on the effect of formulation on the ecotoxicology of the active substance should be submitted (see Chapter 1.2, point 4). Guidelines of the Council Directive 88/379/EEC (as amended) on assessing the effect of a single substance in causing hazard in a preparation may be partly applicable here.
- In addition, a qualitative or, preferably, a quantitative estimate on the possibility of formation of by-products of the active substance during normal use should be submitted on the basis of available data on the active substance and the intended use of the biocidal product.
- Ecotoxicology testing with a product might be required in those cases where a direct release of a product to a compartment is possible (see Chapter 2.5, part B).

7.3.1 Available ecotoxicological information relating to ecotoxicological relevant non-active substances (i.e. substances of concern), such as information from safety data sheets *[Ann. IIB, VII.7.3.]*

- An evaluation of the fate in the environment of ingredients other than the active substances and their toxicity to different organisms must be attached to the application. The sources (literature references or the original studies) of the information presented in a summary form must be attached to the evaluation.

- Guidance on submitting this data is also given in Chapter 4.

8 MEASURES TO BE ADOPTED TO PROTECT MAN, ANIMALS AND THE ENVIRONMENT

8.1 Recommended methods and precautions concerning handling, use, storage, transport or fire. *[Ann. IIB, VIII.8.1.]*

- Provide technical safety precautions, including personal protective equipment when handling the product, e.g. during different stages of the process, to minimise the risk of exposure to humans and the environment. Appropriate precautions for substances/products which are flammable, oxidising, etc., should be given. Handling, storage and transport must take into account any surface which could directly or indirectly come in contact with the product, including for example: processing equipment, piping, ventilators, transport vehicles and their washing and cleaning, as well as protective clothing and shower areas for workers. Storage precautions should include ventilation system to be used for storerooms (in general terms and other conditions for storage, e.g. temperature regime). Precautionary measures during service should especially be considered in addition to the prevention of environmental effects and measures to be taken when the product is released to the environment due to an accident and misuse.
- Materials which are incompatible with the product, e.g. substances and products which may react with the active substance evolving toxic gases, and also other dangers such as reactions resulting in a large increase in volume, aggressive acidity, the possibility of dust explosions, etc., should be indicated.
- The precise type of fire-fighting equipment (i.e. both the type of extinguishing agent, including those to be avoided and any protective equipment), e.g. water or carbon dioxide, should be noted.

8.2 Specific treatment in case of an accident, for example, first aid measures following accidental eye or skin contact, ingestion or inhalation, antidotes, medical treatment if available; emergency measures to protect the environment; in so far as not covered by paragraph A8.3 (data set for the active substance) *[Ann. IIB, VIII.8.2.]*

- Provide precise medical data regarding first aid, proven antidotes, and proven medical treatment. This should detail the effectiveness of first aid, suggested antidote doses, etc. and include full documentation of reference sources. The information here is intended for the purpose of immediate first-aid treatment. It is not intended to replace definitive diagnosis and treatment, which can only be undertaken by a qualified medical doctor.
- Measures and courses of action in response to different kinds of accident scenarios (e.g. threat of release of the biocidal product, the product is actually being released and release has already occurred) should be described. In addition actions to avert or stop release, minimise impacts of release, protect human life and property and recover the product and by-products should be indicated.

8.3 Procedures, if any, for cleaning application equipment. *[Ann. IIB, VIII.8.3.]*

- The procedures should be such that the likelihood of accidental contamination of water or its sediments is minimised.

8.4 Identity of relevant combustion products in cases of fire. *[Ann. IIB, VIII.8.4.]*

- It should be stated what gases are evolved, either by experiment or on the basis of

structure, when the substance burns or when heated in the absence of air so that it simply decomposes, e.g. nitrogen oxides, phosgene or soot. Especially the identity of dangerous substances formed should be given (e.g. analysed according to the ISO standard 9122, Part 3, ISO 1993).

8.5 Procedures for waste management of the biocidal product and its packaging for industry, professional users and the general public (non-professional users), for example, the possibility of re-use or recycling, neutralisation, conditions for controlled discharge, and incineration *[Ann. IIB, VIII.8.5.]* Product-type-specific guidance is given here.

- Information necessary for safe disposal must be given. If preliminary treatment of the waste is necessary, information about this must also be given. If any waste generated is classified as hazardous waste (e.g. according to Council Decision 94/904/EC[2]), this has to be mentioned separately and appropriate handling according to the related legislation indicated.
- The possibility of recovery or recycling should be indicated for both normal uses of the substance and quantities involved in spills.
- A chemical or other disposal method for the product. Disposal methods for the waste generated when using the product (e.g. precipitates generated, instruments for spreading, residues treated with the product).
- Information must be given on how the package is to be emptied and cleaned and on the recycling or disposal method for empty packages.
- Recycling or disposal methods for the waste generated from a treated product, and in the processing of the treated product (e.g. shavings, cuttings or other waste from the treated product) and for treated products no longer in use (e.g. impregnated wood), if applicable.
- The guidance given for the corresponding data requirement for the active substance (paragraph A8.5) applies also here.
- When the product is applied to a system with water which is to be released into surface water with or without pre-treatment, as may be for product type 11 and 12, information on the necessary waste water treatment methods and times and/or the on minimum dilution for the active substance in waste water in order to assure a sufficient decree of degradation or dilution before being released into a water course to protect aquatic organisms from harmful effects.
- Recycling or disposal methods for the waste generated from a treated material (e.g. for chips from metal-cutting where the product is used), and in the processing of the possible treated material (e.g. waste from treated paper pulp or porous sand strata for product type 12) and for treated material or treated process water or metal working fluid no longer used, if applicable.

8.6 Possibility of destruction or decontamination following release in or on the following: (a) Air, (b) Water, including drinking water, and (c) Soil *[Ann. IIB, VIII.8.6.]*

- Prevention of health and environmental effects and measures to be taken when the product is released to the environment due to an accident or misuse. Provide details of measures necessary to quickly limit the consequences of accidental release to the environment, and to decontaminate areas affected by the accidental release. These may include neutralisation, destruction and removal procedures.

2 Council Decision of 22 December 1994 establishing the list of hazardous waste pursuant to Article 1(4) of Council Directive 91/619/EEC on hazardous waste. OJ No L 356/14. 31.12.1994.

8.7 Observations on undesirable or unintended side-effects, for example, on beneficial and other non-target organisms *[Ann. IIB, VIII.8.7.]*

- *E.g. unnecessary suffering and pain for vertebrates* or effects on wildlife. Additionally, observations such as on *adverse reaction to fastenings and fittings used in wood following the application of a wood preservative.* It should also be reported if the substance is anticipated to have adverse effects on the air compartment, for example, which may contribute to the depletion of ozone layer, tropospheric ozone building, acidification, warming the atmosphere or degrading air quality.

8.8 Specify any repellents or poison control measures included in the preparations that are present to prevent action against non-target organisms. *[Ann. IIB, VIII.8.8.]*

9 CLASSIFICATION, PACKAGING AND LABELLING *[Ann IIB, IX.]*

Proposals for packaging and labelling according to the requirements set in the Article 20 of the Directive, including:

- *Justification for the classification and labelling according to the principles of Article 20 of the Directive.*
  - The classification comprises a description of the category/categories of danger and qualifying risk phrases for all dangerous properties.
  - On a basis of the classification, a proposal for labelling including the hazard symbol(s) and indications of danger, risk phrases and safety phrases should be given.
- *Justification for packaging (type, materials, size etc.); compatibility of the preparation with proposed packaging materials to be included.*
- Any requirements related to labelling of the treated materials.

Proposals for safety data sheets, where appropriate.

10 SUMMARY AND EVALUATION OF SECTIONS 2 TO 9

- This section is the risk assessment of the biocidal product. Guidance is given in the guidance document in support of annex VI (on the evaluation of the biocidal product).
- Each sub-Chapter from 2 to 9 should contain a short summary of the main results and conclusions of the studies. These sub-conclusions combined with the exposure assessment are the basis for risk assessment.
- A reporting format is under development.

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* Council Directive 88/379/EEC of 7 June 1988 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous preparations.

* Council Directive 80/778/EEC of 15 July 1980 relating to the quality of water intended for human consumption.

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PART C

PRODUCT TYPE SPECIFIC ADDITIONAL DATA SET FOR ACTIVE SUBSTANCES AND BIOCIDAL PRODUCTS REGARDING ECOTOXICOLOGICAL PROFILE, INCLUDING ENVIRONMENTAL FATE AND BEHAVIOUR

Introduction

The testing strategy should be guided by allowing the performance of a meaningful risk assessment, which the applicant will compile in accordance with paragraph A10 (data set for the active substance). Based on the product type, for which an active substance will be used, additional data to those required for the core data set might be necessary to be able to perform an initial risk assessment. These tests are usually required to be delivered together with the core data. If the initial risk assessment shows an indication of risk for man or the environment, the applicant should conduct further studies according to the guidance in Chapter 3 in order to refine the risk assessment and reach a conclusion.

The detailed exposure scenarios have not yet been developed for the 23 product types, and therefore Part C would need refinement when the exposure scenarios are better described.

In the following sections, for each product type, those tests are listed which are required in addition to the core data set.

Regarding further tests on biodegradation and bioaccumulation (especially for soil exposure the bio-concentration estimation is important), independent testing strategies are described in Chapter 3 and these need to be followed in addition.

A description of the tests listed in the following sections can be found in Chapter 2 (Part A and Part B) or 3.

An overview of the data requirements for the active substances and the products is found as annexes to Part C.

PART I: Additional data set and guidance for active (chemical) substances

General

For all product types, the fate and behaviour of the active substances in the atmosphere has to be estimated:

7.3.1 Phototransformation in air (estimation method).

For substances, which are to be used in preparations for fumigants, independently of the product type, a more in-depth assessment of the fate and behaviour in air is necessary:

7.3.2 Fate and behaviour in air, further studies

Specific requirements for different product types

Product type 1: Human hygiene biocidal products

The release to the environment is usually diffuse. No supplementary test data regarding the ecotoxicological and fate profile beyond those listed in the core data set need to be generated in order to perform a preliminary risk assessment.

Product type 2: Private area and health area disinfectants

Chronic aquatic toxicity data would be necessary for this product type, unless the release is intermittent (Ch.3 part A section7) or the intended use is limited to closed spaces with insignificant aquatic release:

7.4.3.2 Effects on reproduction and the growth rate on an appropriate species of fish
7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species
7.4.1.3 Growth inhibition test on algae (if no NOEC is available from the core data set)

For substances to be used as soil or solid waste disinfectants, direct release to soil is possible. It is necessary to perform initial terrestrial tests:

7.2.3.1 Adsorption / desorption (according to new EC method C.18 or the corresponding OECD guideline 106)
7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

Product type 3: Veterinary hygiene biocidal products

Chronic aquatic toxicity data would be necessary for this product type, unless the release is intermittent or the intended use is limited to closed spaces with insignificant aquatic release:

7.4.3.2 Effects on reproduction and the growth rate on an appropriate species of fish
7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species

7.4.1.3 Growth inhibition test on algae (if no NOEC data is available from the core data set)

Releases into manure storage facilities are possible. It is necessary to perform a test on anaerobic biodegradation for estimation of fate in the manure storage facility:

7.1.2.1.2 Anaerobic biodegradation

As well as initial terrestrial tests:

7.2.3.1 Adsorption / desorption (according to new EC method C.18 or the corresponding OECD guideline 106)
7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

For use in poultry farms, were wild birds are attracted, a test with birds is necessary:

7.5.3.1.1 Acute oral toxicity

If the substance is to be used in marine fish nurseries, the aquatic toxicity tests need to be performed additionally with marine/brackish species and a saltwater biodegradation test is required as well:

7.1.1.2.3 Biodegradation in seawater
7.4.1.1 Acute toxicity to fish
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

Product type 4: Food and feed area disinfectants

For most applications, environmental releases will be diffuse and therefore no supplementary test data regarding the ecotoxicological and fate profile beyond those listed in the core data set are necessary in order to perform a preliminary risk assessment.

Product type 5: Drinking water disinfectants

Chronic aquatic toxicity data would be necessary for this product type, unless the release is intermittent (Ch.3 part A section7) or the intended use is limited to closed spaces with insignificant aquatic release:

7.4.3.2 Effects on reproduction and the growth rate on an appropriate species of fish
7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species
7.4.1.3 Growth inhibition test on algae (if no NOEC is available from the core data set)

Product type 6: In-can preservatives

Chronic aquatic toxicity data would be necessary for this product type, unless the release is intermittent or the intended use is limited to closed spaces with insignificant aquatic release of the product to be preserved:

7.4.3.2 Effects on reproduction and the growth rate on an appropriate species of fish
7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species
7.4.1.3 Growth inhibition test on algae (if no NOEC data is available from the core data set)

Product type 7: Film preservatives

Chronic aquatic toxicity data would be necessary for this product type, unless the release is intermittent or the intended use is limited to closed spaces with insignificant aquatic release of the product to be preserved:

7.4.3.2 Effects on reproduction and the growth rate on an appropriate species of fish
7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species
7.4.1.3 Growth inhibition test on algae (if no NOEC data is available from the core data set)

Product type 8: Wood preservatives

Chronic aquatic toxicity data would be necessary for this product type, unless the release is intermittent or the intended use is limited to closed spaces with insignificant aquatic release:

7.4.3.2 Effects on reproduction and the growth rate on an appropriate species of fish
7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species
7.4.1.3 Growth inhibition test on algae (if no NOEC data is available from the core data set

High releases to the terrestrial compartment are possible. It is necessary to perform initial terrestrial tests:

7.2.3.1 Adsorption / desorption (according to new EC method C.18 or the corresponding OECD guideline 106)
7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

If the substance is to be used for wood in hazard class 5 (salt water) defined in the standard EN 335-1 (CEN 1992), the aquatic toxicity tests need to be performed additionally with marine/brackish species and a saltwater biodegradation test is required as well:

7.1.1.2.3 Biodegradation in seawater
7.4.1.1 Acute toxicity to fish
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

Product type 9: Preservatives for fibres, leather, rubber and polymerised material

Chronic aquatic toxicity data would be necessary for this product type, unless the release is intermittent or the intended use is limited to closed spaces with insignificant aquatic release:

7.4.3.2 Effects on reproduction and the growth rate on an appropriate species of fish
7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species
7.4.1.3 Growth inhibition test on algae (if no NOEC data is available from the core data set)

Product type 10: Masonry preservatives

Chronic aquatic toxicity data would be necessary for this product type, unless the release is intermittent or the intended use is limited to closed spaces with insignificant aquatic release:

7.4.3.2 Effects on reproduction and the growth rate on an appropriate species of fish
7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species
7.4.1.3 Growth inhibition test on algae (if no NOEC data is available from the core data set)

For remedial treatment as well as spray application in general, high releases to the terrestrial compartment are possible. It is necessary to perform initial terrestrial tests:

7.2.3.1 Adsorption / desorption (according to new EC method C.18 or the corresponding OECD guideline 106)
7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

Product type 11: Preservatives for liquid-cooling and processing systems

Chronic aquatic toxicity data would be necessary for this product type, unless the release is intermittent or the intended use is limited to closed spaces with insignificant aquatic release:

7.4.3.2 Effects on reproduction and the growth rate on an appropriate species of fish
7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species
7.4.1.3 Growth inhibition test on algae (if no NOEC data is available from the core data set)

For substances to be used in the cooling systems with an open cooling tower, a high water discharge to air and subsequent deposition onto soil is possible. In these cases, it is necessary to perform initial terrestrial tests:

7.2.3.1 Adsorption / desorption (according to new EC method C.18 or the corresponding OECD guideline 106)
7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

For substances to be used on sites situated near the coast and using marine/brackish water in their cooling systems, the aquatic toxicity tests need to be performed additionally with marine/brackish species and a saltwater biodegradation test is required as well:

7.1.1.2.3 Biodegradation in seawater
7.4.1.1 Acute toxicity to fish
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

Product type 12: Slimicides

Chronic aquatic toxicity data would be necessary for this product type, unless the release is intermittent or the intended use is limited to closed spaces with insignificant aquatic release:

7.4.3.2 Effects on reproduction and the growth rate on an appropriate species of fish
7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species
7.4.1.3 Growth inhibition test on algae (if no NOEC data is available from the core data set

For inland use of drilling and oil recovery preservatives, it is necessary to perform initial terrestrial tests:

7.2.3.1 Adsorption and desorption (according to new EC method C.18 or the corresponding OECD guideline 106)
7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

For offshore use, the aquatic toxicity tests need to be performed additionally with marine/brackish species and a saltwater biodegradation test is required as well:

7.1.1.2.3 Biodegradation in seawater
7.4.1.1 Acute toxicity to fish
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

Product type 13: Metalworking fluid preservatives

Chronic aquatic toxicity data would be necessary for this product type, unless the release is intermittent or the intended use is limited to closed spaces with insignificant aquatic release:

7.4.3.2 Effects on reproduction and the growth rate on an appropriate species of fish
7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species
7.4.1.3 Growth inhibition test on algae (if no NOEC data is available from the core data set)

Product type 14: Rodenticides

For products to be used in animal housing, releases to manure storage facilities are possible. An anaerobic biodegradation study is necessary:
7.1.2.1.2 Anaerobic biodegradation

If used outside of buildings in the form of baits, granulates or powder, avian toxicity tests are necessary. Secondary poisoning is tested on the product.

7.5.3.1.1 Acute oral toxicity
7.5.3.1.2 Short-term toxicity
7.5.3.1.3 Effects on reproduction

Product type 15: Avicides

For products to be used in animal housing, releases to manure storage facilities are possible. An anaerobic biodegradation study is necessary:

7.1.2.1.2. Anaerobic biodegradation

Product type 16: Molluscicides

Chronic aquatic toxicity data would be necessary for this product type, unless the release is intermittent or the intended use is limited to closed spaces with insignificant aquatic release:

7.4.3.2 Effects on reproduction and the growth rate on an appropriate species of fish
7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species
7.4.1.3 Growth inhibition test on algae (if no NOEC data is available from the core data set)

For products used outside buildings in contact with soil, release to soil is possible. It is necessary to perform initial terrestrial tests:

7.2.3.1 Adsorption and desorption (according to the new EC method C.18 or the corresponding OECD guideline 106)
7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

For products to be used in animal housing, releases to manure storage facilities are possible. An anaerobic biodegradation study is necessary:

7.1.2.1.2 Anaerobic biodegradation

If used outside of buildings in the form of baits, granulates or powder, avian toxicity tests are necessary:

7.5.3.1.1 Acute oral toxicity
7.5.3.1.3 Effects on reproduction

For molluscicides used in marine waters, the aquatic toxicity tests need to be performed additionally with marine/brackish species and a saltwater biodegradation test is required as well:

7.1.1.2.3 Biodegradation in seawater
7.4.1.1 Acute toxicity to fish
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

Product type 17: Piscicides

Chronic aquatic toxicity data would be necessary for this product type:

7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species
7.4.1.3 Growth inhibition test on algae (if no NOEC is available from the core data set)

If the substance is to be used in a marine environment, the aquatic toxicity tests need to be performed additionally with marine/brackish species and a saltwater biodegradation test is required as well:

7.1.1.2.3 Biodegradation in seawater
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

Product type 18: Insecticides, acaricides and products to control other arthropods and Product type 19: Repellents and attractants

For products used outside buildings as well as products to be used by gassing, fogging or fumigation, release to soil is possible. It is necessary to perform initial terrestrial tests:

7.2.3.1 Adsorption / desorption (according to the new EC method C.18 or the corresponding OECD guideline 106)
7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

If used outside of buildings in the form of baits, granulates or powder, avian toxicity tests are necessary:

7.5.3.1.1 Acute oral toxicity
7.5.3.1.3 Effects on reproduction

Furthermore, a test with bees is necessary:

7.5.3.2 Acute toxicity to honeybees and other beneficial arthropods, for example predators

For products to be used in animal housing, releases to manure storage facilities are possible. An anaerobic biodegradation study is necessary:

7.1.2.1.2. Anaerobic biodegradation

If the substance is to be used as a shark repellent, the aquatic toxicity tests need to be performed additionally with marine/brackish species and a saltwater biodegradation test is required as well:

7.1.1.2.3 Biodegradation in seawater
7.4.1.1 Acute toxicity to fish
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

Product type 20: Preservatives for food and feedstock

For most applications, environmental releases will be diffuse and therefore no supplementary test data regarding the ecotoxicological profile beyond those listed in the core data set are necessary in order to perform a preliminary risk assessment.

Product type 21: Antifouling products

The biodegradation tests, following the strategy described in Chapter 3, have to be performed using saltwater.
The aquatic toxicity tests need to be performed additionally with marine/brackish species:

7.4.1.1 Acute toxicity to fish
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae (if no NOEC is available from the core data set)

Several additional tests with marine/brackish species are required to accurately assess the risks for these substances:

7.4.3.2 Effects on reproduction and the growth rate on an appropriate species of fish
7.4.3.3.1 Bioaccumulation in an appropriate species of fish
7.4.3.3.2 Bioaccumulation in an appropriate invertebrate species
7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species
7.4.3.5.1 Effects on sediment dwelling organisms
7.4.3.5.2 Aquatic plant toxicity

Product type 22: Embalming and taxidermist fluids

No supplementary test data regarding the ecotoxicological and fate profile beyond those listed in the core data set are necessary in order to perform a preliminary risk assessment.

Product type 23: Products for the control of other vertebrates

For products to be used in animal housing, releases to manure storage facilities are possible. An anaerobic biodegradation study is necessary:

7.1.2.1.2. Anaerobic biodegradation

If used outside of buildings in the form of baits, granulates or powder, avian toxicity tests are necessary:

7.5.3.1.1 Acute oral toxicity
7.5.3.1.3 Effects on reproduction

PART II: Additional data set and guidance for (chemical) biocidal products

Information on the releases due to the use of the product is always required.

Other data requirements due to direct release if a product contains 2 or more active substances, or if other ingredients of the product might enhance the bioavailabilty of the active substance, the effects of the product on non-target organisms might be significantly different to those of the active substances alone. In those cases, where a direct release of a product to a given compartment is possible, so that the composition of the product is maintained, additional tests regarding the effects towards non-target organisms are to be performed with the product.

For the compartments directly exposed, the risk assessment will be performed based on the tests performed with the product.

In the following sections, examples of direct environmental exposure for different product types are presented, together with the tests that would have to be performed on the product. Other uses might exist which give rise to direct exposure, for which additional tests might also be necessary.

Furthermore, data on the average amount of the product which may be left in the package to be disposed of should be submitted.

Product type 1: Human hygiene biocidal products

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Especially for human hygiene biocidal products in order to quantify emission fluxes: as far as not covered in paragraph B5.4 in Chapter 2 (data set for the biocidal product), information should be supplied on the maximum and average amounts of the product that is applied on one person at a time. For disinfectants in general, information should be supplied on how and in what percentage the active substance, its transformation products or the other ingredients in the product are released from the point treated during use and during washing, etc. (e.g. per unit of surface area per unit of time) by evaporation, dissolving in water or another way. Release rates to be given can be either default estimates or measured.

Product type 2: Private area and health area disinfectants

For substances to be used as soil or solid waste disinfectants, direct release to soil is possible. Furthermore, for substances to be used by gassing, fogging, fumigation or aerosol sprays high releases to the atmosphere and subsequent deposition is possible. It is necessary to perform initial terrestrial tests with the product:

7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged

[Ann. IIB, VII.7.1.]

- For disinfectants in general, information should be supplied on how and in what percentage the active substance, its transformation products or the other ingredients in the product are released from the point treated during use and during washing, etc. (e.g. per unit of surface area per unit of time) by evaporation, dissolving in water or another way. Release rates to be given can be either default estimates or measured.

Product type 3: Veterinary hygiene biocidal products

For substances to be used as soil or solid waste disinfectants, direct release to soil is possible. Furthermore, for substances to be used by gassing, fogging, fumigation or aerosol sprays high releases to the atmosphere and subsequent deposition is possible. It is necessary to perform initial terrestrial tests with the product:

7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

For use in poultry farms, were wild birds are attracted, a test with birds is necessary:

7.5.3.1.1 Acute oral toxicity

If the substance is to be used in marine fish nurseries, the aquatic toxicity tests with marine/brackish species also need to be performed with the product:

7.4.1.1 Acute toxicity to fish
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged
[Ann. IIB, VII.7.1.]

- For disinfectants in general, information should be supplied on how and in what percentage the active substance, its transformation products or the other ingredients in the product are released from the point treated during use and during washing, etc. (e.g. per unit of surface area per unit of time) by evaporation, dissolving in water or another way. Release rates to be given can be either default estimates or measured.

Product type 4: Food and feed area disinfectants

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged
[Ann. IIB, VII.7.1.]

- Especially for food and feed area disinfectants to quantify emission fluxes: information should be supplied on how and in what percentage the active substance, its transformation products or the other ingredients in the product are released from the point treated during use and during subsequent washing, etc. (e.g. per unit of surface area per unit of time) by evaporation, their dissolving in

water or another way. The release rates given can be either default estimates or measured.

Product type 5: Drinking water disinfectants

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Especially for drinking water disinfectants to quantify emission fluxes: information should be supplied on how and in what percentage the active substance, its transformation products or the other ingredients in the product are released from the drinking water treatment during or after use (e.g. per volume of treated water per unit of time) by evaporation or are dissolved in water or are released in some other way. Release rates to be given can be either default estimates or measured.

Product type 6: In-can preservatives

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Especially for these in-can preservatives in order to quantify emission fluxes: as far as not covered in paragraph B5.4 in Chapter 2 (data set for the biocidal product), information should be supplied on how and in what percentage the active substance, its transformation products or the other ingredients in the product are released from the preserved material (e.g. per unit of volume per unit of time) by evaporation (volatilisation from the treated material in contact with indoor or outdoor air), dissolving or any other way. Release rates to be given can be either default estimates or measured leaching rates.

Product type 7: Film preservatives

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Especially for these film preservatives in order to quantify emission fluxes: as far as not covered in paragraph B5.4 in Chapter 2 (data set for the biocidal product), information should be supplied on the binding of the active substance to the film treated, on factors influencing binding properties and information should be supplied on how and in what percentage the active substance, its transformation products or the other ingredients in the product are released from the treated film (e.g. per unit of surface area per unit of time) by evaporation, dissolving or any other way. Release rates to be given can be either default estimates or measured leaching rates.
- Different leaching rates required are for example, leaching during the washing of freshly preserved film (e.g. a textile or a film), leaching from a treated film to be placed outdoors with a risk of wetting, leaching from the treated film when washed indoors or otherwise in contact with water during its service life, and volatilisation from the treated film in contact with indoor or outdoor air.

Product type 8: Wood preservatives

High releases to the terrestrial compartment are possible during storage of freshly treated wood. It is necessary to perform initial terrestrial tests with the product:

7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

Alternatively to testing the product, it would be possible to test the leachate. No harmonised methods are currently available though, and further discussion regarding the scope of these tests would be necessary.

If the substance is to be used for wood in hazard class 4 (fresh water) defined in the standard EN 335-1 (CEN 1992), the aquatic toxicity tests with freshwater species are required with the product as well:

7.4.1.1 Acute toxicity to fish
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

Alternatively to testing the product, it would be possible to test the leachate. No harmonised methods are currently available though, and further discussion regarding the scope of these tests would be necessary.

If the substance is to be used for wood in hazard class 5 (salt water) defined in the standard EN 335-1 (CEN 1992), the aquatic toxicity tests with marine/brackish species are required with the product as well:

7.4.1.1 Acute toxicity to fish
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

Alternatively to testing the product, it would be possible to test the leachate. No harmonised methods are currently available though, and further discussion regarding the scope of these tests would be necessary.

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Especially for wood preservatives to quantify emission fluxes: as far as not covered in paragraph B5.4 in Chapter 1 (data set for the biocidal product), information should be supplied on the binding of the active substance to wood or other treated materials, on factors influencing binding properties and information should be supplied on how and in what percentage the active substance, its transformation products or the other ingredients in the product are released from the treated material (e.g. per unit of surface area per unit of time) by evaporation, dissolving or another way. Release rates to be given can be either default estimates or measured leaching rates.
- The different leaching rates required are: leaching during storage of freshly preserved wood, leaching from wood above ground with risk of wetting, leaching from wood in contact with water, leaching from wood in contact with soil and

volatilisation from wood in contact with air. [**Note:** Evaluation methods for leaching from treated wood and related risk assessment guidance are being developed in some Member States and e.g. in the framework of the COST E2 project "Wood durability". Related to this project a protocol for the quantification of the emission fluxes has been developed by the European Wood Preservation Manufacturers' Group.]

Product type 9: Preservatives for fibres, leather, rubber and polymerised material

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Especially for these material preservatives in order to quantify emission fluxes: as far as not covered in paragraph B5.4 in Chapter 2 (data set for the biocidal product), information should be supplied on the binding of the active substance to the material treated, on factors influencing binding properties and information should be supplied on the binding of the active substance to the material treated, on factors influencing binding properties and information should be supplied on how and in what percentage the active substance, its transformation products or the other ingredients in the product are released from the treated material (e.g. per unit of surface area per unit of time) by evaporation, dissolving or any other way. Release rates to be given can be either default estimates or measured leaching rates.
- Different leaching rates required are for example, leaching during the washing of freshly preserved material (e.g. a textile), leaching from a treated textile or plastic in or above ground outdoors with a risk of wetting, leaching from the treated material when washed or otherwise in contact with water during its service life, and volatilisation from the treated material in contact with indoor or outdoor air.

Product type 10: Masonry preservatives

For spray application, high releases to the terrestrial compartment are possible. It is necessary to perform initial terrestrial tests with the product:

7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Especially for these material preservatives in order to quantify emission fluxes: as far as not covered in paragraph B5.4 in Chapter 2 (data set for the biocidal product), information should be supplied on the binding of the active substance to the material treated, on factors influencing binding properties and information should be supplied on how and in what percentage the active substance, its transformation products or the other ingredients in the product are released from the treated material (e.g. per unit of surface area per unit of time) by evaporation, dissolving or any other way. Release rates to be given can be either default estimates or measured leaching rates.

- Different leaching rates required are for example, leaching from a treated construction material in or above ground with a risk of wetting, leaching from the treated material placed indoors and washed or otherwise in contact with water during its service life, and volatilisation from the treated material in contact with indoor or outdoor air.

Product type 11: Preservatives for liquid-cooling and processing systems

For substances to be used in the cooling systems with an open cooling tower, a high water discharge to air and subsequent deposition onto soil is possible. In these cases, it is necessary to perform initial terrestrial tests with the product:

7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- For example, indicate the measured or estimated extent of release: frequency and intensity (e.g. dose and duration).

Product type 12: Slimicides

For inland use of drilling and oil recovery preservatives, it is necessary to perform initial terrestrial tests with the product:

7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

For offshore use, the aquatic toxicity tests with marine/brackish species need to be performed additionally with the product:

7.4.1.1 Acute toxicity to fish
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- For example, give information on the percentage of the active substance or a substance of concern adsorbed to pulp or paper in the manufacturing process. Indicate measured or estimated extent of release: frequency and intensity (e.g. dose and duration).

Product type 13: Metalworking fluid preservatives

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- For example, indicate the measured or estimated extent of release: frequency and intensity (e.g. dose and duration).

Product type 14: Rodenticides

Depending on the outcome of the discussions regarding the scope of the biocide directive, this section might have to be revised.
If used outside of buildings in the form of baits, granulates or powder, an acute avian toxicity test is necessary with the product:

7.5.3.1.1 Acute oral toxicity
7.8.7.2 Studies by acceptance by ingestion of the biocidal product by any non-target organisms thought to be a risk

Furthermore, in order to assess risks to predators residue data in target organisms concerning the active substance and including toxicologically relevant metabolites would be needed (cf. Chapter 2, part B, section 5.11)

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Information should be supplied on the leaching rate of active substances due to weathering of e.g. baits, granules or contact pastes.

Product type 15: Avicides

Furthermore, in order to assess risks to predators residue data in target organisms concerning the active substance and including toxicologically relevant metabolites would be needed (cf. Chapter 2, part B, section 5.11)

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Information should be supplied on the leaching rate of active substances due to weathering of e.g. baits, granules or contact pastes.

Product type 16: Molluscicides

For products used outside buildings in contact with soil, release to soil is possible. It is necessary to perform initial terrestrial tests with the product:

7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

If used outside of buildings in the form of baits, granulates or powder, an acute avian toxicity test is necessary with the product:

7.5.3.1.1 Acute oral toxicity

For molluscicides used in marine waters, the aquatic toxicity tests with marine/brackish species need to be performed with the product as well:

7.4.1.1 Acute toxicity to fish
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

For molluscicides to be used in water, residue studies are necessary:

7.7.1.2 Residue data in fish concerning the active substance and including toxicologically relevant metabolites

Furthermore, possible monitoring data or results of residues studies including toxicologically relevant metabolites, if these cause harmful effects on human health.

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Information should be supplied on the leaching rate of active substances due to weathering of e.g. baits, granules or contact pastes.

Product type 17: Piscicides

For piscicides, the freshwater aquatic toxicity tests need to be performed with the product as well:

7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

If the substance is to be used in a marine environment, the marine/brackish aquatic toxicity tests need to be performed with the product as well:

7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

Residue studies are also necessary:

7.7.1.2 Residue data in fish concerning the active substance and including toxicologically relevant metabolites

Furthermore, possible monitoring data or results of residues studies including toxicologically relevant metabolites, if these cause harmful effects on human health.

Product type 18: Insecticides, acaricides and products to control other arthropods and Product type 19: Repellants and attractants

For products used outside buildings as well as products to be used by gassing, fogging or fumigation, release to soil is possible. It is necessary to perform initial terrestrial tests with the product:

7.5.1.1 Inhibition to microbial activity
7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms
7.5.1.3 Acute toxicity to plants

If used outside of buildings in the form of baits, granulates or powder, an acute avian toxicity test is necessary with the product:

7.5.3.1.1 Acute oral toxicity

Furthermore, a test with bees is necessary:

7.5.3.2 Acute toxicity to honeybees and other beneficial arthropods, for example predators

If the substance is to be used as a shark repellant, the aquatic toxicity tests with marine/brackish species need to be performed additionally with the product:

7.4.1.1 Acute toxicity to fish
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Information should be supplied on the leaching rate of active substances due to weathering of e.g. baits, granules or contact pastes.

Product type 20: Preservatives for food and feedstock

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- For these uses to quantify emission fluxes: information should be supplied on how and in what percentage the active substance, its transformation products or the other ingredients in the product are released from the point treated during use and during subsequent washing, etc. (e.g. per unit of surface area per unit of time) by evaporation, their dissolving in water or another way. The release rates given can be either default estimates or measured.

Product type 21: Antifouling products

The aquatic toxicity tests with marine/brackish species need to be performed additionally with the product:

7.4.1.1 Acute toxicity to fish
7.4.1.2 Acute toxicity to invertebrates
7.4.1.3 Growth inhibition test on algae

Alternatively to testing the product, it would be possible to test the leachate. No harmonised methods are currently available though, and further discussion regarding the scope of these tests would be necessary.

Residue studies are also necessary:

7.7.1.2 Residue data in fish concerning the active substance and including toxicologically relevant metabolites

Furthermore, possible monitoring data or results of residues studies including toxicologically relevant metabolites, if these cause harmful effects on human health.

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Especially for antifouling products in order to quantify emission fluxes: as far as not covered in paragraph B5.4 in Chapter 2 (data set for the biocidal product), information should be supplied on the average and maximum leaching of the active substance from the film, on factors influencing the leaching properties (e.g. time passed after application, temperature, pH, salinity, vessel speed, erosion rate of coating) and information should be supplied on how and in what percentage the active substance, its film (e.g. per unit of surface area per unit of time). Release rates to be given can be either default estimates or measured leaching rates. There is one internationally accepted leaching test method available and it is only for organo-tin based antifouling products (ASTM D5108-90). ISO is also developing methods for the determination of release rates of active substances in antifouling paints. The first methods will be for copper based active substances.

Product type 22: Embalming and taxidermist fluids

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- For embalming and taxidermist fluids, information should be supplied on how and in what percentage the active substance, its transformation products or other ingredients in the product are released from the point during use and during storage of treated material, etc. (e.g. per unit of surface area per unit of time) by evaporation, dissolving in water or another way. Release rates to be given can either default estimates or measured.

Product type 23: Products for the control of other vertebrates

If used outside of buildings in the form of baits, granulates or powder, an acute avian toxicity test is necessary with the product as well:

7.5.3.1.1 Acute oral toxicity

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Especially for these product types: information should be supplied on the leaching rate of active substances due to weathering of e.g. baits, granules or contact pastes.

PRODUCT TYPE SPECIFIC DATA.
AN OVERVIEW OF REQUIREMENTS IN CHAPTERS 2 AND 2.5 CONCERNING THE ENVIRONMENT

PT = product type, + = always required, (+)= product type specific requirement, ++* = core data, always required for more than one environmental compartment (i.e. more than one species) according to exposure. C = required conditionally.
For key to guideline abbreviations, see end of table.

7. ECOTOXICOLOGICAL PROFILE INCLUDING ENVIRONMENTAL FATE AND BEHAVIOUR																								
	Guideline	**PT 1**	**PT 2**	**PT 3**	**PT 4**	**PT 5**	**PT 6**	**PT 7**	**PT 8**	**PT 9**	**PT 10**	**PT 11**	**PT 12**	**PT 13**	**PT 14**	**PT 15**	**PT 16**	**PT 17**	**PT 18**	**PT 19**	**PT 20**	**PT 21**	**PT 22**	**PT 23**
7.1.1.1.1 Hydrolysis *[Ann.IIA, VII.7.6.2.1.]*	EC C.7	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
7.1.1.1.2 Phototransformation in water *[Ann.IIA, VII.7.6.2.2.]*	S 1995 US 835.2210	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
7.1.1.2.1 Ready biodegradability *[Ann.IIA, VII.7.6.1.1.]*	EC C.4 O 305 A-F	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
7.1.1.2.2 Inherent biodegradability *[Ann.IIA, VII.7.6.1.2.]*	EC C.9 / 12 O302 B,C O 306	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**	**c**
7.1.1.2.3 Biodegradation in seawater	OECD 306 ISO14592			**(+)**					**(+)**			**(+)**	**(+)**				**(+)**	**(+)**		**(+)**				
7.1.2.1.2 Anaerobic biodegradation	ISO 11734			**(+)**											**(+)**	**(+)**	**(+)**			**(+)**				**(+)**
7.1.3 Adsorption/desorption screening test *[Ann.IIA, VII.7.7.]*	O 106 EC 18	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
7.2.3.1 Absorption and desorption in soil *[Ann.IIIA, XII.1.2.]*	O 106 EC C.18		**(+)**	**(+)**		**(+)**			**(+)**		**(+)**	**(+)**	**(+)**				**(+)**			**(+)**				
7.3.1 Phototransformation in air *[Ann.IIIA, VII.5.]*	TGD EC 1996	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
7.4.1.1 Acute toxicity to fish *[Ann.IIA, VII.7.1.]*	EC C.1/US 850.1075	+	+	**++***	+	+	+	+	**++***	+	+	**++***	**++***	+	+	+	**++***	+	+	**++***	+	**++***	+	+

	Guideline	PT 1	PT 2	PT 3	PT 4	PT 5	PT 6	PT 7	PT 8	PT 9	PT 10	PT 11	PT 12	PT 13	PT 14	PT 15	PT 16	PT 17	PT 18	PT 19	PT 20	PT 21	PT 22	PT 23
7.4.1.2 Acute toxicity to invertebrates *[Ann.IIA, VII.7.2.]*	EC C.2, O 202 / I 14669/ US 850.1035-850.1035	+	+	++*	+	+	+	+	++*	+	+	++*	++*	+	+	+	++*	++*	+	++*	+	++*	+	+
7.4.1.3 Growth inhibition test on algae *[Ann.IIA, VII.7.3.]*	O 201 / EC C.3 / I 10253 / US 850.5400	+	++*	++*	+	+	++*	++*	++*	++*	++*	++*	++*	++*	+	+	++*	++*	+	++*	+	++*	+	+
7.4.1.4 Inhibition of microbiological activity *[Ann.IIA, VII.7.4.]*	EC C.11 / O 209	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
7.4.2 Bioconcentration *[Ann.IIA, VII.7.5.]*	TGD (EC) 1996	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
7.4.3.2 Effects on reproduction and growth on fish *[Ann.IIIA, XIII.2.2.]*	O 210, 212, 215		(+)	(+)			(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)			(+)					(+)		
7.4.3.3.1 Bio-accumulation in an appropriate species of fish	O 305 EC 13																					(+)		
7.4.3.3.2 Bio-accumulation in an appropriate invertebrate species	US 850.1710																					(+)		
7.4.3.4 Reproduction and growth rate of an appropriate Invertebrate species *[Ann.IIIA, XIII.2.4.]*	O 211/ Dan.Stan 2209/ US 850.1350		(+)	(+)			(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)			(+)	(+)				(+)		
7.4.3.5.1 Effects on sediment dwelling organisms	TGD (EC) 1996																					(+)		
7.4.3.5.2 Aquatic plant toxicity using *Lemna* spp.	US 850-4400																					(+)		
7.5.1.1 Inhibition of microbial activity	14238-16387/ O 216-217		(+)	(+)		(+)			(+)		(+)	(+)	(+)				(+)			(+)				

	Guideline	PT 1	PT 2	PT 3	PT 4	PT 5	PT 6	PT 7	PT 8	PT 9	PT 10	PT 11	PT 12	PT 13	PT 14	PT 15	PT 16	PT 17	PT 18	PT 19	PT 20	PT 21	PT 22	PT 23
7.5.1.1 Inhibition of microbial activity	14238-16387/ O 216-217		**(+)**	**(+)**		**(+)**			**(+)**		**(+)**	**(+)**	**(+)**				**(+)**			**(+)**				
7.5.1.2 Acute toxicity to earthworms or other soil- non-target macro organisms	EC C.8/ O 207		**(+)**	**(+)**		**(+)-**			**(+)**		**(+)**	**(+)**	**(+)**				**(+)**			**(+)**				
7.5.1.3 Acute toxicity to plants	O 208		**(+)**	**(+)**		**(+)**			**(+)**		**(+)**	**(+)**	**(+)**				**(+)**			**(+)**				
7.5.3.1.1 Acute oral toxicity *[Ann.IIIA, XIII.1.1.]*	S 1995			**(+)**											**(+)**		**(+)**			**(+)**				**(+)**
7.5.3.1.2 Short term toxicity *[Ann.IIIA, XIII.1.2.]*	O 205														**(+)**									
7.5.3.1.3 Effects on reproduction *[Ann.IIIA, XIII.1.3.]*	O 206														**(+)**		**(+)**			**(+)**				**(+)**
7.5.4.1 Acute toxicity to honeybees and other beneficial arthropods *[Ann.IIIA, XIII.3.1.]*	IOBC (1985) BBA PartVI (1998B) O 213 and/ or 214																			**(+)**				
7.6 Summary of ecotoxicological effects and fate and behaviour in the environment *[Ann.IIA, VII.7.8.]*		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

BBA = Biologische Bundesanstalt
C = CIPAC
EC = European Communities
I = ISO
IOBC = International Organisation for Biological Control
O = OECD
S = SETAC
UBA = Umweltbundesamt
US = US-EPA

CHAPTER 3

ADDITIONAL DATA REQUIRED FOR ACTIVE SUBSTANCES AND BIOCIDAL PRODUCTS

PART A:

ADDITIONAL DATA AND GUIDANCE FOR ACTIVE (CHEMICAL) SUBSTANCES

DOSSIER REQUIREMENTS

1 APPLICANT *[Ann. IIA, I.]*

1.1 Name and address, etc. *[Ann. IIA, I. 1.1]*
1.2 Active substance manufacturer *[Ann. IIA, I. 1.2.]*

2 IDENTITY *[Ann. IIA, II.]*

2.1 Common name *[Ann. IIA, II.2.1.]*
2.2 Chemical name *[Ann. IIA, II. 2.2.]*
2.3 Manufacturer's development code number(s) *[Ann. IIA, II .2.3.]*
2.4 CAS and EC numbers, if available *[Ann. IIA, II. 2.4.]*
2.5 Molecular and structural formula, molecular mass *[Ann. IIA, II. 2.5.]*
2.6 Method of manufacture of the active substance *[Ann. IIA, II. 2.6.]*
2.7 Specification of purity of the active substance *[Ann. IIA, II. 2.7.]*
2.8 Identity of impurities and additives *[Ann. IIA, II.2.8.]*
2.9 The origin of the natural active substance or the precursor(s) of the active substance *[Ann. IIA, II.2.9.]*
2.10 Exposure data in conformity with Annex VIIA to Directive 92/32/EEC *[Ann. IIA, II.2.10.]*

3 PHYSICAL AND CHEMICAL PROPERTIES *[Ann. IIA, III.]*

3.1 Melting point, boiling point, relative density *[Ann. IIA, III. 3.1.]*
3.2 Vapour pressure *[Ann. IIA, III. 3.2.]*
3.3 Appearance *[Ann. IIA, III. 3.3.]*
3.4 Absorption spectra (UV/VIS, IR, NMR), and a mass spectrum, molar extinction at relevant wavelengths, where relevant *[Ann. IIA, III. 3.4.]*
3.5 Solubility in water *[Ann. IIA, III. 3.5.]*

3.6 Dissociation constant

- The acid-base constant (pKa, pKb) or another such constant should always be given if it can be determined.
- E.g. OECD guideline number 112 (Dissociation constant in water) only if water solubility cannot be measured.

3.7 Solubility in organic solvents, including the effect of temperature on solubility *[Ann. IIIA, III. 1.]*

- *Must be submitted for a purified active substance of stated specification.*
- Must be examined using at least two common solvents with different polarities.
- Results should be given as mg/l of solvent.
- This data is usually not required for the product type 5.

3.8 Stability in the organic solvents used in biocidal products and the identity of relevant breakdown products *[Ann. IIIA, III. 2.]*

- Must be stated if the active substance as manufactured includes an organic solvent.
- *Must be submitted for the active substance of stated specification.*
- This data is usually not required for the product type 5.

3.9 Partition coefficient n-octanol/water *[Ann. IIA, III. 3.6.]*
3.10 Thermal stability, identity of relevant breakdown products *[Ann. IIA, III. 3.7.]*
3.11 Flammability including auto-flammability and identity of combustion products *[Ann. IIA, III. 3.8.]*
3.12 Flash-point *[Ann. IIA, III. 3.9.]*
3.13 Surface tension *[Ann. IIA, III. 3.10.]*

3.14 Viscosity

- This data is always required for liquid substances, excluding product type 5.
- E.g. OECD guideline 114

3.15 Explosive properties *[Ann. IIA, III. 3.11.]*
3.16 Oxidising properties *[Ann. IIA, III. 3.12.]*
3.17 Reactivity towards container material *[Ann. IIA, III. 3.13.]*

4 ANALYTICAL METHODS FOR DETECTION AND IDENTIFICATION

4.1 Analytical methods for the determination of a pure active substance and for relevant degradation products, isomers and impurities of the active substance and additives (e.g. stabilisers) *[Ann. IIA, IV.4.1.]*
4.2 Analytical methods including recovery rates and the limits of determination for the active substance, and for residues thereof, and where relevant in/on the specified materials *[Ann. IIA, IV.4.2.]*

4.3 Analytical methods including recovery rates and the limits of determination for residues in/on food or feedstuffs and other products where relevant *[Ann. IIIA, IV.1.]*

- Required if the active substance or the material treated with it is to be used in a manner which may cause contact with food or feedstuffs (e.g. when used for disinfection in food production or transportation, in the food processing industry or catering services), or intended to be placed on, in or near soils in agricultural or horticultural use. This may be the case for product types 1, 2, 3, 6, 8, 14 and 18. In addition, always required for product types 4, 5 and 20.
- Required if the active substance for product type 12 is to be used for the treatment of paper pulp, paper, paperboard or any other product intended for contact with feedstuffs. Food packaging may be covered by Directive 89/109/EC which is under revision to include food-contact paper. It seems that feedstuffs are not covered by other directives.
- Analytical methods for residues in fish and shellfish must be submitted for product type 21.
- Reference can be made to analytical methods covered in paragraph A4.2 above where relevant.

5 EFFECTIVENESS AGAINST TARGET ORGANISMS AND INTENDED USES

5.1 Function, for example, fungicide, rodenticide, insecticide, bactericide *[Ann. IIA, V.5.1.]*
5.2 Organism(s) to be controlled and products, organisms or objects to be protected *[Ann. IIA, V.5.2.]*
5.3 Effects on target organisms, and likely concentration at which the active substance will be used *[Ann. IIA, V.5.3.]*
5.4 Mode of action (including time delay) *[Ann. IIA, V.5.4.]*
5.5 Field of use envisaged *[Ann. IIA, V.5.5.]*
5.6 User: industrial, other professional, general public (non-professional) *[Ann. IIA, V.5.6.]*
5.7 Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies *[Ann. IIA, V.5.7.]*
5.8 Likely tonnage to be placed on the market per year *[Ann. IIA, V.5.8.]*

6 TOXICOLOGICAL AND METABOLIC STUDIES *[Ann. IIIA, VI.]*

6.1 Acute Toxicity *[Ann. IIA, VI. 6.1.]*
- 6.1.1 Oral *[Ann. IIA, VI. 6.1.1]*
- 6.1.2 Dermal *[Ann. IIA, VI. 6.1.2.]*
- 6.1.3 Inhalation *[Ann. IIA, VI. 6.1.3.]*
- 6.1.4 Skin and eye irritation *[Ann. IIA, VI. 6.1.3.]*
- 6.1.5 Skin sensitisation *[Ann. IIA, VI. 6.1.5.]*

6.2 Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study *[Ann. IIA, VI. 6.2.]*

6.3 Short term repeated dose toxicity (28 days) *[Ann. IIA, VI. 6.3.]*
- 6.3.1 Repeated dose toxicity (oral)
- 6.3.2 Repeated dose toxicity (dermal)
- 6.3.3 Repeated dose toxicity (inhalation)

6.4 Subchronic toxicity 90-day study *[Ann. IIA, VI. 6.4.]*
- 6.4.1 Subchronic oral toxicity test
- 6.4.2 Subchronic dermal toxicity test
- 6.4.3 Subchronic inhalation toxicity test

6.5 Chronic toxicity *[Ann. IIA, VI. 6.5.]*

6.6 Genotoxicity studies, *[Ann. IIA, VI. 6.6.]*)
- 6.6.1 In vitro gene mutation study in bacteria *[Ann. IIA, VI. 6.6.1.]*
- 6.6.2 In vitro cytogenicity study in mammalian cells *[Ann. IIA, VI. 6.6.2.]*
- 6.6.3 In vitro gene mutation assay in mammalian cells *[Ann. IIA, VI. 6.6.3.]*
- 6.6.4 If positive in 6.6.1, 6.6.2 or 6.6.3, then an in vivo mutagenicity study will be required (bone marrow assay for chromosomal damage or a micronucleus test) *[Ann. IIA, VI. 6.6.4.]*
- 6.6.5 If negative in 6.6.4 but positive in some of in vitro tests then undertake a second in vivo study to examine whether mutagenicity or evidence of DNA damage can be demonstrated in tissue other than bone marrow *[Ann. IIA, VI. 6.6.5.]*
- 6.6.6 If positive in 6.6.4 then a test to assess possible germ cell effects may be required *[Ann. IIA, VI. 6.6.6.]*

6.7 Carcinogenicity study *[Ann. IIA, VI. 6.7.]*

6.8 Reproductive toxicity *[Ann. IIA, VI. 6.8.]*
- 6.8.1 Teratogenicity test *[Ann. IIA, VI. 6.8.1.]*
- 6.8.2 Two generations reproduction study *[Ann. IIA, VI. 6.8.2.]*

6.9 Neurotoxicity study *[Ann. IIIA, VI. 1.]*

- This data may be relevant on the basis of the toxicological properties of a substance.
- Neurotoxicity studies detect functional changes and/or structural and biochemical changes in the central and peripheral nervous systems. These changes can be morphological, physiological (e.g. electroencephalographic changes), or behavioural nature, or can be changes in biochemical parameters (e.g. neurotransmitter levels).
- If there are any indications that the active substance may have neurotoxic properties then specific neurotoxicity studies are required. Indications of neurotoxicity can be acquired from the standard systemic toxicity studies. Further investigation is possible using standard repeated dose toxicity tests with incorporation of specific neurotoxicity measures, like sensory activity, grip strength, and motor activity assessment (e.g. EC method B7 or the corresponding OECD guideline 407) and/or acute neurotoxicity testing using the OECD method 424. Expert judgement is required to decide whether a repeated dose neurotoxicity study is needed (see Chapter 1.2, point 4).
- These studies have to be performed for substances of similar or related structures to those capable of inducing delayed neurotoxicity. If anticholinesterase activity is detected a test for response to reactivating agent may be required.
- EC methods number B.37 (Delayed neurotoxicity of organophosphorus substances following acute exposure) and B.38 (Delayed neurotoxicity of organophosphorus substances, 28 repeated dose study) or the corresponding OECD guidelines 418 and 419.

6.10 Mechanistic study - any studies necessary to clarify effects reported in toxicity studies *[Ann. IIIA, VI. 7.]*

- This data may be relevant on the basis of the toxicological properties of a substance.

- Studies of the mechanisms of toxicity may be necessary when there are indications that active substance may have e.g. a non-genotoxic mechanism for carcinogenicity, species specific effects, adverse effects on reproduction, immunotoxicity or hormone related effects.
- Scientific judgement is required to decide whether any supplementary studies are needed (see Chapter 1.2, point 4).

6.11 Studies on other routes of administration (parenteral routes)

- For existing substances, data (if already existing) by alternative routes should be submitted by the applicant.
- New studies will be required only in exceptional cases.
- Studies on parenteral routes may supplement the information received from toxicokinetic studies and give valuable information e.g. in cases when the gastrointestinal absorption of the chemical in question is poor.
- E.g. acute toxicity studies on intraperitoneal, intravenous subcutaneous and intramuscular routes, where conducted, should be submitted.
- A scientific judgement is required to decide whether any supplementary studies are needed (see Chapter 1.2, point 4).

6.12 Medical data in anonymous form *[Ann. IIA, VI. 6.9.]*

6.12.1	Medical surveillance data on manufacturing plant personnel, if available *[Ann. IIA, VI. 6.9.1.]*
6.12.2	Direct observation e.g. clinical cases, poisoning incidents, if available *[Ann. IIA, VI. 6.9.2.]*
6.12.3	Health records both from industry and any other available sources. *[Ann. IIA, VI. 6.9.3.]*
6.12.4	Epidemiological studies on the general population, if available *[Ann. IIA, VI. 6.9.4.]*
6.12.5	Diagnosis of poisoning including specific signs of poisoning and clinical tests, if available *[Ann. IIA, VI. 6.9.5.]*
6.12.6	Sensitisation/allergenicity observations, if available. *[Ann. IIA, VI. 6.9.6.]*
6.12.7	Specific treatment in case of an accident or poisoning: first aid measures, antidotes and medical treatment, if known *[Ann. IIA, VI. 6.9.7.]*
6.12.8	Prognosis following poisoning *[Ann. IIA, VI. 6.9.8.]*

6.13 Toxic effects on livestock and pets *[Ann. IIIA, VI. 2.]*

- An estimation on toxic effects and exposure via different exposure routes (e.g. inhalation, licking, skin contact and ingestion of poisoned bait) and in relevant, but exceptional cases, toxicity testing in livestock and pets is required. Toxic effects for livestock and pets should to be estimated or studied if the substance is to be used in spaces in which animals are housed, kept or transported or exposure is possible via drinking water or feedingstuffs. Information on lethal doses for different species, symptoms of poisoning, details of the time courses in case of poisoning and antidotes should also be submitted, if available.
- This data may be relevant e.g. for product type 3 (substances used for veterinary hygiene purposes), product type 4 (disinfection of surfaces and equipment), product type 5 (drinking water) product types 8 and 10 (treated materials in areas in which animals are housed, kept or transported), product types 14, 15 and 23 (ingestion of baits), product types 16 and 17 (contaminated drinking water), product types 18 and 19 (repellents to be used for veterinary hygiene purposes). An expert judgement is required to decide whether any studies are needed (see Chapter 1.2, point 4).
- This data is usually not required for the product types 1, 2, 6, 7, 9, 11, 12, 13, 20, 21 and 22.

6.14 Other test(s) related to the exposure of humans *[Ann. IIIA, XI.2]*

- Toxicity of degradation products, by-products and reaction products related to human exposure.
- Information is required on the toxic effects of substances generated from an active substance, other than mammalian metabolites, in normal use of biocidal product.
- The decision as to the need for this data should be made on case-by-case basis by expert judgement (see Chapter 1.2, point 4). Where human exposure is significant, toxicity testing may be needed.
- This data may be relevant for many product types. As examples, product types 1 and 2 (reaction products with water when the substance is used for human hygiene purposes or reaction products with water or other materials released in water or air when the substance is used for the treatment of bathing waters), product type 5 (substances produced in a reaction with drinking water), product types 6, 7, 9 and 10 (residuals in treated materials), product type 8 (irritating and sensitising effects of chemical compounds, such as metal salts, developed on the surface of the treated wood) and product type 18 (products, which may produce harmful substances with water during gassing).

6.15 Food and feedingstuffs *[Ann. IIIA, VI. 4.]*

- *If the active substance is to be used in preparations for use where food for human consumption is prepared, consumed or stored, or where feedingstuff for livestock is prepared, consumed or stored, the tests* and results in accordance with paragraphs A6.15.1-6.15.5. *shall be required.*
- The list of the product types for which this data is required is not exhaustive. Decisions as to the need for the following data must be made on a case-by-case basis according to an expert judgement (see Chapter 1.2, point 4).
- Any relevant regulations related to materials and articles indented to come into contact with food and feeding stuffs must be taken into consideration. Examples of such regulations are: Dir. 96/23/EC (residues in food of animal origin), and Dir. 89/109/EEC (on the approximation of the laws of the Member States relating to materials and articles intended to come into contact with foodstuffs) and 2377/90 (veterinary regulation). Applicable residue limits given in relevant legislation must be respected.
- Examples of product types, for which all or some of these tests may be relevant, are product type 1 (products to be used by personnel in food production, the food processing industry or catering services), product type 3 (cleaning eggs), product type 4 (products used for surfaces with which food, feedingstuffs and drinking water may come into contact), product type 5 (drinking water disinfectants), product type 9 (polymerised materials or paper which may come into contact with food, feedingstuffs or drinking water), product type 12 (products used in the production process of materials, which may come into contact with food or feedingstuffs, e.g. paper used for packaging), product types 14 and 23 (products to be used in places where the contamination of food or feeding stuffs is possible, or near soils in agricultural or horticultural use), product types 16 and 17 (residues of the substance in fish or shellfish), product type 20 (food and feedstuff) and product type 21 (residues of products to be used for aqua-culture or fishing equipment, e.g. fish cages).

6.15.1 Identification of the residues (identity and concentrations), degradation and reaction products and of metabolites of the active substance in contaminated foods or feeding stuffs. *[Ann. IIIA, XI. 1.1. and XI.1.3 , XI.1.5.and XI.I.6]*

- Migration into foodstuffs and concentrations of the substances in contaminated food or feeding stuffs should be measured by exposing samples of representative food or feedingstuffs or their simulates for various periods of time to the substances in question. Any possible organoleptic changes in food, feeding stuffs and drinking water must be stated.

6.15.2 Behaviour of the residues of the active substance, its degradation and reaction products and, where relevant, its metabolites on the treated or contaminated food or feeding stuffs including the kinetics of disappearance *[Ann. IIIA, XI. 1.2 .and XI.1.3 , XI.1.5. and XI.I.6]*

6.15.3 Estimation of potential or actual exposure of the active substance to humans or animals through food and feeding stuffs and other means *[Ann. IIIA, XI. 1.4.]*

- Expected exposure via diet taking into account consideration the average consumption of different food types and drinking water should be studied.
- This data is usually not required for product types 11, 13, 14, 15, 16, 17, 18 and 23.

6.15.4 Proposed acceptable residues and the justification of their acceptability *[Ann. IIIA, XI. 1.7.]*

- For product type 5 any relevant regulations relating to acceptable or unacceptable residues in drinking water must be taken into consideration in the justification.
- For product type 21 any directions or restrictions at the Community or national level related to residues in fish and shellfish intended to be used as food or feeding stuffs must be taken into consideration in the justification.

6.15.5 Any other available information that is relevant *[Ann. IIIA, XI. 1.8.]*

- E.g. information from other chemical programmes on ADI, MRL or relevant residues

6.15.6 Summary and evaluation of data submitted under point 6.15 *[Ann. IIIA, XI.1.9]*

- This information is included in 6.18

6.16 Any other tests related to the exposure of the active substance to humans, in its proposed biocidal products, that are considered necessary may be required. *[Ann. IIIA, VI.3.5 and XI. 2]*.

- An expert judgement for suitable tests and reasoned case is needed as to decision that such additional studies are required (see Chapter 1.2, point 4).

6.17 If the active substance is to be used in products for action against plants then tests to assess toxic effects of metabolites from treated plants, if any, where different from those identified in animals shall be required *[Ann. IIIA, VI.6]*.

- Ann. IIIA VI.6. is action against plants, and therefore seen as covered sufficiently by directive 91/414/EC

6.18 Summary of mammalian toxicology and conclusions

7 ECOTOXICOLOGICAL PROFILE INCLUDING ENVIRONMENTAL FATE AND BEHAVIOUR

- These additional studies should clarify the fate and behaviour in the environment of the active substance together with its transformation products and their ecotoxicological effects to the extent that is sufficient for a risk assessment to be carried out addressing the most likely routes of environmental exposure and effects of concern. This guidance to the additional data requirements proposes testing strategies for evaluation of which further data is necessary to address the ecotoxicity and the fate and behaviour in the environment. The nature of the additional data needed depends on the specific properties of the substance, the results of ecotoxicological studies submitted in the common core data set and the intended use(s) of the active substance. A fugacity model may be used to predict the relevant environmental compartments in addition to the exposure scenarios under development.
- The testing strategy should be guided by refining the preliminary risk assessment which the applicant will compile in accordance with paragraph A10 (dataset for the active substance) on the basis of the available test results and other data of the core data set. If the PEC/PNEC ratio is greater than one the applicant should conduct further studies

according to the guidance in this section until sufficient data is available for risk assessment and, where relevant, risk management. Additional trigger values based on qualitative criteria for further testing (e.g. the likelihood of exposure) are given in the paragraphs below describing the data requirements. The applicant may wish to consult with the Competent Authority to ensure the adequacy of the planned further testing. The testing strategy and risk characterisation are refined after each additional test and the applicant can then submit a preliminary risk assessment on the grounds of accompanying test results and other data to the Competent Authority for checking and final acceptance with the rest of the dossier. Guidance on the procedure of this acceptance is given in the guidance document for evaluation of biocidal product (in support of Annex VI) which is under development.

- When in the following requirements under this section there is reference to a risk or (preliminary) risk assessment, it refers to the risk characterisation described above.
- The detailed guidance on the data requirements for ecotoxicological profile given in the paragraphs of this section should be read keeping in mind the overall testing strategy presented in the Figures 1 to 2 under the heading Fate and Behaviour in the Environment, the Figures 3.1 to 4 under the heading Ecotoxicological Studies, and the guidance on risk assessment of the active substance given in Part II and Part III of the Technical Notes.
- For the purpose of guidance given in this section intermittent release is defined as a release taking place one day or less per month. (guidance in Chapter 2.5)

In the future a section on metabolites will be included in the guidance.

Fate and Behaviour in the Environment

- For the purposes of guidance given in this Section, bound residues (e.g. in soil or sediment, also referred to as non-extractable or non-extracted residues), are defined as chemical species originating from an active substance after use according to authorisation granted and that cannot be extracted by methods which do not significantly change the chemical nature of these residues. These non-extractable residues are not considered to include fragments of the active substance having been metabolised by soil organisms to natural constituents of humus.
- The following Figures 1 to 2 illustrate with decision trees the testing strategy for the fate and behaviour of an active substance in the environment. The testing strategy on biodegradation of biocidal active substances is given as a separate section. The detailed criteria for requiring additional data are given in the text thereafter.

7.0 Testing strategy on degradation

7.0.1 TESTING STRATEGY FOR ABIOTIC DEGRADATION

- For the aquatic compartment, the results from the initial abiotic degradation tests on phototransformation (A7.1.1.1.2) and hydrolysis (A7.1.1.1.1) are taken into account in the preliminary risk assessment. If this shows risk then further studies on biodegradation may be required according the testing strategy on biodegradation (see corresponding text and Fig. 1).
- For the atmosphere, estimation of the phototransformation in air (A7.3.1) is required for active substances of all product types as a part of their preliminary risk assessment. Additional data on abiotic degradation in the atmosphere (A7.3.2 Rate and route of degradation in air) are initially required only for active substances which are to be used as fumigants. This study may also be required later for any other active substance if the preliminary risk assessment shows risk for the atmosphere.

7.0.2 TESTING STRATEGY ON BIODEGRADATION OF BIOCIDAL ACTIVE SUBSTANCES

7.0.2.1 Introduction

7.0.2.1.1 Aim

Based on the discussions of the EU biocides working group on environmental fate & behaviour on the Technical Guidance Document on data requirements in the framework of Directive 98/8/EC, a strategy on biodegradation and application in risk assessment has been developed. The objective was to develop a biodegradation test strategy which:

- delivers degradation rate constants for use in the RA
- provides information on (relevant) metabolites formed
- makes use of possible available data
- avoids unnecessary (and expensive) testing as much as possible
- is based on accepted guidance as much as possible

The biodegradation strategy is represented in figure 1.

7.0.2.1.2 Toxicity

Many biocides have an anti-bacterial activity. This may pose a problem for biodegradability testing of biocides. Biocides which are toxic to the inoculum may give false negative test results, which may lead to requirements for further tests and/or will influence the outcome of risk assessments. Therefore it is recommended to test the toxicity to bacteria before commencing with biodegradation studies, and to relate the outcome of the toxicity test to the circumstances (e.g. substance concentration) prescribed for the biodegradation studies foreseen. Thus the most appropriate biodegradation test can be selected. The inhibition of the respiration of activated sludge can be tested using EC method C.11 or the corresponding OECD guideline 209. It must be noted however, that this test is rather insensitive due to the high biomass content used. Notes on the evaluation of chemicals which may be toxic in ready biodegradability tests are given in Annex IV to EC method C.4. A-F or in Annex II of the corresponding OECD 301 guideline. That annex suggests testing substance concentrations at less than 1/10 of the EC50. The ‘closed bottle’ test method EC C.4-E or the corresponding OECD 301 D guideline is normally done with substance concentrations down to 2 mg/l. For lower concentrations, the use of 14C-labelled material will generally be required. Especially for biocides which may be toxic for bacteria at concentrations used in the standard OECD ready or inherent biodegradability tests, it is advised to enter directly into simulation tests for the relevant compartment, using environmentally relevant concentrations of radiolabelled material.

7.0.2.1.3 Temperature

The results of (laboratory) biodegradation studies should be calculated to reflect an average EU outdoor temperature of 12 ^{o}C: DT 50 (12 ^{o}C) =DT 50 (t) x $e^{(0.08x(T-12))}$

7.0.2.2 Screening tests

7.0.2.2.1 Ready biodegradation (Core data)

Ready biodegradability tests are stringent tests which provide limited opportunity for biodegradation and acclimatisation to occur. It may be assumed that a chemical giving a positive result in a test of this type will rapidly biodegrade in the environment and, therefore be classified as ‘readily biodegradable’ in

Annex I of Directive 67/548/EC or according to the corresponding OECD definition. Tests on ready biodegradability are required for the core data set of active substances and are described in EC method C.4-F or the corresponding OECD guidelines 301 A-F (see section 7.1.1.2.1 of Chapter 2 part A).

Information on ready biodegradability tests and the interpretation of their results is summarised on pages 279-281 of Chapter 3 of the TGD for new and existing substances. Ready biodegradation tests provide information on ultimate degradation (mineralization), which can be used to determine whether the parent compound is readily biodegradable or not. To make the results of ready tests useful for risk assessment, EU experts have assigned rate constants to the results of the test. It is considered to be helpful to distinguish why a ready test has not been passed. It may be that the pass level (certain level of mineralization within 28 days) is not reached and/or that the additional kinetic criterion of the 10-days time window is failed. Different rate constants are assigned in these situations (see table). The use of ready tests in this strategy and the proposed rate constants are identical to the TGD for new and existing substances.

7.0.2.2.2 Inherent biodegradability (Core data)

Inherent biodegradability tests are tests which allow prolonged exposure of the test compound to micro-organisms, a more favourable test compound/biomass ratio; chemical, or other conditions, favour biodegradation. A compound giving a positive result in a test of this type may be classified as "inherently biodegradable", but, because of the favourable conditions employed, its rapid and reliable biodegradation in the environment may not be assumed (EC or corresponding OECD definition). Tests on inherent biodegradability are required for the core data set of active substances ‘where appropriate’ and are described in EC methods C.12 and C.9 or the corresponding OECD guidelines 302 A-B and OECD guideline 302 C.

Core-data testing for inherent biodegradability may in general not be appropriate, since these tests do not provide adequate information for risk assessment purposes (see 2.3). Therefore, simulation tests are preferred instead. Nevertheless, if inherent biodegradation data are available (which may well be the case for biocides which are already on the market), the output of the test should be used if the tests fulfil specific criteria:

Zahn-Wellens test:	Pass level must be reached within 7 days, log-phase should be no longer than 3 days, percentage removal in the test before biodegradation occurs should be below 15%.
MITI-II test:	Pass level must be reached within 14 days, log-phase should be no longer than 3 days.
SCAS test:	If a substance is not biodegradable according to the SCAS test, the degradation rate is zero and further (simulation) tests are generally not required (unless metabolite formation is considered relevant).

Information on inherent biodegradability tests and the interpretation of their results is summarised on pages 281-282 of Chapter 3 of the TGD for new and existing substances. The proposed rate constant for inherently degradable substances is identical to the TGD for new and existing substances.

Table 1. Proposed rate constants for biodegradation based on test results.

Test result	**Rate constant STP (h^{-1})**	**Rate constant Surface water (d^{-1})**
Ready biodegradable	1	$4.7 \cdot 10^{-2}$
Ready, but failing 10-d window	0.3	$1.4 \cdot 10^{-2}$
Inherently biodegradable, fulfilling specific criteria	0.1	$4.7 \cdot 10^{-3}$
Inherently biodegradable, not fulfilling specific criteria or not inherently biodegradable	0	0

7.0.2.2.3 Relevance for risk assessment

The screening tests have a long history, are standardised and therefore have been incorporated in many chemical substance legislations.

There are, however a number of drawbacks attached to the current EC test methods and the corresponding OECD ready and inherent biodegradability tests. In general the current tests have been designed to categorise substances in ready vs. not-ready or inherent vs. not-inherent biodegradable. They do not deliver rate constants for primary degradation of parent compounds. Default rate-constants have been attached to these tests in order to be able to use them for risk assessment. For biocides an important drawback may be that they require rather high substance concentrations (2-400 mg/l), which may give toxicity problems (see paragraph 1.2). Furthermore such high substrate concentrations are generally not in line with the circumstances in which biodegradation takes place in reality. Degradation kinetics at high substrate concentrations may differ from those at lower concentrations.

The screening tests do not provide information on the formation of metabolites (other than mineralization products). Substances which are either readily biodegradable or inherently biodegradable (according to the above criteria) can be considered to have such a high mineralization rate that formation of relevant metabolites is highly unlikely. Notwithstanding this consideration, it is recognised that even substances which are readily or inherently biodegradable may form metabolites which are (transiently) available and may lead to exposure under continuous releases. In such cases further (simulation) tests may be required if the PEC/PNEC is more than one and the risk assessment needs refinement in relation to metabolites.

For assessment of substances released to marine environments, the OECD guideline 306 ‘biodegradability in sea water’ may be used. Data from EC method C.4 or the corresponding OECD 301 ready and EC methods C.12 and C.9 or the corresponding OECD 302 A-B and the OECD 302 C guideline inherent tests may also be accepted if the applicant is able to give proper justification for their use instead of OECD 306.

7.0.2.3 Simulation tests

Simulation tests are tests which provide evidence of the rate of biodegradation under some environmentally relevant conditions. Tests of this type may be subdivided according to the environment they are designed to simulate a) biological treatment (aerobic); b) biological treatment (anaerobic); c) river; d) lake; e) estuary; f) sea; and g) soil (OECD definition).

Simulation tests may be performed:
- directly, thus skipping the screening stage biodegradation tests. This may be required for biocides which are toxic to the inoculum.

- if a substance is not ready or not inherently biodegradable and further refinement of the degradation rate and route is needed.

Any simulation test should at least fulfil the following criteria:
- give measured rates for primary and ultimate degradation of the parent compound;
- allow for identification and quantification of metabolites formed during the test.

At this stage in the scheme, it becomes important to which compartment(s) the initial emission takes place.

7.0.2.3.1 Sewage Treatment Plant (STP)

If the biocide first enters a STP before release to the environment, a STP simulation test is required.

The only laboratory EC STP (or the corresponding OECD STP) simulation test currently available is the 'coupled units test' (EC method C.10 or the corresponding OECD test 303A). This test cannot distinguish between biological degradation and other elimination processes such as adsorption and volatilisation. The EC method C.10 or the corresponding OECD 303A test does not fulfil the criteria given above. Investigations with a closed vessel version of the 'coupled units test' using radiolabelled materials have been performed which would allow a determination of the complete mass balance. This modified test is, however, not standardised internationally.

In recent years relatively simple tests using radiolabelled material have been developed which may provide useful information on e.g. aerobic degradation in a STP. An activated sludge die-away test is an example of such a test. Such tests are now discussed at the ISO and therefore not yet standardised. Because they are static tests, one could argue whether they can really be classified as 'simulation' tests or are merely an alternative to 'real' simulation tests. Nevertheless they are well suited for the testing of biocides and risk assessment purposes in general, since they allow for the use of low substance concentrations, give primary degradation rates, account for formation (and disappearance) of metabolites, and are relatively easy to perform.

If the STP simulation test indicates a DT_{50} of more than 3 hours, significant emissions from the STP to water and soil (via sludge) may occur. Then further water or soil simulation studies may be required, depending on the partitioning characteristics of the substance. Substances with a K_p of 5000 l/kg which do not degrade in the STP and are not volatile, partition to the sludge and to water equally (i.e. approx. 50%-50%). Substances with a lower K_p will primarily reside in the water phase and may require a simulation test for degradation in water. Substances with a K_p higher than 5000 l/kg will primarily adsorb to sludge. Since this sludge may be applied to soil, a soil degradation simulation test may be required. The K_p can be derived from the K_{oc} using: $K_p = f_{oc} \times K_{oc}$ using a dry matter content of raw sewage of 450 mg/l and an organic carbon content of 30%.

7.0.2.3.2 Water

If the biocide is directly emitted to water, then a water simulation test is always required. A water-sediment simulation test is required, depending on the partitioning characteristics of the substance:
- K_p > 2,000: water-sediment simulation test (with quantification of bound residues).

The K_p can be derived from the K_{oc} using: $K_p = f_{oc} \times K_{oc}$ using a content of suspended matter in surface water of 15 mg/l (d.wt.) and an organic carbon content of 10%.

There are very few water 'simulation' tests which fulfil the criteria presented in paragraph 7.0.2.3. The ISO 14592 shake flask batch test with surface water is probably the best option currently available. This

test has also been proposed as an OECD test guideline.

For some product types it is relevant to perform a sea water simulation test, and the test system has to be adapted accordingly. Chapter 2.5 gives more guidance on the product types for which this is the case, and 7.1.1.2.3 describes the seawater biodegradation test.

The water-sediment simulation test should be done according to OECD TG 308, with at least two sediments with different characteristics (OECD/JRC workshop in Belgirate in 1995 agreed on two tests for aerobic and one for anaerobic breakdown).

7.0.2.3.3 Soil

If the biocide is directly applied/emitted to soil, then a soil simulation test is required. The route(s) of degradation should be studied in one of the soils tested. Such a test should be done in three different soil types which which, depending on the characteristics of the substance should cover a wide range of relevant soil characteristics.
The OECD TG 307 on aerobic and anaerobic transformation in soil should be used by preference. Furthermore the description of the Eurosoil project could be useful.

An outdoor soil lysimeter study/field study may be relevant as a detail of the soil testing strategy, with identification of suitable protocols e. g. OECD draft guidance document: "Performance of Out-door Monolith Lysimeter Studies" from March 1999, see 7.2.3.2 for further guidance.)

FIG 1. BIODEGRADATION TEST STRATEGY

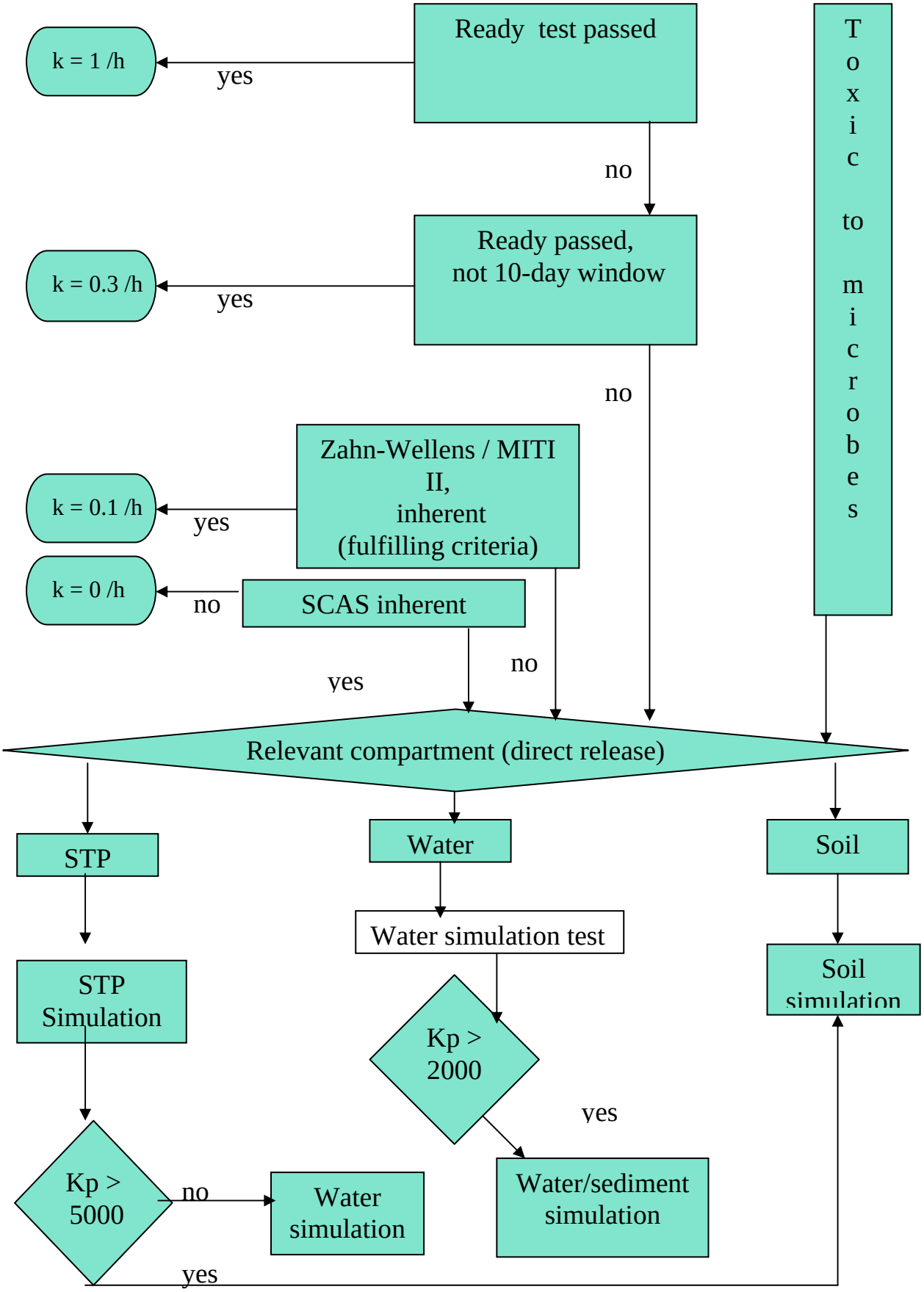
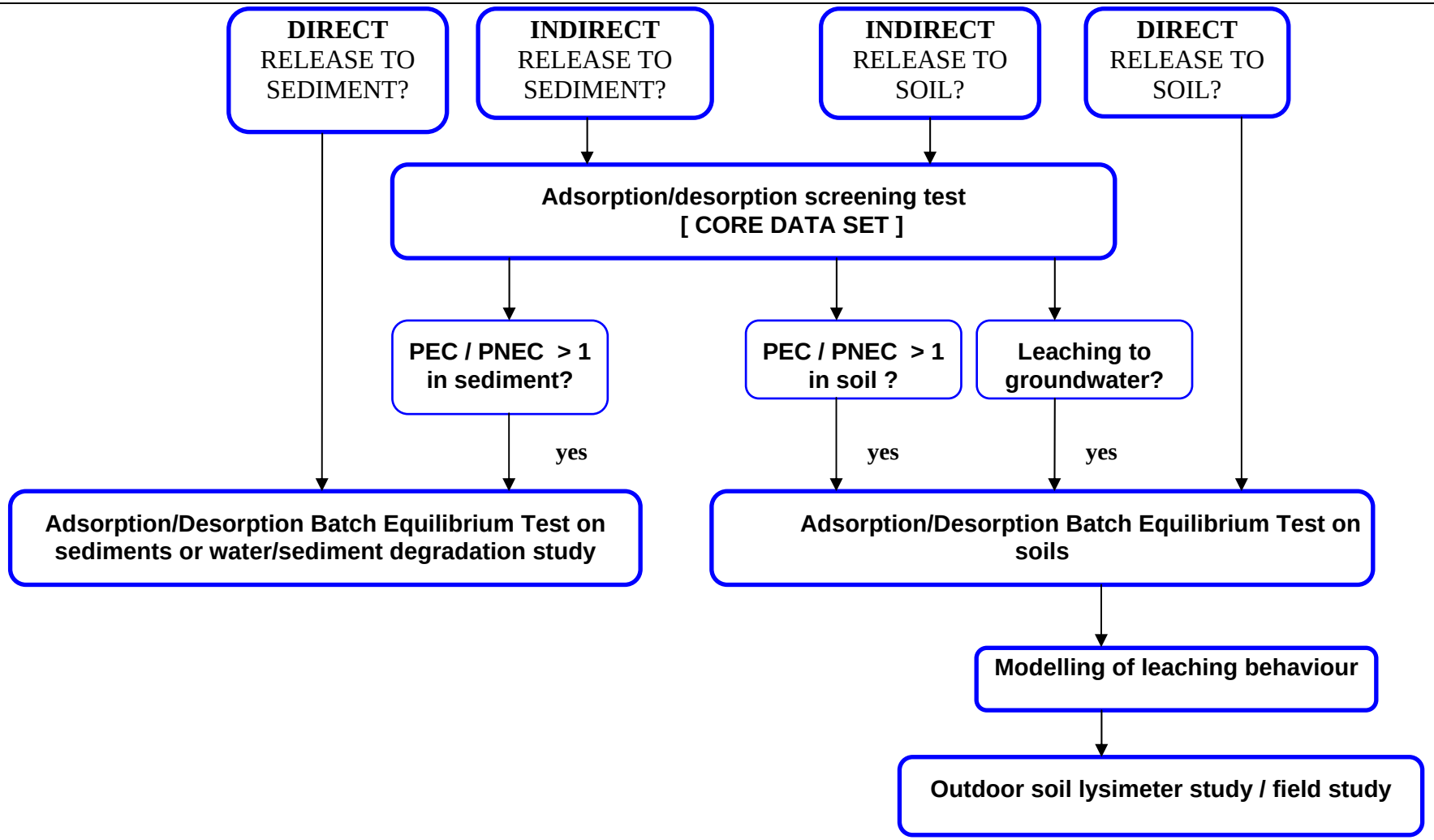


FIG 2 Testing strategy for adsorption and mobility (page 17)



Note: If necessary to characterise more accurately the partitioning behaviour of a substance in a sewage treatment plant, an adsorption/desorption equilibrium test can also be performed with activated sludge.

7.1 Fate and Behaviour in Water

- The data submitted in accordance with this paragraph should clarify, in addition to the degradation of the substance, other relevant routes of dispersion in water, such as volatilisation, adsorption, sedimentation and transformation into bound residues. Accordingly the exposure of organisms living in water and the sediment, and the potential for the contamination of surface water and groundwater should be established.

7.1.1 Degradation, initial studies

7.1.1.1 Abiotic

7.1.1.1.1 Hydrolysis as a function of pH and identification of breakdown products *[Ann. IIA, VII.7.6.2.1.]*

7.1.1.1.2 Phototransformation in water including the identity of the products of transformation *[Ann. IIA, VII.7.6.2.2.]*

7.1.1.2 Biological

7.1.1.2.1 Ready biodegradability *[Ann. IIA, VII.7.6.1.1.]*

7.1.1.2.2 Inherent biodegradability, where appropriate *[Ann. IIA, VII.7.6.1.2.]*

7.1.1.2.3 Biodegradation in seawater

- If a substance is to be used or released in marine environments in considerable amounts (e.g. it is known to be repeatedly used or continuously released in marine environments), then a seawater biodegradation test according to OECD guideline 306 will be required.
- A modified version of ISO 14592 (shake flask batch test) with seawater at environmentally relevant concentrations (^{14}C) may be performed.
- Alternatively a water/sediment degradation study (see paragraph A7.1.2.2.2) in seawater according to modified guidelines may be done.

7.1.2 Rate and route of degradation in aquatic systems including identification of metabolites and degradation products *[Ann. IIIA, XII.2.1.]*

- *If the results from paragraphs A7.1.1.2.1 or (A7.1.1.2.2) above indicate the need to do so, or the active substance has an overall low or absent abiotic degradation, then the tests described in this paragraph shall be required. [Ann. IIIA, VII.6.]*
- See section 7.0 and the testing strategy given in figure 1.
- Testing methods include: water degradation simulation test according to US-EPA guideline OPPTS 835.3100 (US-EPA 1998b); water sediment degradation test according to SETAC procedures (SETAC, 1995) or BBA guideline Part IV, 5.1 (BBA, 1990a); activated sludge biodegradation test according to Federle & Itrich (1997).

7.1.2.1 Biological sewage treatment

7.1.2.1.1 Aerobic biodegradation

- An aerobic simulation test is required if the biocide enters a sewage treatment plant before release to the environment.
- A test according to, for example, Federle & Itrich (1997), Hanstveit et al. (1999) or EC method C.10 or a modified version of the corresponding OECD guideline 303A.

7.1.2.1.2 Anaerobic biodegradation

- An anaerobic degradation study is required if exposure to anaerobic conditions is likely. This may be the case with veterinary hygiene biocidal products and biocidal pest control products to be used in animal housing where release into manure storage facilities is possible.
- A test according to, e.g. ISO method 11734: 1995.

7.1.2.2 Biodegradation in freshwater

7.1.2.2.1 Aerobic aquatic degradation study

- Test according to, for example, ISO method 14592 or US-EPA guideline OPPTS 835.3100 (US-EPA 1998b) is required with non-adapted inoculum.

7.1.2.2.2 Water/sediment degradation study

- Test according to, for example, draft OECD guideline (Aerobic and anaerobic transformation in water/sediment systems), BBA guideline Part IV, 5.1, BBA 1990a, Hoeks/Dekker or US-EPA guideline OPPTS 835.3180 (US-EPA 1998c).
- A water/sediment degradation study under anaerobic conditions should be done if the exposure of the substance to anaerobic conditions is very likely (e.g. when a major proportion of the substance is absorbed in sediment).

7.1.3 Studies on adsorption and desorption in water/sediment systems and, where relevant, on the adsorption and desorption of metabolites and degradation products.
[Ann. IIIA, XII.2.2.]

- Such studies are required where the preliminary risk assessment indicates that this is necessary.
- Screening tests on metabolites and other degradation products are required for compounds which at any sampling time during the soil degradation studies account for more than 10% of the active substance added.
- A full scale adsorption test may be appropriate to refine the PEC value in those cases where:

  -PEC/PNEC > 1 as a result from indirect exposure and the substance is not readily biodegradable.
- The testing strategy, figure 2, indicates when such further tests would be necessary.
- Test according to the new test method EC C.18 or the corresponding OECD guideline 106, or if adsorption to sewage sludge is of concern a test for example, US-EPA guideline OPPTS 835.1110 Activated sludge sorption isotherm (US-EPA 1998a); or draft OECD aerobic or anaerobic transformation in water/sediment systems.

7.1.4.1 Field study on accumulation in the sediment

- If non-extractable residues are formed exceeding 70% of the initial dose in the water/sediment study or if the mineralization rate in the water/sediment system is less than 5% in 100 days, then a field study on accumulation in the sediment should be done.
- There is currently no standardised test guideline available.

7.2 Fate and Behaviour in Soil *[Ann. IIIA, XII.1.]*

- *If the results from paragraphs A7.1.1.2.1 or A7.1.1.2.2 of the data set for the active substance indicate the need to do so, or the active substance has an overall low or absent abiotic degradation, then the tests described in this paragraph shall be required.*
  [Ann. IIIA, VII.6.]
- The data submitted under this paragraph should clarify also, that in addition to the degradation of the substance, other relevant routes of dissipation in soil, such as volatilisation, leaching and transformation into bound residues. The testing strategy on biodegradation of biocidal active substances (fig.1 and text in section 7.0) gives more specific information.

7.2.1 Aerobic degradation in soil, initial study *[Ann. IIIA, VII.4., Ann. IIIA, XII.1.1.]*

- The initial study on degradation in soil should give as the main result the best possible estimates of the time taken for degradations of 50% (DT_{50lab}) of an active substance under more relevant environmental conditions than those of a test on ready or inherent biodegradation. Furthermore, the main route of degradation in soil should be identified with determination of degradation products and bound residues. The aerobic degradation should be studied in the laboratory using one soil for at least 100 days.
- Any metabolites or other degradation products that at any sampling time during the studies account for more than 10% of the active substance added should be identified and their degradation rates should be studied.
- A test is required, for example, according to OECD guideline 304 A, Inherent biodegradability test in soil, or draft OECD guideline on aerobic transformation in soil or BBA or US-EPA guidelines.

7.2.2 Aerobic degradation in soil, further studies

7.2.2.1 The rate and route of degradation including the identification of the processes involved and identification of any metabolites and degradation products in at least three soil types under appropriate conditions *[Ann. IIIA, VII.4., Ann. IIIA, XII.1.1. and Ann. IIIA, XII.1.4.]*

- If the DT_{50lab} determined according to paragraph A7.2.1 above is more than 21 days and the PEC/PNEC > 1 for soil or there is danger for the groundwater or other refinement of the preliminary risk assessment for soil is necessary. The aerobic rate of degradation of the active substance and its relevant metabolites or other degradation products should be further studied in the laboratory in three soil types at 20 ^{o}C, and at 10 ^{o}C, in one of these soil types until such time as a validated Community calculation model for the extrapolation of degradation rates at low temperatures is available.
- The tests should be conducted, for example, according to OECD guideline 304 A, Inherent biodegradability test in soil, or draft OECD guideline on aerobic transformation in soil or BBA or US-EPA guidelines.

7.2.2.2 Field soil dissipation and accumulation *[Annex VI, para. 85]*

- The soil dissipation studies should provide estimates of the time taken for dissipation of 50% and 90% ($DT_{50field}$ and $DT_{90field}$) of the active substance under field conditions.
- Field soil accumulation tests are required in two soil types if the $DT_{90field}$ is over one year and the $DT_{50field}$ is greater than 3 months, or if during laboratory tests non-extractable residues are formed in amounts exceeding 70% of the initial dose after 100 days with a mineralization rate of less than 5% in 100 days.
- The tests should provide sufficient data to evaluate the possibility of the accumulation of the active substance and of its transformation products in soil.
- No standardised test guideline is currently available but some general guidance is given by SETAC (1995).

7.2.2.3 Extent and nature of bound residues *[Ann. IIIA, XII.1.4.]*

- Required if the results in accordance with paragraph A7.2.1 or A7.2.2.1 above indicate that bound residues may be formed which account for more than 10% of the active substance added. Testing should be done according to SETAC procedures (SETAC 1995) with a radio labelled active substance and the nature of the bound residues should be characterised as far as possible according to, for example, Schnitzer (1982) or after an acetone/methanol-ultrasonic treatment according to OECD guideline 304A. It is recommended that testing be combined with other additional soil degradation studies (i.e. the tests in paragraph A7.2.2.1 above).

7.2.2.4 Other soil degradation studies.

- Such further studies should identify rates of degradation in different release conditions and main routes of degradation in soil in detail. Any metabolites or other degradation products that at any sampling time during the studies account for more than 10% of the active substance added should be identified and their degradation rates should be studied. For example, a soil photolysis study is required where the deposition of the active substance at the soil surface is significant (e.g. is over 10% of the substance applied) on the basis of results from paragraph A7.1.1.1.2, data set for the active substance and photolysis is considered to be a major way of degradation.
- An anaerobic soil degradation study according to e.g. SETAC (1995) is required if exposure to anaerobic conditions is likely where the active substance or material treated with it is used. The general guidance given for the corresponding data requirement for an aerobic degradation study (paragraph A7.2.1) applies here also.

7.2.3 Adsorption and mobility in soil, further studies *[Ann. IIIA, XII.1.2.-3.]*

- These further studies should provide detailed information on adsorption and desorption in soil under environmentally relevant conditions. The testing strategy on adsorption/desorption of biocidal active substances (fig. 2) and Chapter 2.5 give more specific information.

7.2.3.1 Adsorption and desorption in at least three soil types and, where relevant, the adsorption and desorption of metabolites and degradation products *[Ann. IIIA, XII.1.2.]*

- Screening tests on the adsorption/desorption of metabolites and other degradation products are required for compounds which at any sampling time during the soil degradation studies account for more than 10% of the active substance added.
- A full scale adsorption test (isotherms, mass balance, desorption) is required if a substance is used directly on, released to or disposed in/on soil in relevant amounts, unless it can be shown that it is readily biodegradable.
- A full scale adsorption test may also be appropriate to refine the PEC value in those cases where:

  -PEC/PNEC > 1 as a result from indirect exposure (e.g. spreading of contaminated sewage sludge on land) and the substance is not readily biodegradable.

  -modelling results indicate that relevant concentrations of the substance may reach groundwater (ref. Council Directive 80/778/EEC).
- The testing strategy, figure 2 and Chapter 2.5, indicate when such further tests would be necessary.
- Test according to the new EC method C.18 or corresponding OECD guideline 106. (Adsorption/desorption using a batch equilibrium method) (including number of soil samples required therein). The criteria for selection of suitable soil types should thereby address the regional conditions of expected use as well as the physico-chemical properties of the substance itself (e.g. pK_a). Although not explicitly mentioned in the guideline the handling procedure can also be applied to sediments.

7.2.3.2 Mobility *[ref. Annex IIIA –XII 1.3]*

- In most cases the mobility of a substance in soil can be estimated by means of running mathematical model calculations, processing adsorption coefficient and degradation rates of the substance (and its transformation products) but also pedological and climatic parameters.
- Where it is indicated from data on adsorption and degradation in soil that relevant amounts of a substance may reach groundwater it may become necessary to carry out an outdoor confirmatory study. For guidance on how to perform a long-term study on mobility of a substance in undisturbed soil under outdoor conditions it is referred to OECD draft guideline (Performance of Outdoor Monolith Lysimeter Studies).

7.3 Fate and Behaviour in Air

7.3.1 Phototransformation in air (estimation method) *[Ann. IIIA, VII.5]*

An estimation of the phototransformation of a substance is necessary for the risk assessment. Although for some chemicals direct photolysis may be an important breakdown process, the most effective elimination process in the troposphere for most substances results from reactions with photochemical generated species like OH radicals, ozone and nitrate radicals. In a first approach, the specific first order degradation rate constant of a substance with OH-radicals can be estimated by (Q)SAR methods. Further details can be found in EC (1996).

- A qualitative discussion of the potential formation of breakdown products should be included.
- Furthermore, an assessment of the global warming potential, the stratospheric ozone depletion potential, the potential for tropospheric ozone formation as well as the acidification potential should be submitted. Further guidance is given in EC (1996).

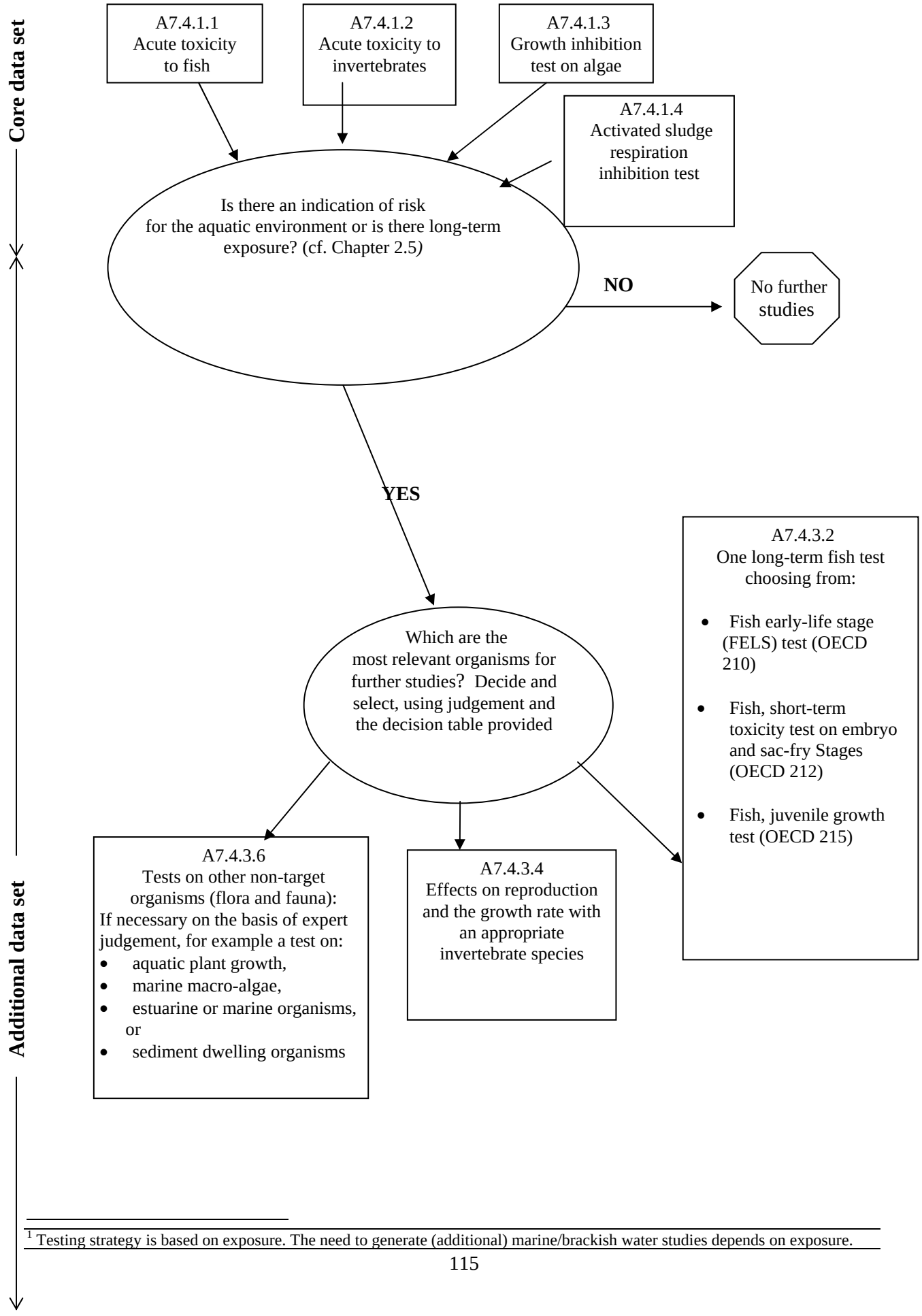
7.3.2 Fate and behaviour in air, further studies *[Ann. IIIA, XII.3]*

- If the active substance is to be used in preparations for fumigants or it causes risk to the atmospheric environment, its degradation behaviour has to be determined experimentally (e.g. according to the methods described in OECD, 1992). For the most important processes, the rate constants should first be estimated theoretically and then, after considering the relative importance of the various processes, confirmed experimentally.
- For experimental estimation the data must be submitted for a purified active substance of stated specification.
- The identification of transformation products which any sampling time account for more than 10% of the active substance added is required unless the half-life of the transformation product is less than 3 hours.
- The data submitted should be applicable to atmospheric conditions (light intensities, spectral distribution, etc.).
- SETAC (1995)

Ecotoxicological Studies

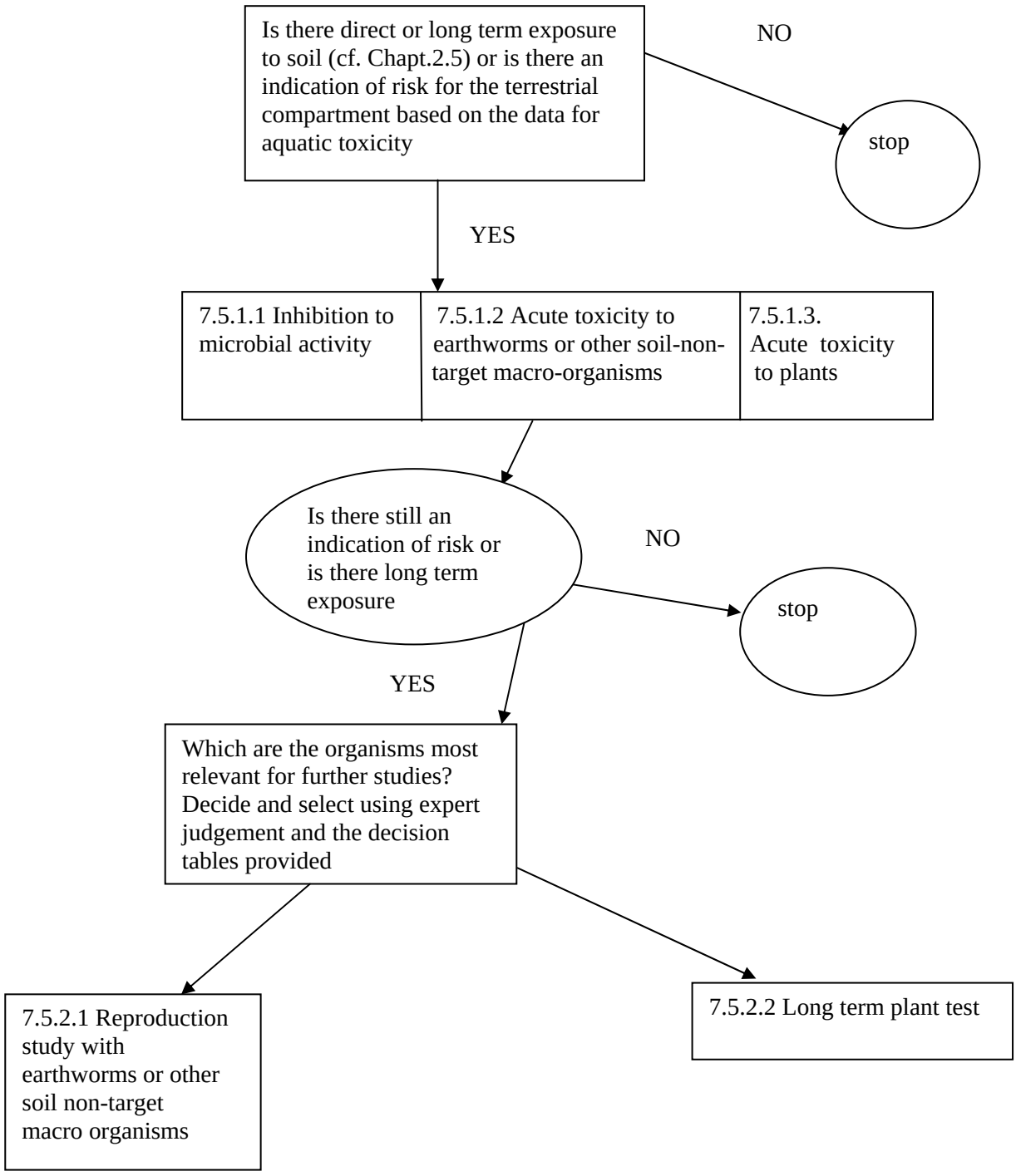
- Data reported must be supported with analytical data on concentrations of the substance being tested in the test media.
- An OECD Working Group is currently elaborating a proposal on testing strategy for endocrine disrupters. This guidance will be later amended according to the agreed testing strategy.
- The following Figures 3.1 to 4 illustrate with decision trees the testing strategy for ecotoxicological studies of an active substance.

FIG. 3.1. TESTING STRATEGY FOR AQUATIC TOXICITY STUDIES[1]



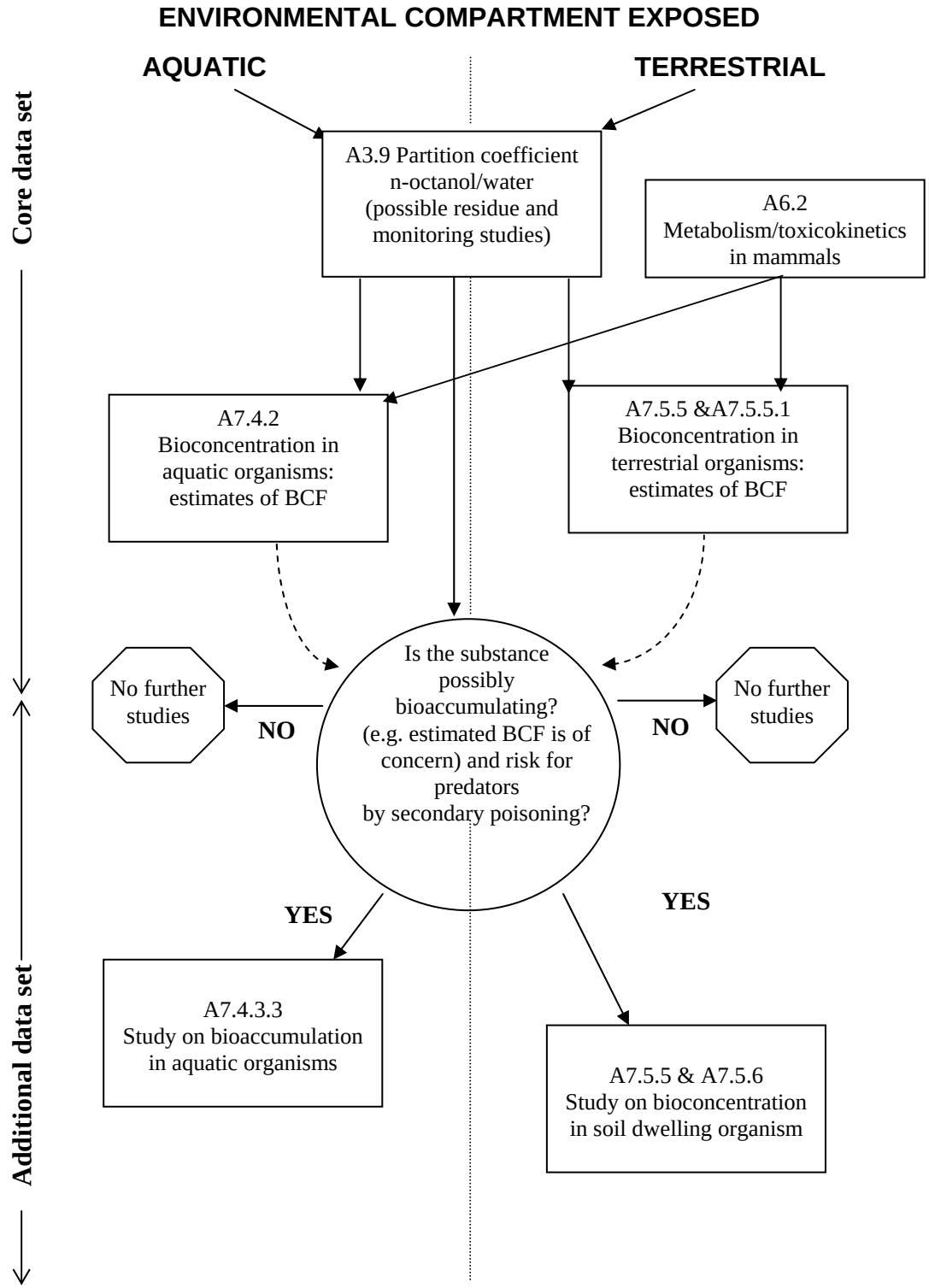
[1] Testing strategy is based on exposure. The need to generate (additional) marine/brackish water studies depends on exposure.

FIG. 3.2. TESTING STRATEGY FOR TERRESTRIAL ECOTOXICITY STUDIES[1]



[1] (7.5.4.1) Acute toxicity tests on honeybees and other beneficial arthropods and (7.5.3.1) tests on birds depend on exposure and are covered in Chapter 2.5

FIG. 4. TESTING STRATEGY FOR BIOACCUMULATION AND BIOCONCENTRATION



7.4 Effects on Aquatic Organisms

7.4.1 Aquatic toxicity, initial tests
- 7.4.1.1 Acute toxicity to fish *[Ann. IIA, VII.7.1.]*
- 7.4.1.2 Acute toxicity to invertebrates *[Ann. IIA, VII.7.21.]*
- 7.4.1.3 Growth inhibition test on algae *[Ann. IIA, VII.7.3.]*
- 7.4.1.4 Inhibition to microbiological activity *[Ann. IIA, VII.7.4 and Ann. IIIA, VII.3.]*

7.4.2 Bioconcentration *[Ann. IIA, VII.7.5.]*

7.4.3 Effects on aquatic organisms, further studies *[Ann. IIIA, XIII.2.]*

- *Criteria for further testing on fate and effects in general: If the results of the above mentioned ecotoxicological studies and the intended use(s) of an active substance indicate a danger to the environment then the tests described in this paragraph shall be required. [Ann. IIIA, VII.2.]*

Examples of such grounds for further testing are given below:

- Additional studies are required where any of the related risk assessments compiled in accordance with paragraph A10 (data set for the active substance) indicate risk.
- However, such further testing would not normally be required on aquatic species for which no short-term toxicity has been demonstrated (L (E) C50 >100 mg/l); exemptions may be substances poorly soluble in water. For these long term testing might be required.
- Detailed guidance on the proper selection of long-term aquatic toxicity tests with fish or daphnia on the basis of results from short-term tests is given in the form of a decision table in the Technical Guidance Document on the risk assessment for new and existing chemicals (EC 1996). There is a copy of this table is in Appendix 1.

7.4.3.1 Prolonged toxicity to an appropriate species of fish *[Ann. IIIA, XIII.2.1.]*

- Usually this test is not required, as it does not add information as needed in the risk assessment. The existing test guidelines are not sufficient.
- Test according to OECD guideline 204

7.4.3.2 Effects on reproduction and the growth rate on an appropriate species of fish *[Ann. IIIA, XIII.2.2.]*

- Test required according to decision table in Appendix 1.
- *Fish early-life stage (FELS) test (OECD 210)*[1] This test is considered as the most sensitive of the fish tests, covering several life stages of the fish from the newly fertilised egg, through hatch to early stages of growth. This is felt to cover most, but not all, of the sensitive points in the life-cycle, and it is the only suitable test currently available for examining the potential toxic effects of bioaccumulation, apart from the full life cycle test. It is, however, a long test typically 60 days post hatch for rainbow trout (*Oncorhynchus mykiss*), or approximately 30 days post-hatch for warm water fish, and is consequently the most expensive of those available. It should be requested where long-term fish toxicity data are required and the substance has the potential to bio-accumulate. For marine environments, the test can be performed *with Cyprinodon variegatus*
- *Fish, Short-term Toxicity test on Embryo and Sac-fry Stages (OECD 212)* This test measures the sensitive early life stages from the newly fertilised egg to the end of the sac-fry stage. It is considerably shorter, and hence cheaper, than the FELS test but is also considered to be less sensitive. It offers an alternative to the FELS test for substances with log Kow less than 4. The conditions under which the egg and sac-fry stage test can be used in place of the FELS test may be clarified following the further discussions at the OECD. For marine environments, the guideline proposes several species, e.g. *Cyprinodon variegatus.*
- *Fish, Juvenile Growth Test (OECD Guideline 215)* This test measures the growth of juvenile fish over a fixed period, and it is considered a sensitive indicator of fish toxicity. Although it is considered to be of insufficient duration to examine all the sensitive points

[1] EC methods are under preparation for OECD 212 and OECD 215.

in the fish life cycle, it provides a shorter and cheaper option to FELS test for substances of log Kow < 5.

7.4.3.3 Bio-accumulation in an aquatic organism *[Ann. IIIA, XIII.2.3.]*

7.4.3.3.1 Bio-accumulation in an appropriate species of fish

- The test is required when there is the risk for secondary poisoning. There may be also other grounds for testing, for example, when the substance has surface activity (i.e. surface tension $\leq$ 50 mN/m at a concentration of up to 1 g/l, see A3.13, data set for the active substance) or structural features indicating bio-accumulation (as in the case of e.g. pyridinium compounds).
- E.g. a test according to EC method C.13 or corresponding OECD guideline 305 (Flow-through fish test). For marine environments, the guideline proposes several species, e.g. *Cyrinodon Variegatu.s*

7.4.3.3.2 Bio-accumulation in an appropriate invertebrate species

- This test may be required for some product types, especially if a direct release to marine/brackish water occurs. A test with oysters or mussels could be performed.
- *A possible test method would be US-EPA OPPTS 850.1710*

7.4.3.4 Effects on reproduction and growth rate with an appropriate invertebrate species *[Ann. IIIA, XIII.2.4.]*

- Test required according to decision table in Appendix 1 or if chronic exposure is expected.
- Test according to OECD guideline 211. For marine environments, a long-term test with *Nitocra spinipes* can be performed (Danish standard 2209). Tests have also been performed with *Macoma baltica* (Bryant et al. 1985 as quoted in OECD DRP on Aquatic Testing Methods for Pesticides and Industrial Chemicals, 1998).
- For marine environments, a test with *Mysidopsis bahia* according to US-EPA method OPPTS 850.1350 can also be performed.

7.4.3.5 Effects on any other specific, non-target organisms (flora and fauna) believed to be at risk *[Ann. IIIA, XIII.3.4.]*

- Such testing may be required if tests on other non-target organisms are needed on the basis of intended use(s) and results from the other tests in section A7 (data set for the active substance) or a preliminary risk assessment compiled in accordance with point A10. For instance, tests on sediment dwelling organisms, aquatic plant growth (including macro-algae), accumulation and elimination in shellfish or tests on marine macro-algae or other additional tests on estuarine and marine organisms may be needed.
- The decision on the need of such further studies should be decided case-by-case after consulting with the competent national authority (see Chapter 1.2, point 4) for those product types not specifically mentioned below.

7.4.3.5.1 Effects on sediment dwelling organisms

- A test in sediment dwelling organisms is required if due to the partition to and persistence of the active substance in aquatic sediments the exposure of sediment dwelling organisms is likely and if effects on sediment dwelling invertebrates are likely. Testing might be required for certain Product types (cf. Chapter 2.5) or if the risk assessment for sediment based on the equilibrium partition method indicates a possible risk to the benthic compartment.
- The risk assessment strategy will indicate whether one or several tests are necessary cf. EC (1996)
- The selection of test species can be made on the basis of their habitat and feeding strategy, to reflect different routes of exposure among sediment organisms. In this context one could make a distinction between epibenthic deposit feeders, (Chironomids) and

endobenthic sediment ingesters (Oligochaetes). To make a distinction between sediments of different composition rather than different species, it is also recognised that the variability of sediment could be as relevant for the outcome of the test as species sensitivity.

- Organisms should be exposed to spiked sediment. The presence of spiked sediment is essential because the substances for which testing is required are very hydrophobic substances or substances that bind covalently to sediment. Long-term tests should be performed and one long-term NOEC should be sufficient at the first stage. The NOEC will be based on the measured bulk sediment concentration. If further refinement of the PNEC would be necessary, test species with different habitat and feeding strategy should be preferred to reflect the possible different ways of exposure.
- The following recommendations can be made with respect to the test species. The recommended species are complementary to each other with respect to feeding strategy and habitat.

1. -Long Term Chironomid Toxicity Test Using Spiked Sediment

- Two draft guidelines are under development within the OECD: (1) Chironomid Toxicity Test Using Spiked Sediment and (2) Chironomid Toxicity Test Using Spiked Water. Only the test using spiked sediment is considered appropriate for the purpose of testing here. This test should be considered first, when further testing is required.

2.-Long Term Oligochaete Test Using Spiked Sediment

- If further testing is needed, preference should be given to an endobenthic sediment ingester to reflect the different habitat and feeding strategy. Oligochaetes (*Tubifex* or *Lumbriculus*) would be suitable candidates. Standardised tests have been described for these species in the international literature (E.g. ASTM method E 1383).

3. -Long Term Test Using Spiked Sediment and *Gammarus* or *Hyalella*

- Finally a test with a third species could be considered to lower the assessment factor. Suitable species would be *Gammarus* or *Hyalella*. These are again epibenthic deposit feeders, but the difference with *Chironomus* is that they spent their whole life cycle on the sediment. Also for these organisms standardised tests have been described (e.g. ASTM E 1383). Instead of testing of a third species, testing with a second sediment could be considered.

7.4.3.5.2 Aquatic plant toxicity

- Test with *Lemna* spp. , e.g. according to US-EPA guideline OPPTS 850.4400 (US-EPA 1996b) An OECD guideline is in preparation. For marine/eustarine higher plants, *Zostera* spp could be tested.

7.5 Effects on Terrestrial Organisms

7.5.1 Terrestrial toxicity, initial tests

- These tests are required if the risk assessment for the terrestrial compartment, based on the equilibrium partitioning method indicates a concern for the terrestrial compartment or there is long term exposure. For some product types, these tests will be required with the core data set (cf. Chapter 2.5). It is necessary to perform all 3 tests to allow a derivation of a more realistic PNEC for the terrestrial compartment than the PNEC based on the equilibrium partitioning method.

7.5.1.1 Inhibition to microbial activity

- For example, test on inhibition of soil non-target micro-organisms according to ISO standard (ISO, 1997, 14238; or 16387 or BBA guideline Part VI, 1-1 (BBA 1990b) or two German standards of DIN 19733 (DIN, 1998). A test on effects on nitrogen

transformation or carbon mineralization in soil according to OECD guideline 216 (Soil micro-organisms, nitrogen transformation test), OECD guideline 217 (Soil micro-organisms, carbon transformation test).

7.5.1.2 Acute toxicity to earthworms or other soil non-target macro-organisms

- E.g. a test according to EC method C.8 or the corresponding OECD guideline 207 (Earthworm, acute toxicity tests).

7.5.1.3 Acute toxicity to plants

- E.g. a test according to OECD guideline 208 (Terrestrial Plants, Growth test)

7.5.2 Terrestrial tests, long-term tests

- These tests are required if the risk assessment for the terrestrial compartment, based on the results from the acute toxicity tests still indicates a concern for the terrestrial compartment. The NOEC from the test on inhibition to microbial activity can be used as long-term result

7.5.2.1 Reproduction study with earthworms or other soil non-target macro-organisms

- E.g. a test according to ISO standard 11268 (part 2, ISO 1998) or 16387 or a C*ollembola* reproduction test according to the draft ISO standard 11267 (ISO, 1996)

7.5.2.2 Long-term test with terrestrial plants[1]

7.5.3 Effects on birds

7.5.3.1 For some product types, direct exposure for birds is possible and some tests with birds would be required (cf. Chapter 2.5). Furthermore, the risk assessment for fish eating birds, using mammalian data for a first approach, might indicate concern, which would trigger tests with birds.

7.5.3.1.1 Acute oral toxicity *[Ann. IIIA, XIII.1.1.]*

- The acute oral toxicity of the active substance must be determined according to SETAC procedures (SETAC 1995). The highest dose used in tests need not exceed 2 000 mg/kg body weight.

7.5.3.1.2 Short-term toxicity *[Ann. IIIA, XIII.1.2.]*

- *An eight-day dietary study in at least one species (other than chickens)* according to OECD guideline 205.
- If the test for effects on reproduction (A7.5.3.1.3) is available this test is not necessary.

7.5.3.1.3 Effects on reproduction *[Ann. IIIA, XIII.1.3.]*

- An avian reproduction study according to, for example, OECD guideline 206.

7.5.4 Effects on honeybees

7.5.4.1 Acute toxicity to honeybees and other beneficial arthropods, for example predators *[Ann. IIIA, XIII.3.1.]*

- At least one test on bees and one on another beneficial arthropod may be generally required for insecticides, acaricides and substances in products to control other arthropods which are used outdoors (product type 18). Such tests are usually not needed for other product types.
- A test on acute oral and contact toxicity on bees should be done according OECD guideline 213 (acute oral) and/or 214 (acute contact) or to EPPO Guideline 170 and OECD guidelines.
- Possible species to be tested in addition to honeybees are, for instance, *Chrysoperla carnea* (according to IOBC methods, IOBC 1985), *Trichogramma cacoeciae* (according

[1] Test will be developed on continuous exposure of plants

to BBA guideline Part VI, 23-2.1.1, BBA 1989a), *Coccinella septempunctata* (according to BBA guideline Part VI, 23-2.1.5, BBA 1989b) or *Aleochara bilineata* (according to BBA guideline Part VI, 23-2.1.10, BBA 199X).

7.5.5 Bioconcentration, terrestrial *[Ann. IIA, VII. 7.5]*

- When released to soil the intrinsic bio-concentration potential needs to be estimated based on, at least, the physical-chemical properties (e.g. partitioning coefficient, surface-active substances, and dissociating or inorganic substances).

7.5.5.1 Bioconcentration, further studies

- A test on bioconcentration in earthworms could be required if the risk assessment for secondary poisoning would suggest a concern for predators
- Test e.g. according to ISO standard 11268 part 3 (ISO, 1999)on earthworms.

7.5.6 Effects on other terrestrial non-target organisms

- Further tests (e.g. field tests) may be required if the risk assessment based on long-term terrestrial tests show that there is still a concern for the terrestrial compartment and ("it is considered more useful to refine the PNEC than PEC").

7.5.7 Effects on mammals

7.5.7.1 For some product types, direct and/or indirect exposure for mammals is possible and some tests with mammals may be required in rare cases on the basis of concern for severe risk for the terrestrial environment. (In most cases tests with mammals will have been carried out for assessing the impact of the substance on man).

7.5.7.1.1 Acute oral toxicity (see also Chapter 2 part B section 6.1.1. and Chapter 2, 6.1)

- When planning new tests, the EC methods B.1.bis, B.1.tris (or the corresponding OECD TGs 420 and 423) and the OECD TG 425 are recommended) EC method B.1 (or OECD TG 401) should not be used. Existing results based on EC method B.1 (or OECD TG 401) are accepted.
- For substances with low acute oral toxicity a limit test at 2000 mg/kg b.w. may be sufficient.

7.5.7.1.2 Short term toxicity (see also Chapter 2, 6.3)

- Repeated oral dose toxicity (28 days)

7.5.7.1.3 Effects on reproduction (see also Chapter 2, 6.5 and 6.8)

- Chronic toxicity
- Reproductive toxicity (two generation study)

7.6 Summary and Evaluation of Ecotoxicological Effects and Fate and Behaviour in the Environment *[Ann. IIA, VII.7.8.]*, *[Ann. IIIA, XII.4.]* and *[Ann. IIIA, XIII.5.]*

- A summary of all studies and data on environmental fate and effects (both those in the core data set and additional studies, and including mammalian studies submitted for the human risk assessment in Section A6, data set for the active substance, and relevant also for the environment) should always be attached to the application. As a minimum the following information should be presented regarding every study:
  - indication of the quality assurance of the test (e.g. a performance according to GLP);
  - an overview of the results of the studies (the results from the ecotoxicological tests and fate and behaviour in the environment together with relevant additional data from Chapter 2.5 should be given here. This is the initial environmental hazard assessment.
- A reporting format is under development.
- In addition to the summary of the common core data set, clarification of the fate and effects of the active substance and its possible transformation products of concern, or substances of concern given by the further tests done according to the testing strategy should be assessed.

8 MEASURES NECESSARY TO PROTECT HUMANS, ANIMALS AND THE ENVIRONMENT

8.1 Recommended methods and precautions concerning handling, use, storage, transport or fire *[Ann. IIA, VIII. 8.1.]*

8.2 In case of fire, the nature of reaction products, combustion gases, etc. *[Ann. IIA, VIII. 8.2.]*

8.3 Emergency measures in case of an accident *[Ann. IIA, VIII. 8.3.]*

8.4. Possibility of destruction or decontamination following release in or on the following:
(a) Air
(b) Water, including drinking water
(c) Soil *[Ann. IIA, VIII.8.4.]*

8.5. Procedures for waste management of the active substance for industry or professional users *[Ann. IIA, VIII.8.5.]*

8.5.1. Possibility of re-use or recycling *[Ann. IIA, VIII.8.5.1.]*

8.5.2. Possibility of neutralisation of effects *[Ann. IIA, VIII.8.5.2.]*

8.5.3. Conditions for controlled discharge including leachate qualities on disposal *[Ann. IIA, VIII.8.5.3.]*

8.5.4. Conditions for controlled incineration *[Ann. IIA, VIII.8.5.4.]*

8.6. Observations on undesirable or unintended side-effects, for example on beneficial and other non-target organisms *[Ann. IIA, VIII.8.6.]*

8.7 Identification of any substances falling within the scope of List I or List II of the Annex to Directive 80/68/EEC on the protection of ground water against pollution caused by certain dangerous substances (OJ No L 20, 26.1.1980, p. 43). *[Ann. IIIA, VIII.1.]*

9 CLASSIFICATION AND LABELLING *[Ann. IIA, IX.]*

10 SUMMARY AND EVALUATION OF SECTIONS 2 TO 9 *[Ann. IIA, X.]*

PART B:

ADDITIONAL DATA AND GUIDANCE FOR (CHEMICAL) BIOCIDAL PRODUCTS

DOSSIER REQUIREMENTS

1 APPLICANT *[Ann. IIB, I.]*

1.1 Name and address, etc. *[Ann. IIB, I. 1.1.]*
1.2 Manufacturer/formulator of the biocidal product and the active substance(s) *[Ann. IIB, I. 1.2.]*

2 IDENTITY *[Ann. IIB, I.]*

2.1 Trade name or proposed trade name and manufacturer's development code number of the preparation, if appropriate *[Ann. IIB, I. 2.1.]*
2.2 Detailed quantitative and qualitative information on the composition of the biocidal product e.g. active substance(s), impurities, adjuvants, and inert components. *[Ann. IIB, I. 2.2.]*
2.3 Physical state and nature of the biocidal product *[Ann. IIB, I. 2.3.]*

3 PHYSICAL, CHEMICAL AND TECHNICAL PROPERTIES *[Ann. IIB, III.]*

3.1 Appearance *[Ann. IIB, III. 3.1.]*
3.2 Explosive properties *[Ann. IIB, III. 3.2.]*
3.3 Oxidising properties *[Ann. IIB, III. 3.3.]*
3.4 Flash-point and other indications of flammability or spontaneous ignition *[Ann. IIB, III. 3.4]*
3.5 Acidity/alkalinity and, if necessary, pH value (1 % in water) *[Ann. IIB, III. 3.5.]*
3.6 Relative density *[Ann. IIB, III. 3.6.]*
3.7 Storage stability - stability and shelf-life *[Ann. IIB, III. 3.7.]*
3.8 Technical characteristics of the biocidal product, e.g. wettability, persistent foaming, flowability, pourability and dustability *[Ann. IIB, III. 3.8.]*
3.9 Physical and chemical compatibility with other products including other biocidal products with which its use is to be authorised *[Ann. IIB, III. 3.9.]*
3.10 Surface tension and viscosity
- Information is usually not required for product type 5.
- EC method A.5 or the corresponding OECD guideline 115 (Surface tension) and e.g. OECD guideline 114 (Viscosity).

3.11 Particle size distribution
- Must be determined and reported for products that are supplied as powders or granules.
- Size, weight, shape (qualitative description as grit, cylindrical shape or precise dimensions of granules) should be produced for granular products, e.g. for product types 16, 18 and 19.
- E.g. OECD guideline 110.

4 METHODS OF IDENTIFICATION AND ANALYSIS

4.1 Analytical method for determining the concentration of the active substance(s) in the biocidal product *[Ann. IIB, IV.4.1.]*

4.2 In so far as not covered by paragraph A4.2 (data set for the active substance), analytical methods including recovery rates and the limits of determination for toxicologically and ecotoxicologically relevant components of the biocidal product and/or residues thereof, where relevant in or on the specified materials *[Ann. IIB, IV.4.2]*.

5 INTENDED USES AND EFFICACY

5.1 Product type and field of use envisaged *[Ann. IIB, V.5.1.]*

5.2 Method of application including description of the system used *[Ann. IIB, V.5.2.]*

5.3 Application rate and if appropriate, the final concentrations of the biocidal product and active substance in the system in which the preparation is to be used, for example cooling water, surface water, water used for heating purposes *[Ann. IIB, V.5.3.]*

5.4 Number and timing of applications, and where relevant, any particular information relating to geographical variations, climatic variations, or necessary waiting periods to protect man and animals *[Ann. IIB, V.5.4.]*

5.5 Function, for example fungicide, rodenticide, insecticide, bactericide *[Ann. IIB, V.5.5.]*

5.6 Pest organism(s) to be controlled and products, organisms or objects to be protected *[Ann. IIB, V.5.6.]*

5.7 Effects on target organisms *[Ann. IIB, V.5.7.]*

5.8 Mode of action (including time delay) in so far as not covered by paragraph A5.4 (data set for the active substance) *[Ann. IIB, V.5.8.]*

5.9 User: industrial, professional, general public (non-professional) *[Ann. IIB, V.5.9.]*

Efficacy Data

5.10 The proposed label claims for the product and efficacy data to support these claims, including any available standard protocols used, laboratory tests, or field trials, where appropriate *[Ann. IIB, V.5.10.]*

5.11 Any other known limitations on efficacy including resistance *[Ann. IIB, V.5.11.]*

6 TOXICOLOGICAL STUDIES *[Ann. IIB, VI]*

6.1 Acute toxicity *[Ann. IIB, VI. 6.1.]*

- 6.1.1 Oral *[Ann. IIB, VI. 6.1.1.]*
- 6.1.2 Dermal *[Ann. IIB, VI. 6.1.2]*
- 6.1.3 Inhalation *[Ann. IIB, VI. 6.1.3.]*
- 6.1.4 For biocidal products that are intended to be authorised for use with other biocidal products, the mixture of products, where possible, shall be tested for acute dermal toxicity and skin and eye irritation, as appropriate [*Ann. IIB, VI. 6.1.4.]*

6.2 Skin and eye irritation *[Ann. IIB, VI. 6.2.]*

6.3 Skin sensitisation *[Ann. IIB, VI. 6.3.]*

6.4 Information on dermal absorption *[Ann. IIB, VI. 6.4.]*

6.5 Available toxicological data relating to toxicologically relevant non-active substances (i.e. substances of concern) *[Ann. IIB, VI. 6.5.]*

6.6 Information related to the exposure of the biocidal product to man and the operator *[Ann. IIB, VI. 6.6]*

This guidance does not reflect annex IIIB, XI, (additional data for biocidal products) as the data requirements are sufficiently covered by the data from Annex II B VI.6.6

7 ECOTOXICOLOGICAL DATA FOR THE BIOCIDAL PRODUCT

- For relevant guidelines, see the guidance in the corresponding paragraph in Part A of Chapter 2, Chapter 2.5 or this Chapter 3.

7.1 Foreseeable routes of entry into the environment on the basis of the use envisaged *[Ann. IIB, VII.7.1.]*

- Point 7.1 is deleted here, the text partly moved the intermediate Part C.

7.2 Information on the ecotoxicology of the active substance in the product, where this cannot be extrapolated from the information on the active substance itself *[Ann. IIB, VII.7.2.]*

7.3 Available ecotoxicological information relating to ecotoxicological relevant non-active substances (i.e. substances of concern), such as information from safety data sheets *[Ann. IIB, VII.7.3.]*

Further studies on fate and behaviour in the environment *[Ann. IIIB, XII]*

7.4 Where relevant all the information required in accordance with paragraphs A7.1 and A7.2 (data set for the active substance) *[Ann. IIIB, XII.1.]*

- The corresponding information is required for the product, for instance, if the composition or the application technique of the product is suspected to influence the degradation and transformation or mobility and adsorption properties of an active substance or a substance of concern in a way that may considerably alter the conclusions of the risk characterisation.

7.5 Testing for distribution and dissipation in the following *[Ann. IIIB, XII.2.]*:

(a) Soil
(b) Water
(c) Air

- A fugacity model can be used to estimate the inherent distribution.

Test requirements B7.4 *and* B7.5 *above are applicable only to ecotoxicologically relevant components of the biocidal product* (see e.g. Chapter 4).

Further ecotoxicological studies *[Ann. IIIB, XIII]*

On occasion the following data could be required, if the data on the active substance (from Chapter 3A of this guidance) cannot give sufficient information, and there are indications of risk due to specific properties of the biocidal product. See also Chapter 2.5, part B. It must be underlined that normally this information, if relevant, is available from the active substance.

7.6 Effects on birds
7.6.1 Acute oral toxicity, if not already done according to Annex IIB, section VII

7.7 Effects on aquatic organisms
7.7.1 In case of application on, in, or near to surface waters.
7.7.1.1 Particular studies with fish and other aquatic organisms.
7.7.1.2 Residue data in fish concerning the active substance and including toxicological relevant metabolites.

- Possible monitoring data or results of residues studies including toxicologically relevant metabolites, if these cause harmful effects on human health.

7.7.1.3 The studies referred to in Annex IIIA, section XIII parts 2.1, 2.2, 2.3, and 2.4 may be required for relevant component of the biocidal product.
7.7.2 If the biocidal product is to be sprayed near to surface waters then an overspray study may be required to assess risks to aquatic organisms under field conditions.

7.8 Effects on other non-target organisms
7.8.1 Toxicity to terrestrial vertebrates other than birds.
7.8.2 Acute toxicity to honeybees
7.8.3 Effects on other beneficial arthropods other than bees
7.8.4 Effects on Earthworms and other soil non-target macro-organisms, believed to be at risk

7.8.5 Effects on soil non-target micro-organisms

7.8.6 Effect on any other specific, non-target organisms (flora and fauna) believed to be at risk

7.8.7 If the biocidal product is in the form of bait or granules

7.8.7.1 Supervised trials to assess risks to non-target organisms under filed conditions.

7.8.7.2 Studies on acceptance by ingestion of the biocidal product by any non-target organisms thought to be at risk.

- Required if the biocidal product is in form of baits, granules, or treated seeds.
- In order to assess risks to predators, residue data in target organisms concerning the active substance and including toxicologically relevant metabolites would be needed.

(cf. Chapter 2, part B, section 5.11)

7.9 Summary and evaluation of ecotoxicological data *[Ann. IIIB, XIII.4.]*

- Risk assessment (the summary and evaluation) may be combined either with the corresponding summary concerning the active substance or with the overall summary concerning the biocidal product.
- Evaluation on the basis of the available data, of if and how, for example, the composition or the application technique of the product affects the fate and effects of the active substance(s) or possible substance(s) of concern.

8 MEASURES TO BE ADOPTED TO PROTECT MAN, ANIMALS AND THE ENVIRONMENT

8.1 Recommended methods and precautions concerning handling, use, storage, transport or fire *[Ann. IIB, VIII.8.1.]*

8.2 Specific treatment in case of an accident, for example, first aid measures, antidotes, medical treatment if available; emergency measures to protect the environment; insofar as not covered by the paragraph A8.3 (data set for the active substance) *[Ann. IIB, VIII.8.2.]*

8.3 Procedures, if any, for cleaning application equipment *[Ann. IIB, VIII.8.3.]*

8.4 Identity of relevant combustion products in cases of fire *[Ann. IIB, VIII.8.4.]*

8.5 Procedures for waste management of the biocidal product and its packaging for industry, professional users and the general public (non-professional users), for example possibility of re-use or recycling, neutralisation, conditions for controlled discharge, and incineration *[Ann. IIB, VIII.8.5.]*

8.6 The possibility of destruction or decontamination following release in or on the following:
(a) Air,
(b) Water, including drinking water, and
(c) Soil *[Ann. IIB, VIII.8.6.]*

8.7 Observations on undesirable or unintended side-effects, for example, on beneficial and other non-target organisms *[Ann. IIB, VIII.8.7.]*

8.8 Specify any repellents or poison control measures included in preparations that are present to prevent action against non-target organisms *[Ann. IIB, VIII.8.8.]*

9 CLASSIFICATION, PACKAGING AND LABELLING *[Ann. IIB, IX.]*

10 SUMMARY AND EVALUATION OF SECTIONS 2 TO 9 *[Ann. IIB, X.]*

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* Council Directive 89/109/EEC of 21 December 1989a on the approximation of the laws of the Member States relating to materials and articles intended to come into contact with foodstuffs.

[* Commission Directive 95/36/EC of 14 July 1995 amending Council Directive 91/414/EEC concerning the placing of plant protection products on the market.]

[* Commission Directive 96/12/EC of 8 March 1996 amending Council Directive 91/414/EEC concerning the placing of plant protection products on the market.]

[* Council Directive 96/23/EC of 29 April 1996 on measures to monitor certain substances and residues thereof in live animals and animal products and repealing Directives 85/358/EEC and Decisions 89/187/EEC and 91/664/EEC.]

APPENDIX 1

DECISION TABLE FOR ADDITIONAL AQUATIC TOXICITY TESTING

This decision table is to be used to select appropriate additional aquatic toxicity tests in order to refine the risk assessment when the initial risk assessments compiled in accordance with paragraph A10 (data set for the active substance) indicates risk when calculated on the basis of the lowest LC_{50} or EC/IC_{50} value in the aquatic toxicity tests of the core data set (full base set, FBS, which includes LC_{50} or EC/IC_{50} values for fish Daphnia and algae) and using an assessment factor.

Variation in base-set data		**Further testing**	**Data available for assessment**	**Assessment factor** [(a)]
No significant difference between the $L(E)C_{50}$ values of fish, Daphnia or algae	A1	Long-term fish test + long-term Daphnia test + determination of NOEC algae	FBS + algae + Daphnia + fish	10
Fish LC_{50} more than 10 times lower than $L(E)C_{50}$ of Daphnia and algae	A2	Long-term fish test + determination of NOEC algae If S/L [(b)] ratio for fish > 20: long-term Daphnia test [(c)]	FBS + algae + fish FBS + algae + fish + Daphnia	50 10
Daphnia $L(E)C_{50}$ more than 10 times lower than $L(E)C_{50}$ of fish and algae	A3	Long-term Daphnia test + determination of NOEC algae If S/L [(b)] ratio for Daphnia > 20: long-term fish test [(c)]	FBS + algae + Daphnia FBS + algae + fish + Daphnia	50 10
Algae $L(E)C_{50}$ more than 10 times lower than $L(E)C_{50}$ of fish and Daphnia	A4	Test on other algae species + long-term fish/Daphnia test [(d)]	FBS + two algae [(d)] +fish/Daphnia	10[(d)]
Fish LC_{50} more than 10 times higher than $L(E)C_{50}$ of Daphnia and algae	A5	Long-term Daphnia test + determination of NOEC algae If S/L [(b)] ratio for Daphnia > 20: long-term fish test [(c)]	FBS + algae + Daphnia FBS + algae + fish + Daphnia	50 10
Daphnia $L(E)C_{50}$ more than 10 times higher than $L(E)C_{50}$ of fish and algae	A6	Long-term fish test + determination of NOEC algae If S/L [(b)] ratio for fish > 20: long-term Daphnia test [(c)]	FBS + algae + fish FBS + algae + fish + Daphnia	50 10
Algae $L(E)C_{50}$ more than 10 times higher than $L(E)C_{50}$ of fish and Daphnia	A7	Long-term Daphnia test + long-term fish test + determination of NOEC algae	FBS + algae + fish + Daphnia	10

NOTES:

(a) AF = the assessment factor must be applied to the lowest NOEC available at this stage, including the NOEC from the algae test.

(b) S/L refers to the short-term to long-term ratio, i.e. the ratio between the $L(E)C_{50}$ from a short-term test and the NOEC from a long-term-test.

(c) Generally testing of a third species will be unnecessary since the toxicity results from the first species should be protective. However, this cannot be a fixed rule given the toxicity variations within taxonomic groups as well as between them. Thus if a short-term $L(E)C_{50}$: long-term NOEC ratio > 20 is found for the species tested, or from the algae study, then the further testing of a third species might be necessary. The use of long-term fish or Daphnia QSARs could help in deciding which species needs to be tested (see Chapter 4 "Use of QSARs" in the EC, 1996[1]). It is considered that such a ratio may be indicative of an abnormal level of toxicity or of a specific mode of action, and thus the acquisition of additional evidence is justified in order to improve confidence in the calculated $PNEC_{water}$. Other factors such as the shape of the toxicity time curve and the presence of sub-lethal effects in the short-term toxicity study for the second species may also be considered. An assessment factor of 10 may be applied to the lowest of the three NOECs. Before a toxicity study on a third species is requested, due consideration should be given as to whether the resultant NOEC will lead to a further revision of the $PNEC_{water}$.

(d) This table is based on the presumption that an NOEC for algae is available at the base set. If this is not the case, an assessment factor of 50 should be used.

[1] EC, 1996. Technical Guidance Document in support of Commission Directive 93/67/EEC on risk assessment for new notified substances and Commission Regulation (EC) No 1488/94 on risk assessment for existing substances. Part II. Environmental risk assessment. European Commission. ISBN 92-827-8012-0.

APPENDIX 2

DECISION TABLE FOR ADDITIONAL TERRESTRIAL TOXICITY TESTING

This decision table is to be used to select appropriate additional terrestrial toxicity tests in order to refine the risk assessment when the initial risk assessment compiled in accordance with paragraph A10 (data set for the active substance) indicates risk when calculated on the basis of the lowest LC50 or EC50 value in the acute toxicity tests (which includes LC50 or EC50 values for micro-organisms, earthworms and plants) and using an assessment factor.

Variation in acute toxicity tests	**Further testing**	**Data available for assessment**	**Assessment factor [a]**
No significant difference between the L(E)C50 values of micro-organisms, earthworm or plant	Long-term earthworm test + long-term plant test + determination of NOEC micro-organisms	Acute tests + micro-organisms + earthworm + plant	10
Earthworm LC50 more than 10 times lower than EC50 of plant and micro-organisms	Long-term earthworm test + determination of NOEC micro-organisms If S/L[b] ratio for earthworms > 20: long-term plant test [c]	Acute tests + micro-organisms + earthworm Acute tests + micro-organisms + earthworm + plant	50 10
Plant EC50 more than 10 times lower than LC50 of earthworm and micro-organisms	Long-term plant test + determination of NOEC micro-organisms If S/L[b] ratio for plants > 20: long-term earthworm test [c]	Acute tests + micro-organisms + plant Acute tests + micro-organisms + earthworm + plant	50 10
Earthworm LC50 more than 10 times higher than EC50 of plant and micro-organisms	Long-term plant test + determination of NOEC micro-organisms If S/L[b] ratio for plants > 20: long-term earthworm test [c]	Acute tests + micro-organisms + plant Acute tests + micro-organisms + earthworm + plant	50 10
Plant EC50 more than 10 times higher than L(E)C50 of earthworm and micro-organisms	Long-term earthworm test + determination of NOEC micro-organisms If S/L[b] ratio for earthworms > 20: long-term plant test [c]	Acute tests + micro-organisms + earthworm Acute tests + micro-organisms + earthworm + plant	50 10
Micro-organisms EC50 more than 10 times higher than L(E)C50 of earthworm and plant	Long-term earthworm test + long-term plant test + determination of NOEC micro-organisms	Acute tests + micro-organisms + earthworm + plant	10

NOTES:

(a) AF = the assessment factor must be applied to the lowest NOEC available at this stage including the NOEC from the test with micro-organisms.

(b) S/L refers to the short-term to long-term ratio, i.e. the ratio between the L(E)C50 from a short-term test and the NOEC from a long-term test.

(c) Generally testing of a third species will be unnecessary since the toxicity results from the first species should be protective. However this cannot be a fixed rule given the toxicity variations

within taxonomic groups as well as between them. Thus if a short-term L(E)C50 : long-term NOEC ratio > 20 is found for the species tested, or from the study with micro-organisms, then the further testing of a third study might be necessary. It is considered that such a ratio may be indicative of an abnormal level of toxicity or of a specific mode of action, and thus the acquisition additional evidence is justified in order to improve confidence in the calculated $PNEC_{soil}$. Other factors, such as the shape of the toxicity time curve and the presence of sub-lethal effects in the short-term toxicity study for the second species may also be considered. An assessment factor of 10 may be applied to the lowest of the two NOECs. Before a toxicity study on a third species is requested, due consideration should be given as to whether the resultant NOEC will lead to a further revision of the $PNEC_{soil}$.

CHAPTER 4

DATA REQUIREMENTS FOR SUBSTANCES OF CONCERN

4.1 INTRODUCTION

This guidance document gives detailed guidance on the identification of the substances of concern and on the data requirements for them in order to provide a proper risk assessment of a biocidal product.

The basic principle is that sufficient information on all substances in the biocidal products has to be submitted in order to be able to assess properly the risks caused by the product and to conclude whether conditions for issue of an authorisation laid down in Article 5(1) are fulfilled. In the risk assessment of a biocidal product, not only active substances are to be taken into consideration, but also all other toxicologically or ecotoxicologically relevant substances on the basis of their physico-chemical, toxicological or ecotoxicological properties.

The first step is to identify those substances other than active substances, which may cause concern. Basic toxicological and ecotoxicological information on these substances is then required but no actual studies have to be submitted if not deemed necessary by the applicant or competent authorities. On the basis of the information available, the risks of substances of concern are characterised by the applicant. When necessary, a more comprehensive risk assessment has to be done on those substances which show specific signs of concern and thus more data, possibly even including studies, may be deemed necessary. Whilst compiling the data package for an application, the applicant should evaluate, in accordance with the agreed principles of risk assessment, the need for further data or testing of the particular substance(s) of concern.

The different steps of the assessment of substances of concern may be described as following:

1) The applicant compiles the basic information on all components in the product (data on identity, classification and concentration in the product)
2) The applicant identifies the substances of concern
3) The applicant compiles available data on identified substances of concern according to the requirements set in this Chapter
4) The applicant does an initial risk characterisation and assesses the need for additional data
5) The applicant submits the data with the application to the competent authority
6) The competent authority does a preliminary risk characterisation and assesses the completeness of the data
7) More data may be required by the competent authority if the risk characterisation shows signs of specific concern
8) Risk assessment is made by the competent authority on the substance of specific concern on the basis of data submitted by the applicant.

These notes for guidance cover only steps 1 - 3. The guidance on risk assessment given in Part II and Part III of the Technical Notes should be also applied to substances of concern. Guidance on criteria relating to the need for additional data or further testing and on testing strategy of active substances given in Chapters 2 and 3 applies also in many cases to the substances of concern. However, expert judgement is usually required when deciding whether any additional data on substances of concern is needed (see Chapter 1.2, point 4).

4.2 WHAT ARE SUBSTANCES OF CONCERN?

The Biocidal Products Directive (98/8/EC) has the following definition for a substance of concern in Article 2(1)(e):

> *Substance of concern: Any substance, **other than the active substance,** which has an inherent capacity to cause an adverse effect on humans, animals or the environment and is present or is produced in a biocidal product in sufficient concentration to create such an effect.*
>
> *Such a substance, unless there are other grounds for concern, would be normally a substance classified as dangerous according to Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to classification, packaging and labelling of dangerous substances, and present in the biocidal product at a concentration leading the product to be regarded as dangerous within the meaning of Article 3 of Council Directive 88/379/EEC of 7 June 1988 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous substances preparations.* (Amended by Directive 99/45/EC)

The substance is regarded as a substance of concern if:

1. the substance is included in Annex I of Council Directive 67/548/EEC, i.e. it is classified as dangerous **and** its concentration in the product exceeds the classification limit set in Council Directive 88/379/EEC, as amended by Directive 1999/45/EC, for a particular dangerous property **or** the other classification limit indicated for the substance in a preparation in Annex I of Council Directive 67/548/EEC **or** causes that the overall sum of the concentrations of dangerous substances in the product exceeds the limit for classification of the preparation set in Council Directive 88/379/EEC, as amended by Directive 1999/45/EC, for a particular dangerous property. Concentration limits set for preparations concerning classification as dangerous to the environment are given Directive 88/379/EEC as amended by Directive 1999/45/EC;

2. the substance is not (yet) included in Annex I of Council Directive 67/548/EEC (or it is included in Annex I of Council Directive 67/548/EEC but not evaluated for this particular dangerous property, e.g. dangerous to the environment) and it is assessed to fulfil the criteria for a dangerous substance specified in Council Directive 67/548/EEC **and** its concentration in the product exceeds the classification limit set in Council Directive 88/379/EEC, as amended by Directive 1999/45/EC, for a particular dangerous property **or** causes that the overall sum of the concentrations of dangerous substances in the product exceeds the limit for classification of the preparation set in Council Directive 88/379/EEC, as amended by Directive 1999/45/EC, for a particular dangerous property. Concentration limits set for preparations concerning classification as dangerous are given in Directive 88/379/EEC and by Directive 1999/45/EC;

3. there are other grounds for concern, for example:
   - serious doubts on dangerous properties not covered by the classification criteria (e.g. toxicity to terrestrial organisms or endocrine effects);
   - a substance in a biocidal product is present below the concentration limit for classification set in Council Directive 88/379/EEC (as amended by Directive 99/45/EC) but the substance is classified in Annex I of Council Directive 67/548/EEC or otherwise known to have non-acceptable characteristics (carcinogenicity, mutagenicity, toxicity for reproduction or sensitising properties)

or the route of exposure is especially relevant for biocides or the route of exposure can increase the concentration of Council the substance following application;
- serious doubts on other unacceptable effects specified in the Directive, Article 5(1) (e.g. unacceptable effects on indoor or workplace air quality or by worker dermal exposure, resistance, unnecessary pain for vertebrates);
- information on dangerous properties of structural relatives of the substance; or
- information on the ability of the substance to form dangerous substances e.g. in reaction with substances present in the environment.

It is always primarily the applicant who must identify all possible substances of concern in the product and submit the basic data for risk characterisation (Art 8(6) in Directive). The competent authority shall ask for more information or further testing if the data submitted is not satisfactory or if additional information or testing is necessary to evaluate the risks of the biocidal product.

4.3 DATA REQUIREMENTS FOR SUBSTANCES OF CONCERN

A basic data set is required for the preliminary risk characterisation of the identified substances of concern. It should be noted that study reports need not be submitted, but all information submitted must include a detailed description of the references and of the actual source of data. Relevant sources include e.g.: databases, scientific publications, handbooks and summaries collected and edited by scientific organisations or authorities. Also data included in the Safety Data Sheet of the substance can be used, however, the original reference should be given as well. The general rules on data protection laid down in the Biocidal Products Directive have to be respected; i.e. a letter of access may in some cases be required.

In some cases there may be only a limited amount of data available. The applicant, however, is responsible to search for data from all sources which he or she may reasonably be expected to have access to. Data and information additional to that indicated below may be required if a preliminary risk characterisation indicates a need for such. No new tests on substances of concern have to be made, unless so required by the competent authority due to a specific concern.
Where appropriate, the corresponding guidance given in Chapters 2 and 3 on the information to be provided on the active substance or the biocidal product applies here also. The number given in parenthesis refers to the detailed data requirements in Chapter 2 or 3. For polymers, the corresponding data which is relevant according to the Commission Directive 93/105/EC, laying down Annex VII D containing information required for the technical dossier referred to in Article 12 of the seventh amendment of Council Directive 67/548/EEC, should be submitted. The general guidance given in Chapter 1 on, for example, acceptable grounds for not submitting data is also applicable to substances of concern. If a preliminary quantitative or qualitative risk assessment compiled in accordance with Chapter 2, paragraph B10 (data set for the biocidal product) on the basis of the available test results and other data, shows the indication of any risk related to a substance of concern, there may be a need for further testing in accordance with guidance of this Chapter and that applicable from Chapters 2 and 3. In particular, it should be considered if it would be more appropriate to do a test with the biocidal product, instead of a substance of concern, in accordance with the guidance in Chapters 2 and 3, Part B, data set for the biocidal product, especially if there are two or more substances of concern in the product.
All available data on the identified substances of concern must be submitted; if the applicant believes that there is reasons for concern for a certain end-point, at least the Annex VII A data (of directive 92/32/EEC) for that end-point is needed.

1 IDENTITY OF THE SUBSTANCE OF CONCERN

- as required in Chapter 2, Part B 2.2 (e.g. chemical name, CAS and EC numbers)
- molecular mass

2 DATA ON PHYSICAL AND CHEMICAL PROPERTIES

- Melting and/or boiling points (Chapter 2, Part A 3.1)
- Volatility (Chapter 2, Part A 3.2)

    - Vapour pressure
    - Henry's law constant
- Solubility in water (Chapter 2, Part A 3.5)
- Partition coefficient n-octanol/water, including if available effect of pH (5 to 9) and temperature (Chapter 2, Part A 3.9)
- Thermal stability and if possible, identity of the thermal breakdown compounds (Chapter 2, Part A 3.10)
- Other relevant data on physical and chemical properties (a full description on physical and chemical properties in tabular form, e.g. reactive, flammable, explosive and oxidising hazard.)

3 TOXICOLOGICAL AND METABOLIC DATA

A short summary evaluation of the basic toxicological properties of the substance of concern (in accordance with the guidance given in Chapter 2, Part B 6.5):

- Information on acute toxicity
    - Information on acute toxicity in oral route should always be given. If exposure in dermal and/or inhalation route is expected, data on acute toxicity in those routes should be given. (See the criteria in the Chapter 2 for testing of inhalation and dermal toxicity).
- Information on skin sensitisation in animal and/or human skin
- Information on dermal absorption should be submitted in cases where the dermal exposure to the product is relevant.
- Information on mutagenicity
- Information on short term repeated dose toxicity,
- Information on long term repeated dose toxicity including carcinogenicity, if available
- Information on reproduction toxicity, if available
- Human medical data and epidemiological data should be included, if available (e.g. information on signs on acute poisonings, antidotes.)
- Other relevant toxicity data (e.g. toxicokinetics, neurotoxicity), if available

4 ECOTOXICOLOGICAL DATA

It has been proposed that the acceptability of providing (Q) SAR estimates for some data gaps instead of test results should be discussed. E.g. for substances for which no data are available at all the aquatic effects should be estimated with the help of (Q) SAR. See Chapter 1 for further information.

- Foreseeable routes of entry into the environment on the basis of the use envisaged (in accordance with the guidance given in Chapter 2, Part B 7.1)
    - Information on how the substance of concern can be released into the environment due to handling it or from a waste water treatment plant, etc., to which compartment of the environment (soil, sediment, water, air), and an estimation on how large the amounts released are.
    - A description of sources of environmental exposure: for example production, distribution, storage, mixing and loading, uses and disposal or recovery. An indication of the measured or estimated extent of release: frequency and intensity (e.g. dose and duration).
    - A definition of aquatic recipients in detail: for instance surface water, ground water, estuaries or a marine environment. An assessment of possible ways of transformation and distribution.
    - Possible information on representative measured concentrations or monitoring data, for example, in waste water or in the environment or on concentrations based on model calculations, using e.g. the EUSES model (see Chapters 2 and 3).

- Available ecotoxicological information such as information from safety data sheets (in accordance with the guidance given in Chapter 3, Part B 7.3) on the following:
    - Abiotic degradation (see Chapter 2, Part A 7.1.1.1)
        - Hydrolysis as a function of pH
        - Phototransformation in water
    - Biotic degradation (see Chapter 2, Part A 7.1.1.2)
        - Ready biodegradability
    - Adsorption/desorption (see Chapter 2, Part A 7.1.3)
    - Aquatic toxicity, basic information (see Chapter 2, Part A 7.4.1)
        - Acute toxicity to fish
        - Acute toxicity to Daphnia magna
        - Growth inhibition test on algae
        - Inhibition of microbiological activity
    - Terrestrial toxicity, basic information
        - Inhibition of microbiological activity (see Chapter 2, Part A 7.5.1)
    - Bioconcentration (see Chapter 2, Part A 7.5.2).

4.4 REFERENCES

1. Commission Directive 93/105/EC of 25 November 1993 laying down Annex VII D, containing information required for the technical dossier referred to in Article 12 of the seventh amendment of Council Directive 67/548/EEC. OJ No L294 p. 21, 1993/11/30.
2. Council Directive 88/379/EEC on the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous substances preparations.
3. Council Directive 1999/45/EC on the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous substances preparations.
4. Council Directive 92/32/EEC of 30 April 1992 amending for the seventh time Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substance

CHAPTER 5

DATA REQUIREMENTS FOR ACTIVE SUBSTANCES AND BIOCIDAL PRODUCTS IN REGARD TO SIMPLIFIED PROCEDURES

5.1 INTRODUCTION

In addition to the normal two-step authorisation procedure for biocidal products, the Biocidal Products Directive defines three types of simplified procedures:

1) authorisation of frame-formulations;
2) registration of low-risk biocidal products, and
3) listing of basic substances.

The data requirements for the products or active substances under these procedures are in part significantly less than for biocidal products in general. This guidance document summarises and clarifies the data requirements in regard to these simplified procedures.

5.2 DATA REQUIREMENTS FOR AUTHORISATION OF FRAME-FORMULATIONS

5.2.1 DEFINITION AND PROCEDURE FOR FRAME-FORMULATIONS

In the Directive frame-formulations are defined in Article 2(1)(j):

> *Specifications for a group of biocidal products having the same use and user type.*
>
> *This group of products must contain the same active substances of the same specifications, and their compositions must present only variations from a previously authorised biocidal product which do not affect the level of risk associated with them and their efficacy.*
>
> *In this context, a variation is the allowance of a reduction in the percentage of the active substance and/or an alteration in percentage composition of one or more non-active substances and/or the replacement of one or more pigments, dyes, perfumes by others presenting the same or a lower risk, and which do not decrease its efficacy.*

In Article 3(4) the procedure for frame-formulations is laid down:

> *Member States shall, on request, or may, on their own initiative, and where relevant, establish a frame-formulation and communicate it to the applicant when issuing an authorisation for a particular biocidal product.*

5.2.2 DATA REQUIREMENTS

Under the concept frame-formulation it is possible to authorise products which presents only minor variations from a previously authorised biocidal product (“mother product”) or a group of products which complies with the conditions laid down in the article 2(1)(j).

The variations between products may not affect the level of risk associated with them and their efficacy. The active substances in frame-formulations must always be included in the Annex I of this Directive. The studies on products must be conducted using a “mother product” which is representative of the whole group of frame-formulations. Data for the frame-formulations is needed only for the assessment of the acceptable similarity of the product and its intended use with those of the previously authorised "mother product".

The dossier for a product to be authorised as a frame-formulation shall include the information listed below. The detailed guidance given in the Chapter 2 (Common core data set) applies to the relevant requirements of frame-formulations. The numbers given in the brackets refer to Chapter 2.

1 Applicant (see Chapter 2, Part B 1 for detailed guidance)

- 1.1 Name and address
- 1.2 Manufacturer/formulator of the biocidal product and the active substances (names and addresses including location of manufacturer of the active substance)
- 1.3 A letter of access to the data of a previously authorised frame-formulation and active substances included.

2 Identity of the biocidal product (See Chapter 2, Part B 2 for detailed guidance)

- 2.1 Trade name
- 2.2 Full composition of the biocidal product
  - This must always be specified both for the “mother product” and the frame-formulation. See Chapter 2, B2.2.
  - This should include the detailed specification of the active substance(s) (see Chapter 2, Part A 2 for guidance).

3 Intended uses

- 3.1 Product type and field of use (see Chapter 2, Part B 5.1)
- 3.2 Category of users (see Chapter 2, Part B 5.9)
- 3.3 Method of application (see Chapter 2, Part B 5.2)

4 Efficacy data

- Data are required to show that the efficacy of the frame-formulation meets the label claim of the previously authorised "mother product" (see Chapters 2 and 3, Part B 5.10). Where the quantity of active substances are same in the frame-formulation and the “mother product”, only a simple justification is needed. Where there are variations in quantities of active substances or the changes in proportions of other compounds may have an effect on efficacy, the need for efficacy testing should be decided on a case-by-case basis (see Chapter 1.2, point 4). An efficacy study is usually needed to demonstrate that the efficacy of the frame-formulation is sufficient, if the concentration of an active substance is lower in a frame-formulation than in the “mother product”.

5 A risk characterisation summary with an initial assessment of similarity of risks with the "mother product". A format is under development.

6 Classification, packaging and labelling, including a draft label, according to Article 20 (see Chapter 2, Part B 9)

7 Safety data sheet, when relevant.

8 Information on which components have been varied and the degree of variation.

5.3 DATA REQUIREMENTS FOR REGISTRATION OF LOW-RISK BIOCIDAL PRODUCTS

5.3.1 DEFINITIONS AND PROCEDURE

In the Directive a low-risk biocidal product is defined in Article 2(1)(b):

A biocidal product which contains as active substance(s) only one or more of those listed in Annex IA and which does not contain any substance(s) of concern. Under the conditions of use, the biocidal product shall pose only a low risk to humans, animals and the environment.

The procedure for registration of low-risk biocidal products is laid down in Article 3(2):

Member States shall, subject to registration, allow the placing on the market and use of a low-risk biocidal product, provided that a dossier in accordance with Article 8(3) has been submitted and verified by the competent authorities. Unless otherwise specified, all provisions relating to authorisation under this Directive shall also apply to registration.

The procedure for registration is, according to Article 2(1)(k) *an administrative act by which the competent authority of a Member State, following an application submitted by an applicant, after verification that the dossier meets the relevant requirements of this Directive, allows the placing on the market of a low-risk biocidal product in its territory or in a part thereof.*

5.3.2 DATA REQUIREMENTS

The prerequisite for a registration of a low-risk biocidal product is that all the active substances contained therein are listed in Annex IA ("List of active substances with requirements agreed at community level for inclusion in low-risk biocidal products") and the possible conditions laid down in that Annex are fulfilled. For the first inclusion of an active substance into Annex IA, a complete dossier for the active substance and a complete dossier for a relevant biocidal product must be submitted. The active substances can only be added in Annex IA after a full risk assessment. This means that the data requirements for the inclusion of a substance to Annex IA are essentially the same as for other active substances. In addition, according to the Article 10(1) of the Directive the applicant must always provide data to demonstrate that an active substance is not carcinogenic, mutagenic, toxic for reproduction or sensitising, or is not bioaccumulative and readily degrades, according to classification in agreement with the provisions of Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to classification, packaging and labelling of dangerous substances.

The data requirements for a low-risk biocidal product are presented in Article 8(3). The detailed guidance given in Chapter 2 (Common core data set for biocidal products) also applies to the corresponding requirements of low-risk biocidal products. The numbers given in the brackets refer to Chapter 2.

5.4 DATA REQUIREMENTS FOR BASIC SUBSTANCES

In Article 2(1)(c) of the Biocidal Products Directive the basic substance is defined:

A substance which is listed in Annex IB, whose major use is non-pesticidal but which has some minor use as a biocide either directly or in a product consisting of the substance and a simple diluent which itself is not a substance of concern and which is not directly marketed for this biocidal use.

According to Article 3(2)(ii) *Member States shall allow the placing on the market and use of basic substances for biocidal purposes once they have been entered in Annex IB.*

Examples on possible basic substances are given in the Directive. A substance may be listed in Annex IB (List of basic substances with requirements agreed at community level) only after a full risk assessment. This means that the data requirements for the inclusion of a substance to Annex IB are essentially the same as for all other active substances (see Chapter 2, Part A). The major difference is that usually there is no actual biocidal product based on the basic substances but the substance is usually marketed and used for all purposes as such or with a simple diluent.

No data or only limited information on products based on basic substances is required. In cases, where the substance may be used in a product with a simple diluent, data on the compositions (see Chapter 2, Part B 2) of the possible products and the identity of the diluents used is required. The data on diluents must be sufficient for the preliminary risk characterisation i.e. for concluding that the diluent is not a substance of concern. For the basic substance with a diluent the relevant information on efficacy (see Chapter 2, Part B, 5.10) is also required. Usually only a simple justification on efficacy is sufficient. A short description of the non-biocidal uses of the basic substance and an estimation on the tonnage to be used for these purposes should be included in order to determine its minor use as a biocide. Classification and labelling should be given in accordance with Article 9(b) of the Directive 98/8/EC.

Many basic substances may differ from most biocidal active substances e.g. due to their physical and chemical properties. Also the data available on basic substances may differ from that on other active substances. There may be long practical experience on the use of basic substances and possibly also a large amounts of data in the general literature on the properties of the chemical but a lack of studies conducted according to standardised test guidelines. This makes it necessary to use careful expert judgement when compiling the documentation and assessing the acceptability of data (for expert judgement, see Chapter 1.2, point 4).

In certain cases, the risks of a basic substance may already be evaluated under e.g. the regime of existing chemicals (Regulation (EEC) No 793/93). The dossier and scientifically acceptable risk assessment reports can be used directly without any supporting data in cases when the biocidal use of the substance has been included in the original risk assessment and the applicant has a valid letter of access for the dossier.

CHAPTER 6

GUIDANCE ON GOOD LABORATORY PRACTICE

6.1 INTRODUCTION

This document gives guidance on for the acceptability of studies and data submitted in accordance with the requirements of Annexes IIA, IIB, IIIA and IIIB of Directive 98/8/EC of the European Parliament and of the Council, concerning the placing of biocidal products on the market with regard to the principles of good laboratory practice (GLP).

6.2 LEGAL PROVISIONS

As a general principle it is provided in the Biocidal Products Directive in the article 8(8) that, *where appropriate, tests must be conducted in accordance with the provisions laid down in Council Directive 87/18/EEC of 18 December 1986 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of Good Laboratory Practice and the verifications of their applications for tests on* chemicals (and adapted to technical progress by 1999/11/EC). According to article 10(3) of the Biocidal Products Directive *the inclusion in Annex I, IA or IB of an active substance shall be restricted to those product types in Annex V for which relevant data have been submitted in accordance with article 8*. Member States shall bring into force this Directive not later than 24 months after its entry into force.

Council Directive 87/18/EC (OJ No L 15, 17.1.1987, p.29.) (adapted to technical progress by 1999/11/EC) provides in article 1(1) that Member States shall take all measures necessary to ensure that laboratories carrying out tests on chemicals, in accordance with Council Directive 67/548/EEC, comply with the principles of good laboratory practice. According to article 1(2) this applies also where other Community provisions provide for the application of the principles of GLP in respect of tests on chemical products to evaluate their safety for people and/or the environment. The principles of good laboratory practice are specified in Annex 2 to the Decision the Council of the OECD, 12 May 1981 on the mutual acceptance of data for the evaluation of chemical products.

According to article 6 of Council Directive 87/18/EC (and as adapted to technical progress by 1999/11/EC), Member States must have brought into force the laws, regulations and administrative provisions necessary to comply with this Directive not later than 30 June 1988.

6.3 GENERAL PRINCIPLES

The general GLP principles are aimed at the chemicals defined in Council Directive 67/548/EEC. Thus, the laboratory studies on active substances or other substances (substances of concern) of a biocidal product must have been performed in accordance with the GLP Directive if the study was started after 30 June 1988. Laboratory studies on biocidal products performed later than 13 May 2000 must be conducted in compliance with the GLP Directive.

GLP is applied to the organisational processes and conditions under which the studies are planned, performed, recorded, archived and reported. The regulations are not concerned with the interpretation and evaluation of test results.

All physical-chemical studies and non-clinical health and environmental safety studies, i.e. toxicological, ecotoxicological, the analysis of the specimens of tests, field studies and residue trials have to be performed in accordance with the principles of GLP. The GLP principles, however, need not be applied to the efficacy and exposure studies. These studies should be done to an appropriate protocol and suitable QA (Quality Assurance) standards.

6.4 EXEMPTIONS

In general, the Biocidal Products Directive does not provide any flexibility for the acceptance of studies that have not been performed to GLP if they were started after 30 June 1988. Where a study was started before 30 June 1988, or a study did not require GLP certification before 13 May 2000 (e.g. physico-chemical studies on products) repeat testing will not normally be necessary provided the study is scientifically valid. The acceptance of other studies that have not been performed to GLP but were started after 30 June 1988 must always be decided on a case-by-case basis (see Chapter 1.3, point 4). In particular, in accordance with Article 8(8) of the Biocidal Products Directive needless repetition of testing on animals should be avoided.

Article 16(1) in the Biocidal Products Directive provides that Member States may continue to apply their national regulations for data requirements of existing active substances until those substances have been included in Annex I.

6.5 CERTIFICATES OF GLP IN A STUDY REPORT

Final study reports should include all necessary indications that the study was performed in accordance with GLP. The report should be signed and dated by the study director to indicate the acceptance of responsibility for the validity of the data and to confirm compliance with principles of GLP. Any deviations from full GLP compliance should be stated. A certificate/statement by a Quality Assurance Unit (QAU) must be attached to a study report and a certificate from a GLP monitoring authority may also be attached, if available. The certificate/statement from the QAU must be signed by a member of the QAU staff stating that the study has been monitored by the QAU (the dates of inspection should be given where appropriate) and that the final report is a fair representation of the results obtained in the study. The study report should also include:

- the name and address of test facility;
- the dates of commencement and completion of the experimental work;
- the name of the Study Director and other principal scientists involved in the study (when appropriate); and
- statement indicating where all specimens, raw data and the final report is stored.

Where there is a sufficient reason to believe that a laboratory in a Member State claiming GLP compliance has not carried out a test according to GLP, further information may be requested from the national GLP monitoring authority and a study audit may be requested (Council Directive 88/320/EEC, art. 6).

6.6 REFERENCES

Council Directive 87/18/EEC of 18 December 1986 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances. Amended by Council Directive 1999/11/EC of 8 March 1999.

Council Directive 88/320/EEC of 9 June 1988 on the inspection and verification of Good Laboratory Practice (GLP) amended by Council Directive 1999/12/EC of 8 March 1999.

Council Directive 88/379/EEC of 7 June 1988 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous preparations. Amended by Directive 1999/45/99

Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances.