TECHNICAL NOTES FOR GUIDANCE

IN SUPPORT OF ANNEX VI OF DIRECTIVE 98/8/EC OF THE EUROPEAN PARLIAMENT AND THE COUNCIL

CONCERNING THE PLACING OF BIOCIDAL PRODUCTS ON THE MARKET

COMMON PRINCIPLES AND PRACTICAL PROCEDURES FOR THE AUTHORISATION AND REGISTRATION OF PRODUCTS

SHORT TITLE: TNsG on Product Evaluation

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The Technical Notes for Guidance on Product Evaluation were formatted and edited in one single document in pdf format.

No changes have been made with respect to the content of the Guidance Document.

CHAPTER 1 GENERAL INTRODUCTION

1.1 GENERAL INFORMATION

1.1.1 Background

The Parliament and the Council Directive 98/8/EC ('the Directive') requires that active substances used in biocidal products placed on the market must be listed on Annex I, IA or IB of the Directive, and that European Union Member States establish a competent authority to authorise or register products before they can be placed on the market in their territory. This document provides guidance on how to perform the administrative and scientific evaluation of applications for authorisation and registration.

Authorisation is an administrative act by which the Member State competent authority allows a biocidal product to be placed on the market in some or all of its territory. It involves the consideration of the risks, efficacy and benefits arising from the use (and manufacture and disposal, where relevant) of that product and treated material. A product can be authorised once the competent authority is satisfied that the risks are acceptable, that it is sufficiently efficacious, and that it has no other unacceptable effects (such as causing unnecessary suffering in vertebrates).

Registration is a simplified authorisation procedure for products that comply with the definition of low risk as given in Article 2 of the Directive. Although efficacy assessment is required products for registration do not normally require a risk assessment, provided that

- all conditions associated with the Annex IA entry for the active substance(s) are met; a full risk assessment will have been conducted for the use of the product during the evaluation of the active substance at Annex IA inclusion and
- the proposed use pattern does not pose additional risks that were not considered by the Standing Committee on Biocides (SCB) for the inclusion decision.

Basic substances in biocidal products are not addressed in this document as product authorisation or registrations does not apply to basic substances listed in Annex IB.

1.1.2 Whom the guidance is for

The guidance document is intended for use by the competent authorities appointed by Member States under the provisions of the Directive. It is issued by the European Commission to help competent authorities carry out their obligations when considering applications for the authorisation or registration of products. The role of the competent authority is to determine whether proposed use patterns are acceptable and to ensure that decisions are transparent, supportable and derived from the best available sources of information.

The guidance is also intended to be useful to those making applications for authorisation or registration of products. It should help them understand how the risk and efficacy assessments are conducted and how decisions or conclusions are reached, including, on occasion, the need to request further data.

1.1.3 Why the guidance is needed

Annex VI of the Directive lays down harmonised principles ('Common Principles') for the appropriate evaluation of risk and efficacy for biocidal products, to enable decisions resulting in a high level of protection for humans, animals and the environment. This document is primarily intended to amplify

and explain the Common Principles, and it gives detailed practical guidance about how to assess risks and efficacy for the purposes of authorisation or registration. In addition, it provides guidance on practical aspects of administration, in particular the use of frame formulations, data protection and confidentiality.

Risk and efficacy assessment methodologies are continually developing. Consequently, the technical procedures relevant to the different aspects of both risk and efficacy assessment described in this guidance (or other guidance to which reference is made) may, where appropriate, be subject to further refinement and development in the future.

1.1.4 Scope of the guidance

These Technical Notes for Guidance give guidance for the risk and efficacy assessment of individual biocidal products, **assuming that all the active substances present in the product are already listed on Annex I/IA** for the required product type(s). It is closely linked to two other TNsGs, which give guidance on data requirements for the 23 product types and procedures for the inclusion of active substances in Annex I/IA (TNsG on data requirements and Annex I inclusion respectively). The Guidance is also partially applicable to the provisional authorisations refered to in Article 15 (2) of the Directive.

These Technical Notes for Guidance do not cover:

- how to appraise data for each of the end-points listed in Annexes II and III of the Directive. Instead this document is mainly concerned with how to use study results to reach an authorisation decision;
- evaluation of methods for chemical analysis. Guidance on analytical methods is given in the Technical Notes for Guidance on data requirements. Additionally, guidance on analysis of plant protection products can be found on the homepage of DG Health and Consumer Protection (http://europa.eu.int/comm/food/fs/ph_ps/pro/index_en.htm).
- assessment of research and development applications;
- assessment of effects resulting from the simultaneous use of products containing the same active substance(s) by different users. Guidance is given for effects which might arise where a number of products are intended to be used together by the same user (e.g. chemical compatibility), and on additive, synergistic or antagonistic effects of components in an individual biocidal product;
- assessment of additive effects resulting from non-biocidal use of active substances in other types of applications;
- assessment of effects resulting from accidents (e.g. release during transport) or gross abuse (e.g. suicide attempts). Accident scenarios are dealt with under industrial major accident and transport legislation. Minor spills that arise during normal use are covered, however, as is reasonably foreseeable misuse (including swallowing by a child); and
- the risk assessment for animals in a specific manner, which needs to be performed on a case-by-case basis when animal exposure is reasonably foreseeable, and considered to be relevant. This is particularly the case for products that may be used on animals directly. The guidance does not invalidate existing protection measures provided by other legislation or conventions.

1.2 GENERAL PRINCIPLES OF AUTHORISATION

Figure 1.1 outlines the general procedure for obtaining an authorisation for a biocidal product. This document deals with 'stage 2' ('stage 1', relating to active substance inclusion on Annex I/IA is dealt with in the TNsG on Annex I inclusion).

As mentioned above, authorisation requires the assessment of risk, efficacy and, if needed, benefit. (Assessment of benefit would normally only require the submission of a short justification by the

applicant as a part of the product dossier. Less clear cases may require a more detailed justification but only occasionally should a detailed risk-benefit analysis be required.) Detailed assessment of risk and efficacy are required for authorisation, as described here below.

1.2.1 Risk assessment

Risk assessment will always be required for applications for authorisation. Essentially, an assessment of the hazards posed by the product is made, together with an assessment of exposure for humans, animals and the environment. The hazard is then compared to the actual or predicted exposure for each relevant population or compartment to determine the risk.

This guidance document refers to the Technical Guidance Document on Risk Assessment of chemical substances published by the European Commission (2002), where relevant. However, most products are mixtures of several substances, each with its own intrinsic hazards. While these hazards are not necessarily expressed by the product (due for example to dilution), the substances can sometimes interact in complex ways so that the hazard from one substance is enhanced or diminished compared to that which would normally be expected. In addition, once out of the container the composition of the product can change because of differential volatilities and solubilities, etc. In most cases, however, ***the hazard of the product can be assessed by careful consideration of the hazard data on the individual components***, with the assumption that the components operate independently, unless other information suggests otherwise.

For some of the 23 product types environmental emission scenario documents have already been developed and a contract is on-going to address the remaining product types. For the human exposure assessment a project will be finalised by mid-2002 on exposure estimations and models for the 23 product types. Models and risk scenarios developed for other regulatory purposes may be relevant (e.g. models used for plant protection products may be useful where fate in soil is of particular interest; the EUSES model for risk assessment of industrial chemicals may for some product types be used to estimate exposure). Chapters 3-5 deal with product risk assessment in detail.

1.2.2 Efficacy

Efficacy assessment is required for both authorisation and registration. Unlike risk assessment, there are no existing guidelines. For example, there are no international agreements on what constitutes a label claim, on the data to support such claims or on the design and quality assurance aspects of how such data are produced. Detailed guidance in these areas is therefore given in Chapter 7.

1.2.3 Product purpose and design

Article 3(7) of the Directive states that Member States shall prescribe that biocidal products are properly used and that the use of biocidal products is limited to the minimum necessary. In order to achieve this, competent authorities will have to be satisfied that appropriate products are authorised and that sufficient information on how the product should be used is provided. Three issues can be identified consequent to this provision in the Directive.

- Intended uses and any efficacy claims must be presented clearly and accurately on the product label and in product information. Applicants should avoid efficacy claims that might result in the inappropriate use of a biocidal product.

- Applicants should provide appropriate information about how and when a product should be used (and if relevant when a product is inappropriate for use) on the label and in other product information in order to limit biocidal product use to the minimum necessary.

- In addition, the applicant should consider the principles and procedures of the Directive in relation to the product design and proposed pattern of use. Exposure of humans and the environment should be as low as possible so that when a product is used the consequent exposure is minimal. Applicants should then consider the guidance available on risk assessment (chapters 3-6 of this document) to identify any potential problem areas and resolve them before submitting their application. This should maximise the chances of the application being quickly and successfully processed. Specifically, it should avoid the need for refinements of risk assessments at a late stage.

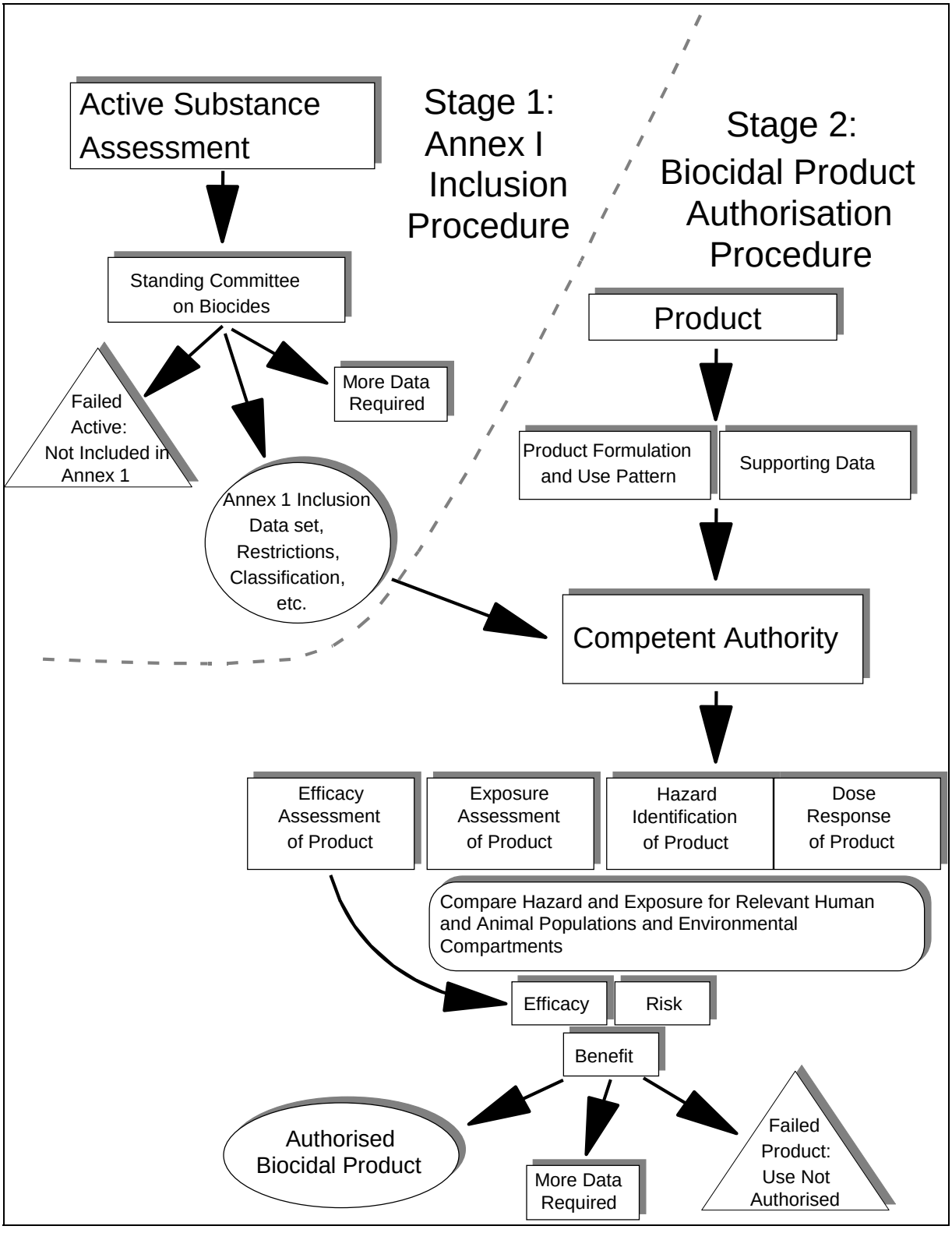


Figure 1.1 ***Overview of the authorisation process***

1.3 INTEGRATION AND CONCLUSIONS

The conclusions from the risk assessment and those following assessment of efficacy will be integrated to produce an overall conclusion, which must be balanced with the benefit of using the product.

In reaching the final conclusion, the competent authorities apply the Precautionary Principle according to the guidance given by the European Commission, where appropriate (Communication from the Commission on the precautionary principle).

The final conclusion will be one of the following:

- the biocidal product can be authorised or registered for the use as applied for, subject to specific conditions/restrictions;
- more data are required before a decision on authorisation or registration can be made; or
- the biocidal product cannot be authorised or registered for the use as applied for.

It is recommended that a consultation process be established between the competent authority and the applicant for all applications to ensure that the assessments make the best possible use of all information available to the applicant, particularly regarding detailed use patterns of the product. Assessments should be re-evaluated and possibly revised in the light of any further information on the properties of the product and/or exposure, whenever such information becomes available. Guidance on how the risk assessment and its conclusions can be structured have been proposed in the TNsG on Dossier Preparation and Study Evaluation.

CHAPTER 2 INITIAL ADMINISTRATIVE PROCEDURES

2.1 INTRODUCTION

When an application for authorisation or registration of a biocidal product has been received, the competent authority should undertake an initial evaluation to determine whether:

- the application is for a product as defined by the Directive;
- the application is covered by a current Annex I or IA entry; and
- the application dossier is complete.

The following sections give guidance in these areas.

Application dossiers should be presented in a structured format to avoid undue delay in processing the application as laid down in the TNsG on Dossier Preparation and Study Evaluation.

2.2 INITIAL CONSIDERATIONS

2.2.1 Is the application for a biocidal product as defined by the Directive?

Article 2 of the Directive presents key definitions:

- Biocidal product
  "Active substances and preparations containing one or more active substances, put up in the form in which they are supplied to the user, intended to destroy, deter, render harmless, prevent the action of, or otherwise exert a controlling effect on any harmful organism by chemical or biological means."
- Active substance
  "A substance or micro-organism including a virus or fungus having general or specific action on or against harmful organisms. "
- Harmful organism
  "Any organism which has an unwanted presence or a detrimental effect for humans, their activities or the products they use or produce, or for animals or for the environment."
- Low-risk biocidal product
  ”A biocidal product which contains as active substance(s) only one or more of those listed in Annex I A 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.”
- Frame-formulation
  ”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.”

The competent authority should determine whether the product is within the scope of the Directive and to which product type in Annex V of the Directive it pertains. If it is outside the scope, no authorisation or registration as a biocidal product is required.

The above definitions are the initial basis for the decision on whether or not the product is within the scope of the Directive together with the exemptions laid down in Article 1. Further guidance on this issue is given in the Manual of Decisions, the borderline documents and the scope documents (which are planned to be published at DG ENV's homepage) and should also consider the following points:

- **Does the product act by chemical, biological or physical means?**

  See borderline documents

- **Is the product within scope of any of the Directives or Regulations listed in Article 1 (2) of the Directive?**

  See borderline and scope documents

- **Does the product claim to destroy, render harmless, deter, prevent the action of or exert a controlling effect on a harmful organism?** If the product does not make such a claim, is there intention to exert these effects through the use pattern or content of the product? (The competent authority may come across this situation if a potential applicant makes an enquiry.)

The competent authority should ensure that products are not excluded from authorisation or registration through misrepresentation of product claims, when the competent authority has reason to suspect that this is the case. For example: A product claim may be that it is for use only as a decorative wood finish even though it contains an active substance known to be used in wood preservatives.

In some situations it will not be clear whether or not the biocidal product is in or out of the scope. In cases where consulting among competent authorities can not solve the matter, the competent authority in question should refer it to the SCB for decision. A decision should be made within the timescales allowed, but with an emphasis on a quick decision so that there are no undue delays to the applicant.

2.2.2 Are the active substances in the product included in Annex I/IA and within the scope of these entries?

For a biocidal product to be authorised or registered the active substance(s) must be on Annex I or IA respectively. The competent authority must check that the intended product type and the applicant's proposed conditions of use for the product are permitted under the Annex I/IA entry. If they are not, or if the applicant provides active substance data that have not previously been evaluated, the Annex I/IA entry must be revised by following the procedures described in the TNsG on Annex I inclusion. The results of the evaluation must be considered by the SCB in the usual way. If the conclusions of the competent authority's evaluation of new data are significantly different from those reached by the SCB for the original data used for Annex I/IA inclusion, then the matter must be referred to the SCB before authorisation or registration of the product can be granted.

In addition to the Annex I/IA check, the competent authority should also ensure that the proposed use of the biocidal product conforms with any conditions imposed by other community legislation, for example:

- restrictions under Directive 76/769/EEC (concerning restrictions on the marketing and use of dangerous substances and preparations) which would affect or prohibit possible authorisation or registration of the product.

2.2.2.1 Low risk products

Risk is related to both hazard and exposure. "Low risk" is not the same as "low hazard". For example, a low-risk product can be hazardous provided that it only gives rise to insignificant exposure.

A low-risk product can therefore either be a "low hazard" one or a “hazardous” one which, under specified conditions, can be used without grounds for concern for human health and the environment.

In addition, Article 2 (1)(b), (e) and Article 10(1) definitions prescribe that a low-risk product can not contain:

- an active substance that is bioaccumulative and which does not readily degrade, or that is classified according to Directive 67/548/EEC as Carcinogenic, Mutagenic, Toxic for Reproduction or Sensitising; nor

- any non-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 at a concentration sufficient to create such an effect. This applies even if the product is already classified for the adverse effect on the basis of the active substance concentration, or if the product is classified as dangerous because of the combined contributions of a number of substances which individually are present at concentrations below the classification cut-offs for the product. In other words, if the substance has a hazard, it can only be allowed if it is present at a concentration so low that the hazard is not expressed in the product. Such a substance, unless there are other grounds for concern, would normally be classified as dangerous according to Directive 67/548/EEC and be present in the biocidal product at a concentration leading the product to be regarded as dangerous within the meaning of Articles 5, 6 and 7 of Directive 1999/45/EC.

The dossiers for inclusion of an active substance into Annex IA are the same as those for Annex I, because the active substance has to be fully evaluated in order to demonstrate that it indeed meets the criteria for inclusion on Annex IA. The accompanying complete product dossier(s) have to represent the patterns of use for which the active substance should be evaluated and thus these dossiers should be full dossiers. For the format see the TNsG on Dossier Preparation and Study Evaluation.

If the application is for registration, the product composition must also be checked to ensure it does not contain any substance(s) of concern (if it does, the application must be revised to one for authorisation).

2.2.2.2 Frame Formulations

The use of frame formulations:

- reduces the complexity of the authorisation system by permitting products to be authorised in ranges of colours and fragrances without the need for specific data on every formulation variation. This reduces the amount of data needed and the need for multiple assessments on virtually identical products; and

- does not compromise human or environmental safety or the efficacy of a product resulting from their use. This is because there will have been an assessment completed on a dossier of one formulation within this frame and all other formulation variations only represent minor differences from that which the dossier supported.

Further guidance on the use of frame-formulations is provided in section 9.6.

This section does not deal with ‘sub-authorisations’ of identical products which have been re-named for commercial reasons.

2.2.3 Is the submitted dossier complete?

The application for authorisation or registration must be complete before it can be progressed (i.e. there must be a study report, reasoned case or letter of access for each data requirement). A completeness check is laid down in the TNsG on Dossier Preparation and Study Evaluation. The competent authority should therefore perform an initial administrative check to ensure that the relevant dossiers have been submitted and are sufficiently complete to enable a subsequent scientific evaluation to be performed. The data requirements are given in Article 8(2) of the Directive, and explained further in the technical notes for guidance (TNsG) on data requirements.

All of the dossier information is required to enable the competent authority to properly evaluate the application. However, Article 8 (3) of the Directive specifically derogates some of these dossier requirements for low risk biocidal products (i.e. those requiring only registration), the major exemptions being:

- toxicology studies for the biocidal product
- ecotoxicology studies for the biocidal product

If the initial completeness check indicates that the application package is inadequate, the competent authority should advise the applicant in accordance with Article 8 (6). This advice could be on appropriate modifications to the application such that the dossier could meet the criteria for a restricted use pattern, or on the further data needed to support the uses applied for. The responsibility for progressing the application remains with the applicant. Competent authorities could adopt a flexible approach as follows:

- **Inadequate dossier.** The main evaluation clock is not started. The applicant should be informed of the inadequacies (e.g. where certain study reports are missing and these studies have not yet been conducted) and given a deadline to respond, and the application either put into temporary storage or returned to the applicant. Work will only begin when the missing items are provided or the application is resubmitted in complete form within the agreed deadline.
- **Some information submitted in summary form but detail is clearly available.** The scientific evaluation can continue whilst such information is supplied in detailed form (for example where a test report has been summarised and the full report has not been submitted). In this case a timetable will need to be discussed with the applicant to ensure that the clock is stopped if the required information is not received by the competent authority by the agreed deadline.
- **Minor details omitted.** The evaluation can continue whilst such details are supplied. Again a timetable will need to be discussed with the applicant to ensure that the clock is stopped if the required information is not received by the competent authority by the agreed deadline.

2.3 LETTERS OF ACCESS

2.3.1 Background

Data protection provisions within the Directive require that only companies who own data, or have access to data via a letter of access can use the data to support their applications whilst data are protected (see Chapter 9 for further details on data protection). When considering an application for authorisation/registration the competent authority should therefore check:

- whether data are subject to protection;
- if so, who owns it; and
- whether the applicant has legitimate access to it.

Where the applicant is not the data holder for the dossier associated with the Annex I or IA entry, a letter of access will be required for each active substance in the proposed biocidal product if these

active substances are still subject to the provisions of data protection covered by Article 12 of the Directive.

Similarly, if the applicant is not the data holder for the dossier associated with the biocidal product then a letter of access will need to be supplied for the proposed product for all use areas applied for.

A letter of access is defined in Article 2 of the Directive as:

> "A document, signed by the owner or owners of relevant data protected under the provisions of the Directive, which states that these data may be used by the competent authority for the purpose of granting authorisation or a registration of a biocidal product under this Directive."

Letters of access are the major tool in the Directive by which data submitted by another applicant under this Directive can be shared. They:

- do not compromise the provisions of data protection;
- reduce unnecessary testing;
- reduce unnecessary photocopying and delivery of test reports; and
- reduce unnecessary evaluations by the competent authority (by removing the need to assess test reports for every requirement under Annex II, III and IV for every product application).

The two major uses of letters of access are:

- letters of access to an active substance dossier, where the active substance supplier supports many applications for authorisation/registration of individual products in one or more product types; and
- letters of access to a product dossier, where read across amongst broadly similar products is possible.

The letter of access is under the responsibility of industry. It should be valid for the authorization period. The letter of access covers data to a specific substance supplier and change of supplier may change the impurities and the purity of the substance.

2.3.2 Acceptability of a letter of access

To determine whether a letter of access is acceptable in supporting a product application, the competent authority will need to check that the following details are included:

- the name of the data holder;
- name of the applicant to which data access is granted - if this is different from the formulator company, the formulator company must also be quoted;
- name of the applicant's product(s) for which authorisation/registration is sought;
- the product type for which access is granted, unless this is clear from the product name;
- the nature of the data package to which access is granted, i.e. whether it is active substance data, product data or both. The specific active substance(s) and/or product(s) must be named;
- a description of the data package including the type of studies to which access is granted, i.e. a complete data package or only certain elements such as toxicity test data, environmental toxicity data or efficacy data; and
- the competent authority to which the original data package was first submitted where relevant

Assuming the example that an application based on mutual recognition for registration or authorisation of a biocidal product in one MS refers by a letter of access to a data package of a different product first submitted to the CA of another MS. The details of the application for authorisation or registration can then be checked against the summary provided by the competent authority, which authorised the original product (as detailed in section 9.2 of Chapter 9) and the active substance(s) data can be checked against the Annex I/IA entry and associated submission presented to the SCB.This check should determine whether the data to which access has been granted are sufficient to meet the requirements of Annexes II, III and IV for the product type and its use.

Access should be granted to whole documents (for example, test reports) and not particular values or parts of the document.

If a data holder later wants to cancel a letter of access then they must inform the CA in writing.

2.4 ASSESSMENT OF DATA

2.4.1 General requirements

It is the responsibility of the applicant to produce (or gain access to), collect and submit all relevant information required to support the proposed authorisation, in accordance with the data requirements as listed in Annexes IIA, IIB, IIIA, IIIB, IVA and IVB of the Directive. Specific guidance on the data which must be submitted is given in TNsG on data requirements. The active substance dossier does not need to be resubmitted for the application, provided, if the applicant is not the owner of the data, that the applicant has written permission from the data owner to use the results of the studies (see section 2.4.2). The same principle applies when the applicant has permission to use previously submitted product data.

Data from any source will be considered, provided they are valid and relevant to the application. The identity, purity and the impurities of the substance have to be defined in the publication and to be comparable with the notified substance. Sources of data may include:

- unpublished scientific/technical reports, including reliable data from human experience (e.g. case reports); and
- published work in reputable, refereed journals.

An applicant might also provide anecdotal evidence or testimonials from individuals for some end points. Although these are a potential source of information, they are unlikely to be sufficiently reliable for use in product authorisation, and should never be used alone.

In addition, an applicant can present justifications for not supplying certain pieces of data, provided they are acceptable to the competent authority (see TNsG on data requirements for further guidance).

2.4.2 Data protection

The Competent Authorities are drafting a guidance document on data protection. When finished it will be published on DG ENV's homepage.

2.4.3 Data submission

The data submission should be presented in a structured and logical manner, and all relevant test reports etc., regardless of positive or negative results, should be submitted in accordance with the guidance given in the TNsG on data requirements. Accompanying the data should be a completeness check list as described in section 4.6 of Part 1 of the TNsG on Dossier Preparation and Study Evaluation.

The competent authority should have access to individual data sets, where relevant, together with summary tables/graphs and, if appropriate, statistical analyses using methods, which are fully described by reference to published work. The competent authority may on occasion need to request the raw data with, if necessary, explanatory notes concerning erratic results.

2.4.4 Evaluation of data

The competent authority must critically evaluate each study or item in detail (cf. TNsG on Dossier Preparation and Study Evaluation.). An evaluation should fulfil the following aims:

- to ensure that the study actually meets any standards it claims to meet and to note and comment on any deviations from these standards;
- to assess the overall scientific integrity of the study and the report with respect to both its completeness and adequacy;
- to describe routine and unusual observations made throughout the study; and
- to summarise the result of the study.

It should be noted that the effects values for active substances that are agreed by the SCB must be used by the competent authority for the product assessment. The same applies to the classification and labelling of the substance except the cases where a different classification and labelling has been confirm in accordance with Directive 67/548/EEC.

2.5 FINAL DECISION ON THE INITIAL ADMINISTRATIVE EVALUATION

The competent authority should consider all of the above information and, on judging that:

- the application is within scope of the Directive;
- the active substances are included in Annex I or IA; and
- the dossier is sufficiently complete and suitable for evaluation,

should begin the main scientific evaluation as described in Chapters 3-7 for authorisation, or Chapters 6-7 for registration. In accordance with Article 8 (6), the time period for the scientific evaluation of the dossier should only start after the initial administrative completeness check is complete and the package judged adequate.

If the package is judged adequate, an application for authorisation should be decided upon without undue delay, in accordance with Article 3(3)(i) of the Directive. The timescale should be appropriate for the level of work required for an evaluation for authorisation.

When a subsequent application for authorisation for a new biocidal product is based on a frame-formulation, the competent authority shall take a decision with regard to this application within a period of 60 days (Art. 3(4) of the Directive).

An application for registration of a low-risk product should be accompanied by the data listed in Article 8(3) of the Directive in accordance with the guidance provided in the TNsG on Data Requirements. The Competent Authority will then evaluate the submission to determine whether or not it meets the conditions outlined in Article 2(1)(b) and Article 3(2). The decision shall be taken within a period of 60 days of receipt of application (Art. 3(3)(ii)).

2.6 MUTUAL RECOGNITION

Where an applicant already holds an authorisation (or registration) for a particular biocidal product in one Member State (and provided there is a suitable Annex I or IA entry for the active substance), they can apply to competent authorities in other Member States for that authorisation (or registration) to be mutually recognised so that the product can also be placed on the market there. Mutual recognition should be based on harmonised models and established evaluation procedures. For example, as long as no harmonised worker exposure model exists, an authorisation based on an exposure model cannot be mutually recognised. Since the risk, efficacy and benefit will already have been assessed, and

hence a precedent set, the applicant only has to provide the competent authority in the second Member State with some limited information as detailed in Article 4(1) of the Directive. Essentially this is:

i) for authorisation:

(a) a summary of the dossier on the product in the language(s) required by that Member State in accordance with Annex IIB, IVB and, where relevant, Annex IIIB;

(b) a certified copy of the first authorisation granted in the language(s) required by that Member State. If relevant, a copy of any letters of access may also be required in order to allow the competent authority to identify and retrieve the information if needed; and

(c) safety data and label with instruction of use for the product all in the language(s) required by that Member State.

ii) for registration: the same data as for a normal registration, except that only a summary of the efficacy data is required (a copy of the first registration should also be submitted although this is not specified in the Directive).

The applications for mutual recognition should be approved by the second Member State under the provisions laid down in Article 4 of Directive 98/8/EC. The receiving competent authority must therefore assess the application in relation to conditions in its own territory. In particular it will consider the following points:

(i) is the target organism different, or is it absent or only present in numbers that do not need control or can it be controlled by non-chemical means, or are there special national provisions for its conservation or control?;

(ii) is there unacceptable tolerance or resistance of the target organism to the biocidal product?; and

(iii) do the relevant circumstances of use differ significantly from those in the Member State where the biocidal product was first authorised? Examples of issues to consider:
- environmental conditions (e.g. is the climate significantly hotter or wetter?; if disposal is to water, are receiving waters similar?),
- breeding period of the target species, and
- working and consumer practices and circumstances (e.g. are worker protection requirements markedly different?).

If the answer to these is no, an authorisation can be issued with the same conditions as the first authorisation, provided that administrative items are in order (e.g. letters of access must allow the applicant to use the data in the Member State. Letters of access may not always be required, e.g. if data protection has expired in the Member State or if acceptable public literature data has been used.), i.e. the first authorisation is mutually recognised. This is expected to be the case for the majority of applications of this type. According to Art. 4(1) of the Directive this mutual recognition procedure shall be without prejudice to measures taken by Member States pursuant to Community law intended to protect the health of workers.

However, if the answer to any of these questions is yes, the competent authority must consider how the original risk, efficacy and benefit assessments would be affected. For example, the climatic or aquatic conditions may prevent an active substance from degrading in the environment to the same extent, or the target organism may be a different strain of the same species, or an unrelated species, with implications for efficacy.

It may be possible for the competent authority to accept the authorisation or registration subject to modifications such as those in relation to, for example:

- directions for use and the dose rate;
- particulars of likely direct or indirect adverse side effects and any directions for first aid;
- directions for safe disposal of the biocidal product and its packaging, including, where relevant, any prohibition on reuse of packaging;
- the period of time needed for the biocidal effect, and retreatment times;

- methods of decontamination, and precautionary measures during use, storage and transport; and where applicable
- information on any specific danger to the environment particularly concerning protection of non-target organisms and avoidance of contamination of water.

If the competent authority cannot fully assess the new risks or efficacy on the basis of the summary received, it should proceed as described in Article 4(3) of the Directive by provisionally refusing the application and entering into discussions with the original authorising competent authority. This might include requesting a copy of the full dossier and the original competent authority's risk assessment to clarify the evaluation (see also chapter 9.2). If the outcome of the evaluation is that the application is refused, the competent authority must proceed according to Article 4(4) of the Directive, i.e. it shall notify the Commission, other Member States and the applicant and shall provide them with an explanatory document containing the name of the product and its specification and setting out the grounds on which it proposes to refuse or to restrict the authorisation.

In all cases the competent authority must reach a decision within 120 days for an authorisation or 60 days for a registration. Refusal to grant an authorisation/registration or modifications to conditions must be justified, and communicated to the Commission, other Member States and the applicant.

CHAPTER 3 RISK ASSESSMENT FOR PHYSICO-CHEMICAL PROPERTIES

3.1 GENERAL INTRODUCTION

3.1.1 Background

A risk assessment for physico-chemical properties will always be needed before a biocidal product can be authorised. No specific risk assessment is normally required for registration of low-risk biocidal products. This section gives guidance on the assessment of the physico-chemical risks posed by biocidal products. Article 5(1)(b) of the Directive requires that a biocidal product must have no unacceptable physical or chemical effects. Such effects can arise from the intrinsic properties of the product, such as flammability and explosivity. Effects can also occur indirectly through, for example, chemical incompatibility between the biocidal product and other materials.

3.1.2 Risk characterisation of physico-chemical effects

Unlike risk characterisation for human health and the environment, the main parts of the physico-chemical risk characterisation are normally **qualitative**. Competent authorities need to consider whether the identified hazard is likely to express itself during realistic worst case use (and, if relevant, manufacture and disposal) scenarios. Other considerations include:

- the chemical and physical nature of the biocidal product, e.g. whether the product is a concentrate or ready-for-use, plus the nature of the diluents;
- the physico-chemical hazards posed by any post-treatment residue, e.g. some kerosene-containing aerosol surface treatments can pose a residual flammability risk until the solvent has evaporated;
- the quantities involved;
- any environmental conditions (e.g. temperature, humidity, presence of other materials, etc.); and
- the severity and the likely consequences of any such reaction.

A risk assessment for explosivity, oxidising properties and flammability is not necessary provided that none of the product's constituents possess such properties, and, in addition, that on the basis of information available to the applicant, the product is unlikely to present dangers of this kind.

3.2 EXPLOSIVITY

3.2.1 Hazard identification

- ***Biocidal product***

The explosive properties of a biocidal product must be identified. This could be by an explosivity test carried out on the biocidal product. If studies are not available, it may be possible to derive information from a frame formulation or from a read-across from a product with a similar formulation.

- ***Active substances***

The explosive properties of the active substance will have been agreed at the time of its inclusion in Annex I/IA. If the active substance is classified, this would include which stimuli (such as shock, heat or friction) that lead to the classification for explosivity and other important factors such as particle size and moisture content.

- ***Substances of concern***

Substances of concern are those classified for explosivity under Directive 67/548/EEC. If information on the classification is not available, they may be identified by analogous substances or by structural alerts.

Table 3.1 lists examples of chemical groups which can decompose violently. The list is not exhaustive and further information can be found in, e.g., Urben (1995).

Table 3.1: ***Examples of structural alerts for explosive properties***

Structural Alert	Name
$-NO_2$	nitro compounds
$-C-N_3$	organic azides
-C-N=N-C-	aliphatic azo compounds
-O-O-	peroxides
$-CN_2^+ Z^-$	diazonium salts
>N-N=O	*N*-nitroso compounds
$-SO_2-NH-NH_2$	aromatic sulfohydrazides
R-NH-NH-R	hydrazides

The oxygen balance is another means of assessing the explosive potential of substances containing groups such as nitrate, peroxide or chlorate. It is a measure of the lack of oxygen in the molecule necessary for stoichiometric combustion. The oxygen balance enables the availability of oxygen in the substance to be compared with known explosives. Further information is available in Urben (1995).

- ***Classification of the biocidal product for explosivity***

Competent authorities should note that some of the additional risk phrases from section 2.2.6 of Annex VI of Directive 67/548/EEC may be appropriate. The component(s) of the biocidal product that cause the product to be classified should be identified for use in risk characterisation.

3.2.2 Risk characterisation

Risk characterisation is required when a biocidal product is classified as Explosive or where there are other grounds for concern. Other grounds for concern include, e.g., if the product:

- contains other substances classified as Explosive;
- can form peroxides during storage, e.g. ethers or unsaturated compounds;
- is thermally unstable or unstable at ambient temperatures;
- can form sensitive metallic derivatives; and
- is put on the market in solution or in a wetted form because it is explosive when dry.

3.2.3 Risk management options

Examples of general risk management conditions, which competent authorities may consider, are given below. This list is not exhaustive and the biocidal product should be considered on a case by

case basis. Depending on the nature of the hazard, expert judgment may be needed to properly control the risks arising from the storage, use and disposal of the biocidal product.

Engineering control

- Controls on use, e.g. specially designed equipment or containers.
- Control of ignition sources.
- Storage conditions, e.g. in an inert or temperature-controlled atmosphere.

Formulation

- Control of any critical aspects such as particle size and moisture content or concentration of reaction inhibitors above the critical level.

3.3 OXIDISING PROPERTIES

3.3.1 Hazard identification

- ***Biocidal product***

The oxidising properties of a biocidal product must be identified nomally by a test carried out on the biocidal product. If studies are not available, it may be possible to derive information from a frame formulation or from a read-across from a product with a similar formulation.

- ***Active substances***

The oxidising properties of the active substance will have been agreed at the time of its entry on to Annex I/IA.

- ***Substances of concern***

Substances of concern are those classified as Oxidising under Directive 67/548/EEC. If information on the classification is not available, the structure should be examined for oxidising groups. Examples are given in table 3.2.

Table 3.2: ***Examples of structural alerts for oxidising properties***

Structural Alert	Group
-O-O-	inorganic peroxides
-O-OH	hydroperoxide
ClO_3 ; ClO_4 ; I_2O_6 ; IO_4	Chlorate, perchlorate, iodate, periodate
NO_3 ; NO_2	nitrate, nitrite
most oxo-elemental groups	

- ***Classification of the biocidal product for oxidising properties***

Biocidal products should be classified as Oxidising in accordance with Article 5 and Annex I of Directive 1999/45/EC. Competent authorities should note that some of the additional risk phrases from section 2.2.6 of Annex VI of Directive 67/548/EEC may be appropriate.

3.3.2 Risk characterisation

Risk characterisation is required when the biocidal product is classified as Oxidising or where there are other grounds for concern. Other grounds for concern include if the product:

- contains other substances classified as Oxidising.

3.3.3 Risk management options

Examples of general risk management conditions which competent authorities may consider are given below. This list is not exhaustive and the biocidal product should be considered on a case by case basis. Depending on the nature of the hazard, expert judgment may be needed to properly control the risks arising from the storage, use and disposal of the biocidal product.

Engineering control

- Temperature, e.g.:
  - control of maximum and minimum temperatures during storage, handling and use; and
  - storage of packaged oxidisers below the self-accelerating decomposition temperature (this depends on both package size and the stacking arrangement of the packaged product).
- Process isolation or segregation.
- Suitable ventilation.
- Special storage conditions to avoid contamination and to take account of the possibility of sudden decomposition and any associated hazard.

Professional and non-professional

- Requirements to avoid incompatible materials such as water; inorganic acids, combustible material, reducing agents and other oxidisers.
- Prevention of contact with sources of ignition or other physical stimuli to which the product is sensitive.

Special requirements for organic peroxides

Organic peroxides are highly reactive, combustible and thermally unstable substances which may undergo self-accelerating decomposition. They will react, often violently, with, e.g., acids, heavy metal compounds, amines etc. Specialist expert advice may be needed to determine whether or not the risks involved can be properly controlled and, if so, how. It should be noted that organic peroxides are classified by limits of concentration of peroxide or active oxygen (cf. Annex VI to Directive 67/548/EEC).

3.4 FLAMMABILITY

3.4.1 Hazard identification

Flammability covers several properties of the biocidal product such as its flash point, pyrophoricity, spontaneous ignition, auto-ignition temperature, etc.

- ***Biocidal product***

Flash point and other indications of flammability or spontaneous ignition must be determined, e.g. from suitable studies, including:

- Relative self-ignition temperature for solids
- Auto-ignition temperature (liquids and gases)
- Flammability (solids)
- Flammability (gases)
- Flammability (contact with water)
- Pyrophoric properties of solids and liquids
- Flash point

If studies are not available, it may be possible to derive information from a frame formulation or from a read-across from a product with a similar formulation.

In addition to the information specified in Annex IIB, other relevant information may be available from the product safety data sheet for products for professional use (e.g. vapour density and evaporation rates).

- ***Active substances***

The properties of the active substance will have been agreed at the time of its inclusion in Annex I/IA. This will have addressed the following aspects, where applicable:

- Relative self-ignition temperature for solids
- Auto-ignition temperature (liquids and gases)
- Flammability (solids or gases)
- Flammability (contact with water)
- Pyrophoric properties of solids and liquids
- Flash point

- ***Substances of concern***

Substances of concern are those with the classification as Extremely Flammable, Highly Flammable or Flammable.

Other information on the co-formulants could include: the upper and lower flammability limits, flash points and auto-ignition temperatures.

- ***Classification of the biocidal product for flammability properties***

Biocidal products should be classified for flammability in accordance with Article 5 and Annex I of Directive 1999/45/EC if it is proven that such estimation methods are valid with respect to the composition of the biocidal product. Competent authorities should note that some of the additional risk phrases from sections 2.2.6 and 3.2.8 of Annex VI of Directive 67/548/EEC may be appropriate.

Competent authorities should note that some materials such as water/solvent mixtures or emulsions only release vapours slowly. These materials can flash during a flash point determination and be assigned a flash point, but may not have the ability to sustain combustion at the temperatures encountered in normal use, although these may well be in excess of the measured flash point.

Biocidal products marketed in the form of pre-pressurised aerosols can be classified for flammability in accordance with Directive 94/1/EC, if it is known that the product does not cause risks because of its flammability. Competent authorities should note that this Directive allows for the person putting the aerosol on to the market to derogate from the flammability classification through testing. If the applicant for a biocidal product authorisation or registration chooses to use the derogation, they should be in possession of, or have access to, the relevant test data.

3.4.2 Risk characterisation

Risk characterisation is required for biocidal products classified as Flammable, Highly Flammable or Extremely Flammable, or where there are other grounds for concern. Other grounds for concern include if:

- any of the product components are classified as Flammable, Highly Flammable or Extremely Flammable, or have a self-ignition temperature of below 250 ºC. If this is the case, the following situations could lead to a flammable hazard:
  - release of the product under pressure as a mist or spray;
  - spreading of the product as a thin film over a large area or spills onto clothing;
  - evaporation of volatile non-flammable components to leave a flammable residue;
  - evaporation of volatile components to form a flammable vapour-air mixture;
- the product is used at temperatures above its flash point; and
- it is mixed with low flash point materials.

The risk characterisation should consider whether the three conditions necessary for a fire (fuel, air and an ignition source) are likely to be present, along with the steps needed to control them.

3.4.3 Risk management options

Examples of general risk management conditions which competent authorities may consider are given below. This list is not exhaustive and the biocidal product should be considered on a case by case basis. Depending on the nature of the hazard, expert judgment may be needed to properly control the risks arising from the storage, use and disposal of the biocidal product.

Engineering control

- A requirement for good ventilation. This will mean that any vapours emitted from a spill, leak, or release from any process, will be rapidly dispersed.

Administrative controls

- Requirements to remove ignition sources from the storage and handling areas.
- A requirement to store and use flammable substances well away from other processes and general storage areas.
- Requirements for the use of suitable containers.

Special requirements for flammable gases

Specialist expert advice may be needed to determine whether or not the risks of flammable gases such as phosphine can be properly controlled and, if so, how. Gases in cylinders are often stored at very high pressures, and so their uncontrolled release can be physically dangerous. A small amount of released gas can fill a large area with a potentially explosive mixture. Competent authorities may require:

- stored cylinders to be suitably restrained and their valves protected from impact damage; and
- gas cylinders to have special valves, fittings and hoses. Manufacturers' or suppliers' instructions should specify the correct equipment.

3.5 STORAGE-STABILITY

3.5.1 Hazard identification

During storage, biocidal products may undergo chemical and physical changes and competent authorities should assess the hazards and risks these may pose. No simple method exists of determining all the possible changes arising from storage of the biocidal product. The following gives general guidance only on sources of available data, its evaluation and possible outcomes.

- ***Biocidal product***

Information on the storage-stability of the biocidal product including shelf-life, reactivity towards container material, and the effects of light, temperature and humidity on relevant technical characteristics of the product. Competent authorities should consider:

- ***chemical changes of the biocidal product:*** possible formation of hazardous materials and amounts formed; the possibility of a hazardous exothermic reaction; the possibility of degradation to unstable products, e.g. bromochloro-5,5-dimethylhydantoin can decompose to chlorine and bromine during storage;
- ***the nature of the active substance(s) and the formulation type***;
- ***physical changes of the biocidal product:*** any safety significance of any changes to the technical characteristics of the product;
- ***the need for and the presence of stabilisers***;
- ***storage conditions to avoid:*** conditions such as temperature (high and low), light, humidity, pressure, shock, etc., which may cause an adverse change in the characteristics of the product, e.g. natural pyrethroids are rapidly destroyed by light;
- ***packaging:*** there should be no significant interaction between the product and the packaging (to ensure that the stability of the packaging and the product are not affected); and

- ***shelf-life:*** a short shelf-life may indicate that the product is not stable over prolonged periods.

- ***Active substances***

Information on the inherent stability of the active substance (e.g. hydrolysis, photolysis, etc.) will have been agreed at the time of its entry onto Annex I/IA. Other stability information may be available from development work conducted on the active substance.

- ***Substances of concern***

Information on the storage-stability of co-formulants may be available from product storage-stability data.

- ***Other information***

Information may be available from a frame formulation or from a read-across from a product with a similar formulation.

Although a hazard may be identified, information may be available to show that in use there is no significant risk. Conversely there may be evidence available to show that although a hazard has not been identified, one may develop during storage and subsequent use. Such information may include pre- or post-marketing surveillance carried out on the product or from uses outside of the EU. Competent authorities should consider this information on case-by-case basis, depending on the relevance of the climate, storage conditions, etc.

- ***Classification***

The classification and labelling should take into account the hazards posed by the product through storage. In particular, competent authorities should note that some of the risk phrases from section 2.2.6 of Annex VI of Directive 67/548/EEC may be appropriate.

3.5.2 Risk characterisation

Risk characterisation is required when the biocidal product is classified as a result of any hazards during storage or when there are other grounds for concern. In risk characterisation the competent authority should consider the information available and whether there is the potential for a significant adverse effect during or following storage of the biocidal product.

3.5.3 Risk management options

Examples of general risk management conditions which competent authorities may consider are given below. This list is not exhaustive and the biocidal product should be considered on a case by case basis. Depending on the nature of the hazard, expert judgment may be needed to determine whether or not the risks arising from the storage of the biocidal product can be properly controlled and, if so, how.

Making the product safer

- Requiring modifications to the formulation, for example through the addition of stabilisers.
- Requirements for more suitable packaging.
- Requiring a shorter shelf-life.

Professionals

- Engineering controls, for example through controlled atmosphere and temperature for storage.

3.6 COMPATIBILITY AND REACTIVITY OF THE BIOCIDAL PRODUCT WITH OTHER PRODUCTS

3.6.1 Hazard identification

Competent authorities should consider the possibility of hazardous reactions occurring under the use and disposal of the biocidal product, and the likely worst case scenario, and characterise the resulting risk. The guidance given here has been adapted from the annex to Directive 91/155/EC.

There is no simple method of predicting whether a biocidal product will react with other products or what the consequences of such a reaction will be. If a product is authorised for use with other products, the biocidal product should be compatible with these products.

- ***Biocidal product (includes any substances of concern)***

Information on the reactivity and stability of the co-formulants can be taken from their chemical structure supplemented by expert judgment, because the presence of certain reactive or labile functional groups may indicate a concern (e.g. acids/alkalis).

For products for professional users the safety data sheet should contain sufficient information to allow the competent authority (and the intended user) to identify and assess possible risks such as identifying incompatible materials. Information may also be available from a frame formulation or from a read-across from a product with a similar formulation.

- ***Active substance and substances of concern***

Information on the reactivity and stability of the active substance can be taken from its chemical structure supplemented with expert judgment.

Observations from the tests conducted on the active substance such as the partition coefficient, the water solubility and hydrolysis studies may give information on the general reactivity of the active substance with water or alcohols.

- ***Other information***

Development work carried out on the biocidal product or active substance may be relevant.

As well as the formulation of the biocidal product, competent authorities should consider the conditions and materials/ products to avoid, e.g. temperature, light, acids, bases oxidising agents etc., which may affect the reaction rate or cause a dangerous reaction.

Although a hazard may be identified, information may be available to show that in use there is no significant risk. Conversely there may be evidence available to show that although a hazard has not been identified, one may develop during storage and subsequent use. Such information may include post-marketing surveillance carried out on the product or from uses outside of the EU. Competent authorities should consider this information on case-by-case basis, depending on the relevance of the climate, use pattern, etc.

- ***Classification***

Classification is not specifically required for stability and reactivity, but competent authorities should note that some of the risk phrases from sections 2.2.6 and 3.2.8 of Annex VI of Directive 67/548/EEC may be appropriate.

3.6.2 Risk characterisation

Risk characterisation is required where:

- contact with water leads to dangerous reactions;
- the biocidal product is intended to be deliberately used with other products;
- the biocidal product is deliberately mixed with other materials before use (e.g. because it is a concentrate); or
- the proposed use pattern of the biocidal product indicates that mixing or contact with incompatible materials and preparations is likely.

Risk characterisation is not required if reactions and incompatibility are unlikely given the formulation and the likely use, storage and disposal pattern.

3.6.3 Risk management options

Examples of general risk management conditions which competent authorities may consider are given below. This list is not exhaustive and the biocidal product should be considered on a case by case basis. Depending on the nature of the hazard, expert judgment may be needed to determine whether or not the risks arising from the storage, use and disposal of the biocidal product can be properly controlled and, if so, how.

Professional use
- Engineering controls.
- Personal protective equipment.

Non-professional use
- Label warnings not to mix with unsuitable materials (e.g. acid cleaners).

3.7 VISCOSITY AND SURFACE TENSION - ASPIRATION HAZARD

As a result of developments in legislation (specifically Directive 96/65/EC), competent authorities should consider the kinematic viscosity and the surface tension of certain **liquid** biocidal products[1] to ensure that they are correctly classified in accordance with Article 20 of the Directive. The kinematic viscosity is used to classify products for aspiration hazard. The surface tension may be used to derogate from the classification requirements.

3.7.1 Hazard identification

- ***Biocidal product***

For products to which this hazard may apply, data may be obtained from a kinematic viscosity study, or a flow time study, conducted on the biocidal product. Alternatively the kinematic viscosity can be derived from the dynamic viscosity and density of the biocidal product. Data from a surface tension study on the product may be used to derogate from the classification requirements, where relevant.

If studies are not available, it may be possible to derive information from a frame formulation or from a read-across from a product with a similar formulation.

If a biocidal product does not meet the viscosity and chemical composition criteria defined in Directive 67/548/EEC, information based on practical human experience can be used to classify the biocidal product. Competent authorities should use expert judgment to decide whether to accept such information.

[1] i.e. liquid preparations (but not aerosols) containing aliphatic, aromatic or alicyclic hydrocarbons in a total concentration equal to or greater than 10%.

- ***Active substance*** *and substances of concern*

Labelling for the aspiration hazard is dependent on the physico-chemical properties of the biocidal product only.

- ***Classification***

The biocidal product should be classified and labelled with R67 for aspiration hazard in accordance with Directive 1999/45/EC (Annex V, Part B 11) or according to paragraph 3.2.3 of Annex VI to Directive 67/548/EEC.

3.7.2 Risk characterisation

Risk characterisation is required when the biocidal product is classified for aspiration hazard. Competent authorities should consider:

- whether the product is a concentrate or a ready-for-use formulation - the product may not pose an aspiration hazard in use;
- whether accidental ingestion of the biocidal product is likely under the reasonable worst case uses of the product (consider quantities and likely availability); and
- the severity and the likely consequences of ingestion.

3.7.3 Risk management options

Examples of general risk management conditions which competent authorities may consider are given below. This list is not exhaustive and the biocidal product should be considered on a case by case basis. Depending on the nature of the hazard, expert judgment may be needed to determine whether or not the risks arising from the storage, use and disposal of the biocidal product can be properly controlled and, if so, how.

Professional use

The aspiration hazard results from ingestion of the product. It is not expected that professionals will require specific risk management measures in this regard, since they are expected to have good standards of hygiene and to keep product containers away from members of the public.

Non-professional use

- Use of child resistant closures.
- Limiting pack sizes (and hence the amount of product that could be ingested).

3.8 COMBUSTIBLE DUSTS

The dust of many organic materials can explode when dispersed in air to form a cloud if an ignition source is present. In authorising a biocidal product, competent authorities should consider:

- particle size of the formulation and any dust that may be formed in use (e.g. through transport, on drying, or activities such as milling, etc.) - particles with diameters above 500 micrometres are unlikely to pose a hazard;
- available information on the ability of the dust to disperse in air and form a cloud; and
- dust explosivity test data, if available.

The risk characterisation should consider whether dusts can be formed at any stage of the life cycle of the product, and any foreseeable potential for accumulation.

Control options include:

- appropriate design and construction of process plant;
- removal or control of sources of ignition, including sources of static electricity;
- control of dust cloud formation, e.g. by a high standard of housekeeping (through removal of dust and prevention of dust accumulation), full enclosure of plant so that it is leak tight, dampening or pelleting the product, etc.;
- control and monitoring of an inert atmosphere if applicable; and
- special safety features built into equipment handling dusty materials.

Note: Assessment of inhalation hazards from dusts is dealt with in Chapter 4.

CHAPTER 4 RISK ASSESSMENT FOR HUMAN HEALTH

4.1 INTRODUCTION

A biocidal product can only be authorised if the risk assessment confirms that, in foreseeable application including a realistic worst-case scenario, the product presents no unacceptable risk to humans. Thus, a risk assessment for human health is always needed before a biocidal product can be authorised. However, no product specific risk assessment is normally required for registration of a low risk biocidal product.

Detailed guidance on the human health risk assessment of single substances is given in the Technical Guidance Document on Risk Assessment published by the European Commission (2002) and in the TNsG on Annex I inclusion. A TNsG on exposure assessment to active substances in biocidal products is being elaborated and will be placed on the ECB web page when finished at http://ecb.jrc.it/biocides/

Biocidal products are often multi-component mixtures. When assessing the overall health risks the competent authority must consider the effects arising from the formulated product itself and, if this data is not available, from the active substance(s) and individual substances of concern. Careful consideration must be given to the possibility of any enhancement of effects, due for example to vehicles/solvents or to any additive, synergistic or other effects which can reasonably be foreseen (such as those arising from metabolism and reactions to form harmful products).

The assessment should cover the proposed normal use of the biocidal product and treated material, together with realistic worst case scenarios (including reasonably foreseeable misuse, such as ingestion by a child, but not accidents). It should also include relevant production and disposal issues for both the biocidal product and treated material, if appropriate.

4.2 HEALTH EFFECTS ASSESSMENT

Risk assessment of a biocidal product should be focused on the health effects arising specifically from the product itself. This assessment is based on studies on the product or frame formulation, together with information from the evaluation of active substances and substances of concern. Where product data are not required for an effect, the assessment must be based on the known effects of the components.

Product and active substance data requirements for the 23 product types (and for substances of concern) are described in the TNsG on data requirements. An applicant should provide all the relevant data but can present scientifically based justifications for not supplying certain pieces of data, provided they are scientifically valid and acceptable to the competent authority.

The following potential human health effect end-points need to be considered as part of the product risk assessment:

- acute, repeated dose and chronic toxicity;
- irritation/corrosivity;
- sensitisation;
- genotoxicity;
- carcinogenicity;
- reproduction toxicity;
- neurotoxicity; and
- any other special properties of the active substance or substance of concern (for example endocrine disruption and immunotoxicity).

Data on the health effects of the active substance(s) that have already been evaluated by the Standing Committee on Biocides (SCB) for Annex I or IA inclusion or for addition to Annex I of

Directive 67/548/EEC (or modification of an existing entry in Annex I of Directive 67/458/EC) do not need to be re-assessed. The conclusions of the SCB on, e.g., NOAELs for various end-points as well as agreed hazard classification according to Directive 67/548/EEC must be used.

The purpose of hazard identification is to identify the inherent capacity of a biocidal product for causing adverse effects. Assessments should be carried out in accordance with appendices 4.1-4.7 of this document, and regarding assessment of individual substances the relevant parts of the Technical Guidance Document on Risk Assessment (European Commission 2002).

The hazard identification should describe all the information needed to determine the dose-response (concentration-effect) assessment, to enable the product to be classified and to enable a risk characterisation to be conducted and margins of exposure to be determined. Therefore, information is required not only on relevant NOAEL, LOAELs or LD50 values but also on the clinical effects, their severity and the doses at which they occurred as well as information on endpoints for which thresholds for effects do not exist.

Normally, only limited hazard data for the biocidal product will be available and in many cases the hazard classification of the product and NOAELs will have to be based on data for the constituents according to Directive 1999/45/EC. However, product data take precedence where they are available for classification. As a check, the hazards identified from product data (if available) should also be compared to those predicted using Directive 1999/45/EC (where applicable).

Biocidal products sometimes contain two or more active substances or substances of concern that may have additive, synergistic, antagonistic or other combination effects. It is the responsibility of the applicant to obtain relevant information (e.g. from the literature or data on similar products), and if combination effects are suspected, further product data may be required (bearing in mind the need to minimise unnecessary animal testing). The competent authority must consider whether such effects are likely to occur or can be predicted. In general, effects on the same target organ from different substances should be treated as additive unless better information exists. Substances that have effects on different target organs should be treated separately. Greater weight should be given to data on the product if these are available. If the results of any hazard identification study on the biocidal product itself are significantly different from those predicted using Directive 1999/45/EC (where relevant), then expert judgement will be required in determining other effects for which product data are not available and deciding whether further product data are required.

Figure 4.1 summarises the points that need to be considered for the hazard identification procedure.

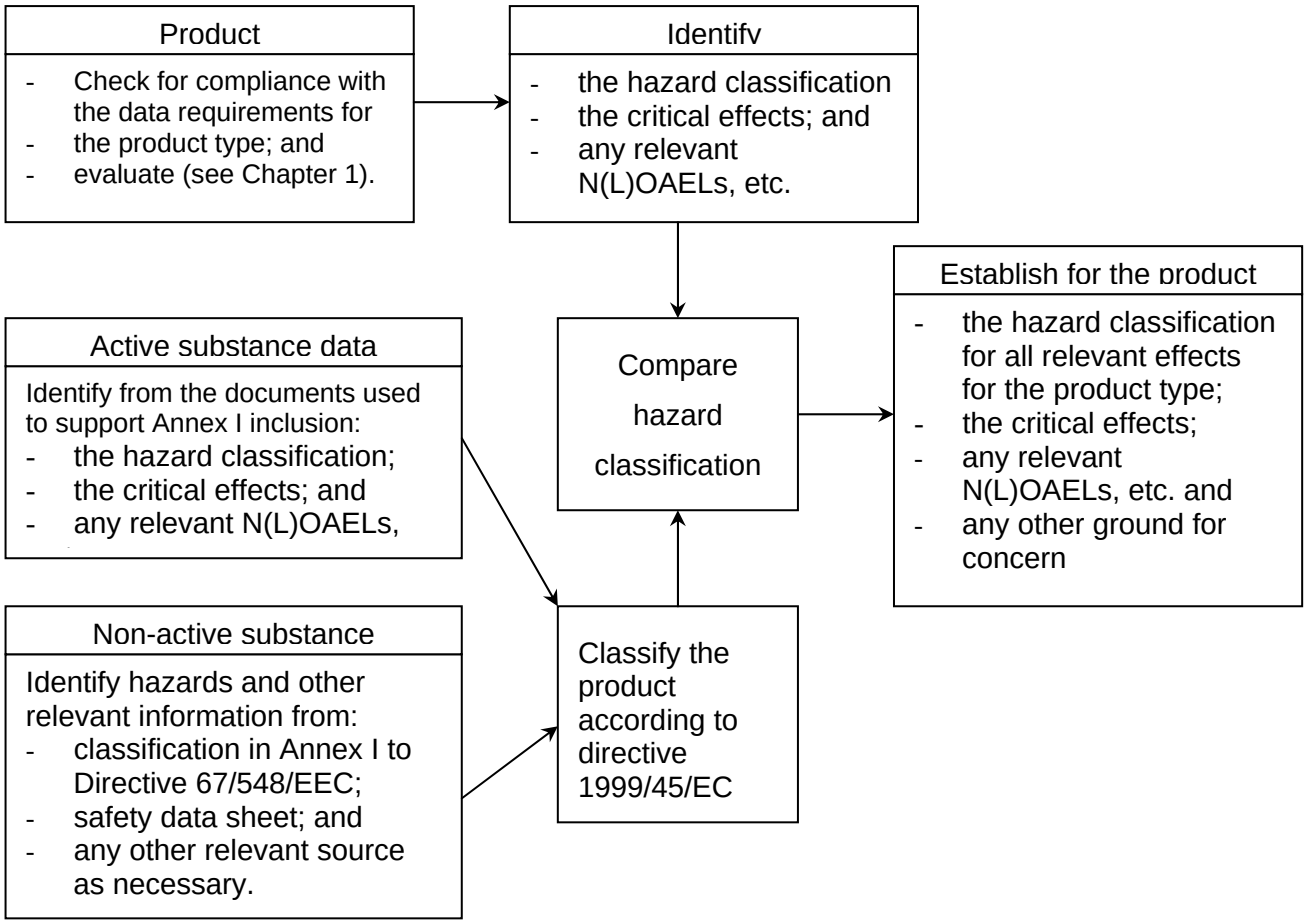


Figure 4.1: ***Summary flow chart of hazard identification procedure***

4.3 EXPOSURE ASSESSMENT

An exposure assessment shall be carried out for each of the human populations for which exposure to a biocidal product occurs or can reasonable be foreseen such as professional users, non-professional users and humans exposed indirectly via the environment. The objective of the assessment shall be to make a quantitative estimate of the dose/concentration of each active substance or substance of concern to which a population is, or may be exposed during and after use of the biocidal product. Exposure can be either primary (application), secondary (non-users, bystanders, people sometimes not being aware of exposure) and/or via the environment (consumer exposure). The likely exposure depends on how the product is intended to be used. Guidance on the exposure estimation for different product types is given in the Technical Notes for Guidance on the “Human exposure to biocidal products”. A detailed description of the pattern of use of the biocidal product should be submitted to give information in detail on how the product is likely to be used and how populations are exposed (categories of human populations exposed, duration and frequency of exposure, routes of exposure, human habits, practices as well as the technological processes).

The possible combinations of exposure of a person from professional and non-professional use of a product, and/or via the environment and by different exposure routes should be considered in each case. It is important to recognise that simple summation of precautionary estimates can lead to gross overestimates of the likely exposure which should be considered if revising the exposure estimate. The results of the quantitative exposure assessment are taken forward to the risk characterisation where they are combined with the results of the effects assessment in order to decide whether or not there is concern for the human population exposed to the substance.

4.3.1 Methods of exposure assessment

The potential exposures may be measured or modelled. Exposure measurements represent precise observations for a limited number of cases. They can be carried out in the workplace, in the residential environment or through laboratory or workshop studies. Further details are issued in the

TNsG on human exposure which is expected to be finalised in 2002 and will be available at the ECB home page at http://ecb.jrc.it/biocides/.

In the absence of representative measured exposure data or data on analogous substances or products, exposure must be estimated using recommended modelling approaches (suitable validated exposure models). Exposure can be estimated from underlying physical processes, the physico-chemical properties of the chemical, the characteristics of the formulation and an understanding of the nature of the contact with the chemical. Specific models for estimating human exposure following the use of biocidal products are still under development. Until specific validated models are available, models and risk scenarios developed for other regulatory purposes may be used, with suitable expert judgment.

In both cases it may be possible to use existing information on preparations with analogous use and exposure patterns or analogous properties to the biocidal product.

Combined exposure for one person occurs as a consequence of that person being the member of different exposure populations (e.g. primary exposure as worker and secondary exposure as bystander). Where this scenario is considered relevant, exposures should be totalled and carried forward to the risk characterisation.

4.4 RISK CHARACTERISATION

The competent authority must evaluate on the basis of the applicant's risk characterisation, the likelihood that an effect on human health will occur at the expected exposure on the basis of the applicant's risk characterisation. The evaluation should be quantitative if an exposure threshold for the effect can be defined. In general, the comparison of exposure with potential health effects is done separately for each population group exposed (by the dermal, inhalation and/or oral routes, as relevant) and for each component that gives rise to concern. Thus, not all effects have necessarily to be covered by detailed risk assessment. Specific aspects of risk characterisation are presented for each effect in Appendices 4.1-4.7.

Risk characterisation of a specific effect is necessary when there are reasonable grounds for concern. Beside identified hazards that lead to classification and labelling of the product it also includes:

- where the exposure assessment indicates that exposure by a relevant route or to a relevant population can occur:
  - if a substance is classified for certain effects (acute effects, carcinogenicity, genotoxicity or reprotoxicity) but is not present at a concentration high enough for the product itself to be classified;
  - if repeated exposure can occur;
  - when a classified component can increase in concentration following application (e.g. through evaporation of solvent);
  - where other information indicates that a hazard may still exist (e.g. human data);
- use by non-professionals (all relevant critical end-points must be considered in such cases); and
- effects for which classification criteria have not been developed (e.g. endocrine or immunological effects).

4.4.1 Quantitative Human Health risk characterisation

Quantitative risk characterisation should be carried out in the first instance assuming no use of personal protective equipment (PPE) or respiratory protective equipment (RPE). Assessment factors taking into account the protective effects of PPE and/or RPE can be used to refine risk characterisations for appropriate endpoints if no other risk management is adequate to reduce risk to an acceptable level. The need for the wearing of personal protective equipment as the only means of reducing the risk from a product to an acceptable level would exclude the possibility of authorisation for use by the general public.

Where a critical effect is threshold-based and exposure data are reliable, quantitative risk characterisations should be carried out. The most appropriate endpoint(s) for use in risk characterisation must be identified and then compared with the exposure estimate for the relevant use situations. Until sufficient experience has been achieved the risk characterisation should be performed using both the MOE (margin of exposure) and the AOEL (acceptable operator exposure levels) approach as described in the TNsG for Annex I inclusion.

NOAELs for active substances will have already been identified by the SCB, except for procedures under article 15 of Directive 98/8/EC. The competent authority will need to identify critical NOAELs for other substances of concern. In all cases the choice of a NOAEL should derive from the identification of the critical effect in the most relevant and sensitive animal species in the appropriate exposure time. Consideration then needs to be given to the overall assessment of the product, and whether effects should be considered to be additive or (in rare cases) synergistic or antagonistic. It is important that consideration is also given to any vehicles/solvents used and the likely effects of these on bioavailability (taking into consideration the route, toxicokinetics, frequency, duration and amount of likely exposure for the population being considered)

When data are lacking for a relevant route of human exposure, the possibility of using route:route extrapolation may be considered. Data on toxicokinetics identifying differences in bioavailability and kinetics and metabolism (e.g. first pass metabolism) and on dermal penetration take on extra significance. Competent authorities should very carefully consider the need for further route-specific studies.

4.4.2 Qualitative risk characterisation

Where it is not possible to determine a NOAEL or a LOAEL (e.g. for effects where it is prudent to assume the absence of a threshold such as genotoxicity and genotoxic carcinogenicity) risk characterisation needs special attention and shall be conducted qualitatively. The likelihood that the effect will occur has to be evaluated on the basis of a qualitative estimate of the likely exposure levels, routes, duration and frequency. If the likely exposure is not significant or prolonged, and all available opportunities have been taken to reduce exposure to a very low level, authorisation may be possible (particularly when the benefits of using the product are taken into account). Expert judgement will be required. The same principle is usually applied to effects such as skin and eye irritation, and skin sensitisation.

4.4.3 Decision making

Initially, it is useful to assess the risk on realistic worst case assumptions. If for the MOE approach there is a satisfactory margin between the predicted exposure and the NOAEL or LOAEL the risk assessment for humans does not need to go further and the biocidal product can be authorised for that use. For the AOEL approach an acceptable operator exposure level, derived from the most relevant

NOAEL under consideration and the appropriate safety margin must not be exceeded by the exposure level to grant an authorisation. As long as both approaches have to be used both should arrive at pass criteria for approval.

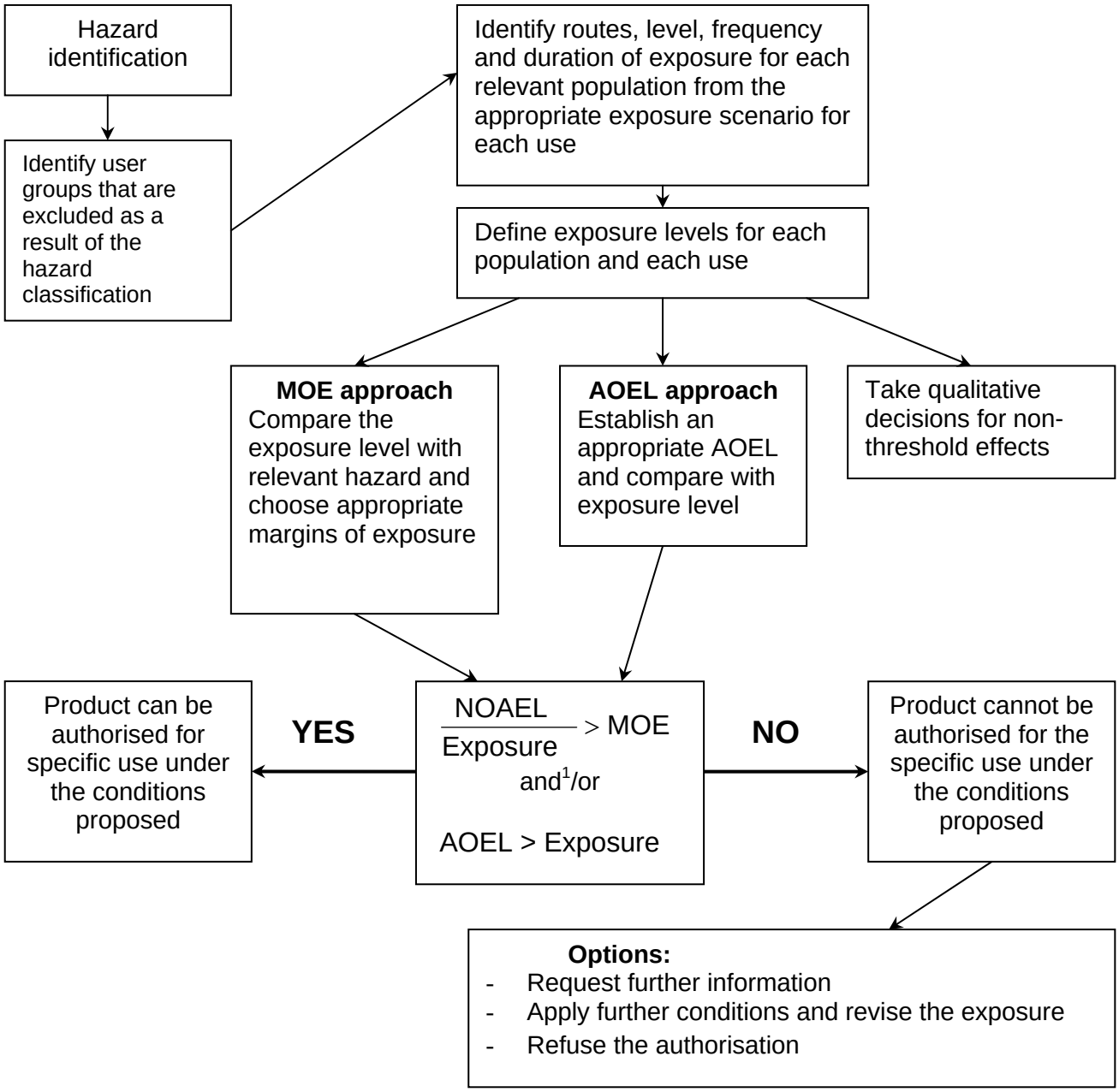
If the biocidal product cannot be authorised on the basis of realistic worst case estimates, the competent authority must consider the likelihood of the occurrence and the severity of adverse effects, the acceptability of the risk at more typical exposures and the ease of exposure control.

The margin between the NOAEL or LOAEL and the exposure may be revised using further data (in terms of the hazard, or exposure, or both), or risk reduction measures may be imposed that will reduce the risk to an acceptable level. However, the applicant should have incorporated all relevant risk management measures into the design of the use of the product at the time of submission of the application for authorisation.

Examples of further risk reduction measurements are:

- limiting the concentration of the active substance in the product;
- changing the formulation type (e.g. adding a dust suppressant);
- changing the form of packaging (e.g. enclosing the product);
- labelling (e.g. restrictions on the method of use); or
- limiting the container size.

Before deciding that further data are required, the competent authority must ensure that the best possible estimates of both exposure and effect have been used in the risk assessment process so that the decision is clearly justified. Careful thought must be given as to how useful the additional data will be. In any event, the necessary information should be obtained using the least amount of testing, particularly if it involves vertebrate animals.



[1] See under 4.4.1 Quantitative Human Health risk characterisation and 4.4.3 Decision Making. For both sections the relevant information is at the end of first paragraph.

Figure 4.2: Summary flow chart of risk characterisation procedure

CHAPTER 5 RISK ASSESSMENT FOR THE ENVIRONMENT

5.1 GENERAL INTRODUCTION

In accordance with Article 5(1)(b) of the Directive Member States shall only authorise a biocidal product if it has no unacceptable effect itself, or as a result of its residues, on the environment having particular regard to:

- its fate and distribution in the environment; in particular contamination of surface waters (including estuarine and seawater, and sediments, where relevant), groundwater and drinking water, and
- its impact on non-target organisms.

In addition, it must have no unacceptable effects on human or animal health through drinking water or food. A risk assessment for environmental effects will therefore always be needed before a biocidal product can be authorised.

Detailed guidance on the environmental risk assessment of single substances, which need assessment in the biocidal product, is given in the Technical Guidance Document on risk assessment, and general guidance on risk assessment of the product in Annex VI of the Directive. The Technical Guidance Document does not include a generic scenario for the estuarine environment, as the assessment is considered sufficiently covered by the inland and marine scenarios. However, the risk assessment principles described pertain to this environment as well and risk assessment of biocides may thus be performed for estuaries if needed. This section does not seek to reproduce the detail given in these documents. It presents guidance on how the conclusions from earlier considerations of environmental effects, usually on the active substance(s) and substance(s) of concern, or with available studies on the biocidal product or frame formulations, are used in assessing risks from the biocidal product.

Biocidal products are often multi-component mixtures. When assessing the overall environmental risk, the competent authority must consider the effects arising from the active substance(s) and individual substances of concern (including metabolites, and reaction and degradation products where relevant). Careful consideration should be given to the possibility of any enhancement of effects, due for example to vehicles/solvents or to any additive, synergistic or other effects which can reasonably be foreseen (such as those arising from degradation, food residues and reactions to form harmful products).

Whilst evaluating data for the product, consideration should be given to other relevant technical or scientific information which is reasonably available with regard to the properties of the biocidal product, its components, metabolites, or residues. Figure 5.1 summarises the points that need to be considered. In addition, justifications submitted by the applicant for not supplying certain data should be evaluated.

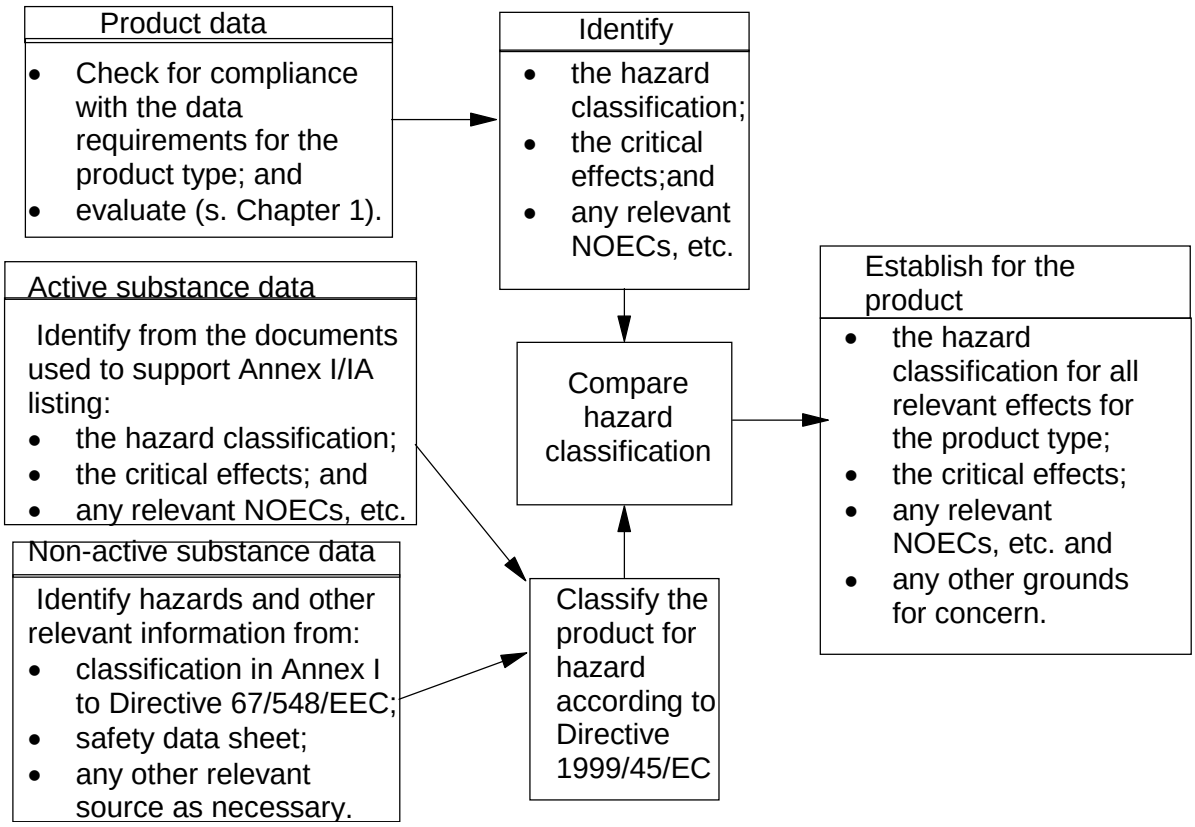


Figure 5.1: ***Summary flow chart of hazard identification procedure***

Where the biocidal product contains two or more active substances or substances of concern, and there is the potential for direct exposure of a particular compartment, the competent authority should take into account possible additive, synergistic or other effects.

The assessment should cover the proposed normal use of the biocidal product and treated material, together with realistic worst case scenarios but not release arising from accidents. Emission scenario documents have been prepared (or are under preparation) for all of the most relevant product types and/or major uses. The assessment should also include relevant production and disposal issues for both the biocidal product and treated material.

Annex VI of the Directive gives specific details on criteria to use on different protection goals. They are detailed in Chapter 5.3 of the TNsG on Annex I inclusion. They should be followed when deciding on the authorisation of the biocidal product, i.e. also any substance of concern should comply with the criteria.

5.2 RISK ASSESSMENT FOR PRODUCTS

The BPD requires that the risks from products are assessed. For products consisting of an active substance with a simple diluent, the assessment of the active substance is sufficient to cover the risks from the product. Guidance on the assessment of active substance and other constituents can be found in the TNsG on Annex I inclusion and the Technical Guidance Document on risk assessment [EC 2002]. A different approach is needed for products containing two or more active substances or when the product is a complex formulation (cf. Annex VI Par. 15 and 53 of the Directive). A formulation can also change the properties of the active substance in the environment (fate and behaviour, effects). An interaction between the active substances might result in additive, synergistic or antagonistic effects that would remain unaccounted for if the active substances were assessed

separately. The same situation arises if the product contains a diluent enhancing the bioavailability of the active substance. It could then be argued that it is necessary to test the effects of products towards ecosystems whenever it is apparent that there is an interaction between the components of the product.

Upon release into the environment though, the individual components will usually have very different transport and transformation behaviour. The integrity of the initial composition of the product will not be maintained. Thereby the interaction between the constituents can be disrupted as well. Even before reaching the environment, the composition of the product can be changed. For example, after application of a wood preservative product, some ingredients will interact with the wood while others may e.g. evaporate. If the treated wood is used in contact with water, the leaching rate out of the wood will be specific to each of the components. The relative concentration of each component in the leachate from the wood will be very different from its relative concentration in the initially applied product. Moreover, artefacts from ingredients of a biocidal product and constituents of the wood (e.g. phenolic resins) may be formed during treatment (e.g. pressure and elevated temperature during impregnation of timber). In particular, when complex interaction between the ingredients of a biocidal product and the treated material and/or the environmental matrix is likely, it will be hardly possible to predict the ecotoxic potential of an aqueous leachate, even from tests on the thorough product. Additional to the TGD Risk assessment this approach may serve as a valuable method for screening any unforeseen effect, [cf. provision of TNsG on Data Requirements, April 2000 – chapter 2.5 p. 74], although being not fully in line with the risk assessment scheme, as laid down in the TGD on risk assessment of chemicals, which does not take into account complex formulations and treated materials. Such kind of tests might in particular be used in the refinement of risk assessment for products, under relevant field and use conditions.

In other situations, a more direct contact of a biocidal product with an environmental compartment is possible. For example, a masonry preservative applied by spraying of aerosols can give rise to spray drift and deposition onto soil. In the same way, the use of a cooling water preservative in a once-through system can cause direct release of all product components in their respective initial composition to surface water.

Two distinct approaches towards assessing products can therefore be proposed.

(1) For substances whose composition changes radically before reaching an environmental compartment, all relevant components of the product need to be assessed separately, which means that PEC/PNEC ratios need to be estimated for each component. For complex mixtures, a risk assessment scheme has been proposed for petroleum substances [Technical Guidance Document on risk assessment, EC 2002]. For aromatic and aliphatic hydrocarbons, it can usually be assumed that they act by the same mode of action upon aquatic organisms, which is by non-polar narcosis and the contribution of each component to the risk of the product is therefore additive. A PEC/PNEC ratio for the product in a compartment can be estimated as:

$$(PEC/PNEC)_{product} = \Sigma\ (PEC/PNEC)_{components}$$

A recently published literature review (Deneer, 2000) has shown that this “concentration addition” model is also valid for mixtures of pesticidal active substances. Based on test results on different aquatic organisms from 202 mixtures of two or more pesticidal active substances, the “concentration addition” model predicts correct effect concentrations (within a factor of two) compared to the experimental results for more than 90% of the mixtures. Even for combinations of compounds with presumably dissimilar modes of action, correct results were predicted for more than 90% of the mixtures. It can therefore also be suggested that the “concentration addition” model can be used for biocidal products.

(2) For products for which a direct exposure of a given compartment is possible, test results with whole products can be taken into account. A PEC and a PNEC can be derived for the whole product as for a single substance and a corresponding risk characterisation can be performed for the product:

$$(PEC/PNEC)_{product} = PEC_{product}/PNEC_{product}$$

The approach is usually not possible throughout a risk assessment for all compartments.

5.3 FURTHER CONSIDERATIONS IF THE PEC/PNEC RATIO IS ABOVE 1

In general, if the PEC/PNEC ratio for any given environmental compartment or population is equal to or less than one, the conclusion shall be that the risk is acceptable. If the PEC/PNEC ratio is greater than one, the competent authority must judge, based on the size of that ratio and other relevant factors[2], if:

- further information and/or testing are required to clarify the concern;
- conditions or restrictions of use can be applied to reduce the risk to an acceptable level; or
- the product cannot be authorised.

5.3.1 Further information and/or testing

In cases where the PEC/PNEC ratio is greater than one, the competent authority should consult the applicant to see if additional data on exposure and/or ecotoxicity can be obtained in order to refine the risk assessment. However it is the duty of the applicant to supply data and provide a revised risk assessment.

If the competent authority considers that the risk characterisation can be revised but the necessary data are not available, further information and/or testing will be required. A decision must be taken on a case by case basis as to whether both the PEC and PNEC need to be revised or only one of them. Consideration should be given to which of the parameters will be more sensitive to revision as a result of further testing. **Efforts should be made to refine the PEC before further data from vertebrate animal studies are requested to refine the PNEC.** This iterative approach has precautionary aspects as data gaps are filled by worst-case assumptions or high assessment factors.

The decision by the competent authority to request the generation of additional data should be transparent and justified and should be based on the principles of lowest cost and effort, highest gain of information and the avoidance of unnecessary testing on animals. Guidance on which tests to conduct is given in TNsG on data requirements.

There may be cases where, assuming PEC values are realistic and cannot be refined further (e.g. by representative measured data), any further testing which lowers the assessment factor cannot decrease the PEC/PNEC ratio below one. In such cases, testing is not necessary, because the product in question poses an unacceptable risk.

5.3.2 Conditions or restrictions of use

In some instances a route of likely exposure may be prevented, or the exposure reduced, by the use of appropriate control/preventative measures. Examples include use of proofing to prevent wildlife from entering areas where the biocide is being applied. The risk assessment should determine the measures necessary to protect humans, animals and the general environment during both the proposed normal use of the biocidal product and in a realistic worst case situation. The proposed instructions for use of the biocidal product, including procedures for cleaning application equipment, must be such that the likelihood of accidental contamination of the environment is minimised. The competent authority shall also take the necessary measures to ensure that the applicant proposes packaging and,

[2] The PEC/PNEC ratio should always be considered with due regard to a chemical's specific properties (e.g. persistence and bioaccumulation) and the degree of confidence in the exposure data. Expert judgment is important.

where appropriate, the procedures for destruction or decontamination of the biocidal product and its packaging or any other relevant material associated with the biocidal product, which conforms to the relevant regulatory provisions.

5.3.3 Cases where the product cannot be authorised

If further refinement of the PEC/PNEC ratio does not reduce its value below 1, and conditions or restrictions cannot reduce exposure of the compartment or non-target organisms to an acceptable level, then the product cannot be authorised for the particular use. (This decision may be reversed under the conditions laid down in the TNsG on Annex I inclusion). However, in this decision also the benefit of the use of the biocidal product must be taken into account.

An authorisation shall not be given for a biocidal product if the risk assessment confirms that, in realistic worst-case use, the biocidal product presents an unacceptable risk to non-target animals. It shall not be given either if the risk assessment confirms that the active substance, or any substance of concern, or any degradation or reaction product present an unacceptable risk in any of the environmental compartments, water (including sediment), soil and air. This shall include the assessment of risks to non-target organisms in these compartments.

CHAPTER 6 ASSESSMENT OF OTHER UNACCEPTABLE EFFECTS

6.1 GENERAL INTRODUCTION

6.1.1 Background

The evaluation of unacceptable risks to humans, animals and the environment (including to non-target organisms (e.g. beneficial insects) and the atmosphere (e.g. ozone depletion)) are dealt with in Chapters 3-5. This chapter provides guidance for the assessment of other effects which contribute to the overall performance of the product but which are not directly linked to its intrinsic properties or efficacy.

In accordance with Article 5 (1) (b) of the Directive, the competent authority must assess the potential unacceptable effects of the product on target organisms, such as unacceptable resistance, and any unacceptable suffering caused by use against vertebrates. Annex VI also requires competent authorities to evaluate the possibility of any other unacceptable effects occurring if there are indications that they may do so.

6.1.2 Objective of the guidance

This chapter, used together with expert scientific judgment, gives guidance for competent authorities on the evaluation of unacceptable effects data so they can decide how these will influence the authorisation.

The range of potential unacceptable effects is very broad and there are no internationally agreed guidelines for their assessment. In addition, relevant information can be complex, and may be obtained from a variety of sources. Consequently the guidance is of a general nature and information for each product must be assessed on a case by case basis. Detailed information about specific properties and effects is available in a variety of reference texts (e.g. Buckle & Smith, 1994).

Resistance, humaneness and 'other' effects are dealt with in three separate sections, and particular attention is paid to the types of data which might be available and the decision making process. **In all cases it is the responsibility of the applicant to provide all relevant information for the competent authority, in a structured and readily accessible format.** The guidance is valid for all countries in the European Union. However, situations within certain territories may vary due to different working practices, environmental conditions, and the relevance and breeding biology of the target species.

6.2 RESISTANCE

6.2.1 Introduction

Annex IIA of the Directive requires information on the occurrence and possible development of resistance, and appropriate resistance management strategies, for chemical active substances. Annex IIB of the Directive requires information on any known limitations on efficacy of the biocidal product including resistance.

The evaluation of resistance must be done on a case-by-case basis taking into account the possible development of resistance (see chapter 6.2.3.3). A number of factors need to be considered:

- **Resistance**

This term refers to a genetically inherited characteristic which cannot be acquired during the lifetime of the individual. It may be defined as a significant loss of performance due to the ability of a target organism to withstand the effects of normally applied concentrations of a biocidal product. The term resistance is often used loosely, and incorrectly, to explain treatment failure which may be attributed to inadequate treatment, behavioural resistance, target pest tolerance or other contributory factors.

The level of resistance of a particular genetic strain can be quantified in laboratory studies by the *resistance factor (or ratio)*, which is the number of times the amount of product given to a resistant strain has to be increased above the normal dose to achieve the same effect as that dose in the normal strain. Cross-resistance can also occur.

The level of resistance, its geographical spread and frequency of occurrence can all change with time for any one biocidal product (indeed there can be a wide variation in resistance levels across a single country). It should be noted that some biocides will continue to have commercial usefulness even at reduced levels of efficacy towards a particular target species.

- **Cross-resistance**

  Cross-resistance, where target organisms resistant to one active substance are also resistant to others to which they have not previously been exposed, can also occur (particularly for active substances from the same chemical class).

- **Behavioural resistance**

  Treatment failure as a result of behavioural resistance can be displayed in a number of ways, e.g. bait preference and neophobia. Behavioural resistance does not involve actual systemic resistance to a biocide's action, and it can be reversible.

  An example of bait preference is the altering of feeding habits by ants from protein- to carbohydrate-based baits. Obviously if bait preference changes or is different depending on the stage in the life cycle of the pest, then the biocidal product will have varying degrees of efficacy.

  Neophobia or "new object reaction" is exhibited by some rodent species, and refers to individuals who avoid a new object (such as a bait) placed in the environment until they become used to it. As a result the individual may only take small, sub-lethal amounts of bait, and may consequently avoid the bait if it learns to associate it with an unpleasant response.

  Some of these behavioural aspects can be anticipated and tested through experimental design when biocidal products are being developed but others can only be overcome by the expert use of the biocide by trained professional operators.

- **Tolerance**

  Tolerance can be defined as the ability of an organism to withstand the effect of a normally lethal dose of a biocide by ingestion of increasingly large sub-lethal doses over a short period of time (e.g. due to enzyme-induction). An example of this has been reported for the use of alphachloralose against mice.

  Tolerance is different from resistance because if the normal lethal dose is administered as a single dose the individual will die (resistant individuals would not).

The competent authority must therefore evaluate the nature and extent of both existing and potential resistance to an active substance in the biocidal product by the target organism, and anticipate its development, so that a balanced authorisation decision can be made. It should be noted that many products will be intended for use against a range of target species.

6.2.2 Types and availability of data

Whilst data should be relevant to the target species, requirements must be flexible because of the variable nature of resistance. Evidence of resistance may come from:

- laboratory studies specifically addressing resistance (including simulated use and dose-response tests), e.g. efficacy studies on strains which are known to be resistant to the active substance. For vertebrates there may be specific, non-lethal methods of resistance assessment, such as blood clotting tests for rodenticide anticoagulants; or
- field studies (in which data are generated using the product in the actual service conditions and in the manner described on the product label). Field observations may also be provided as additional evidence (however, see section 6.2.3.1).

If valid data are available in connection with resistances to existing active substances, these should be added or references made to the relevant publications. These data will usually be available for existing active substances following review for Annex I/IA inclusion, but it is unlikely that there will be any data for new active substances. However, the competent authority may be able to make a decision based on relevant information on products containing an active substance from the same chemical class with a similar mode of action. Similarly, data are not necessarily required for every product because an extrapolation may be possible from data on similar products containing the same active substance.

6.2.3 Evaluation

6.2.3.1 General principles

The applicant's data submission should include, where relevant, all information necessary to allow a reasonable evaluation of target organism resistance to the biocidal product at the recommended dose/application rate, when used in accordance with the label instructions. Data on the active substance itself will have been considered at the Annex I/IA inclusion, and must not be re-interpreted. Where product data are provided, the competent authority should perform the evaluation with regard to:

- test objective;
- study content and methodology (including use of controls and reference products, test procedures, results and analysis, etc.);
- acceptability of the method;
- robustness;
- quality assurance;
- completeness; and
- adequacy (i.e. its reliability and relevance to the proposed use of the candidate product).

Expert judgement is needed for proper interpretation of resistance data. For example, data generated on laboratory strains may not be reliably extrapolated to wild individuals in the field situation. In addition, field observations should be viewed with caution. For example, persistent infestations are often caused by re-invasion from untreated surroundings or poor application techniques rather than resistance. Apparent resistance may also be caused by behavioural factors, such as neophobia (as is often the case for rats). For this reason, the competent authority will need evidence to show that other possible causes of treatment failure have been excluded. Corroborating data would usually also be needed from laboratory tests on captured specimens.

Conclusions about the performance of the product should usually be valid for all areas of the Member State in which it is to be authorised, and all conditions under which its use is proposed. However, where there are pockets of resistance within a Member State’s territory, the competent authority should decide whether continued use of the product can be allowed elsewhere within the territory (e.g. it may be possible to contain the resistant pockets by a suitable management strategy (see 6.2.3.4)). Decisions may also need to be made regarding read-across of resistance data for similar species, especially where the intention is to extend the label claim.

6.2.3.2 Cross-resistance

The problem of cross-resistance also needs to be addressed for products. This will be necessary when the active substance has a similar mode of action (or belongs) to a particular chemical class, which is known to cause resistance problems in particular situations (e.g. pyrethroids used to control fly problems in intensive animal units). Information on known resistance problems with related active substances should be provided in meeting the Annex IIA data requirements for the active substance. In such cases, the competent authority should ensure that adequate data on the activity of the product against these resistant strains have been provided.

6.2.3.3 Development of resistance

As well as assessing the immediate likelihood of resistance for the product, the competent authority must, where relevant, evaluate the possibility of the development of resistance to the active substance by the target organism. This will normally be considered at the Annex I/IA inclusion, but it may be appropriate to consider this for particular products as well. However, it is likely that resistance development will only become evident as the product is used. The ability of laboratory tests to predict such development can be relatively low, because they often show only the symptoms of resistance rather than the underlying cause or because resistance has not been established in the genetic pool within the relatively short duration of the test. Factors that may promote the development of resistance are related to the mode of action of the active substance, the lifestyle of the target organism and the proposed use pattern of the biocidal product. Examples of such factors include:

- active substances that act by a “one site” (as opposed to a “multi-site”) mechanism;
- target organisms with rapid breeding cycles (i.e. many generations per year);
- pest infestations that are confined in some way (where resistant individuals are unable to disperse and so remain localised);
- use of the biocide over large areas and/or for long periods with frequent application rates (creating a continual evolutionary selection pressure on the target population); and
- use of a number of biocidal products against the same pest which contain either the same active substance or active substances with similar modes of action.

6.2.3.4 Resistance management strategies

Where resistance is considered likely to be a problem for use of a particular active substance at the Annex I/IA inclusion, an overall management strategy should be implemented in order to help delay or reduce the likelihood of resistance development, and minimise any consequences. The competent authority must evaluate the proposed use of the product in the light of any strategy agreed by the Standing Committee on Biocides (SCB), and where necessary ensure that the applicant submits a supplementary management strategy for particular products (such a strategy may be based on the principles of integrated pest control, but should be distinguished from actions which are tailored to control site-specific resistant infestations).

The competent authority must assess these proposals to determine their acceptability, and whether they are appropriate to the use of the product, on a case by case basis. For example:

- a strategy which aims to limit the number of resistant individuals rather than eradicate them may be suitable for housefly control in intensive animal units but would not be acceptable for the control of cockroaches in food-handling premises.

Proposals for resistance management could include:

- the incorporation of appropriate label warnings or provision of other labelling advice, e.g. the product should only be used over a distinct period of time, alteration with other products not containing the same active substance is recommended;
- specific conditions of authorisation, e.g. restrictions on the use of the active substance(s) in a particular situation or geographical area.

Post-authorisation resistance monitoring will normally be required for any product authorised in this way to determine the effectiveness of the strategy.

6.2.4 Examples

Resistance should be considered for all product types where there is a possibility of its development (this will usually be identified at the Annex I/IA inclusion for the active substance). The following list gives some examples of product types with well-known resistance problems, but it is not exhaustive.

Product type 14: Rodenticides
e.g. resistance of rats to first and second generation anti-coagulant rodenticides.

Product type 18: Insecticides, acaricides and products to control other arthropods
e.g. resistance of houseflies to synthetic pyrethroid insecticides in intensive animal units.

In addition, biocidal products for control of micro-organisms may be prone to resistance problems. Relevant product types include disinfectants (Product types 1-5), preservatives for liquid cooling and processing systems (Product type 11), slimicides (Product type 12) and metal-working fluids (Product type 13).

6.2.5 Decision making

Having evaluated all the available data, the competent authority must determine whether resistance to the biocidal product is likely now or in the future, the significance of this in relation to performance, and possible management strategies to control the problem and minimise any consequences. Based on this assessment the competent authority will decide which of the following will apply:

- authorisation/registration can be granted without specific conditions, because the data demonstrate a level of resistance which will have little effect on product performance, and the potential for any further development of resistance is low;
- the level of resistance or its development may affect product performance, but the biocidal product can be authorised/registered subject to specific conditions (e.g. a management strategy) or for a specific time period (followed by a review);
- a decision on authorisation/registration cannot be given until additional data/information are available to resolve a particular point or item of concern; or
- the biocidal product cannot be authorised/registered because product performance will be unacceptably affected by resistance, and/or the potential for the development of resistance is of concern and the proposed management strategy is considered inadequate to control it.

This decision must be a reasoned balance between the benefits of using a product and the loss of performance caused by any resistance problems (real or potential), taking into account the availability of other control methods and the implications of the loss of the product through refusal of authorisation (the wider the diversity of active substances that are available, the easier it will be to control future resistance problems).

6.3 HUMANENESS

6.3.1 Introduction

"Humaneness" is a term which is difficult to define, but it infers the degree of pain, distress and discomfort to the target organism. Article 5(1)(b) of the Directive requires that products authorised for use against vertebrate target organisms will not cause them "unnecessary" suffering and pain. In other words, there must be a reasoned justification for the need for a product if that product is considered, from an evaluation of the submitted data, to cause suffering or pain. In particular, Annex VI of the Directive states that an authorisation for a biocidal product intended to control vertebrates will not be given unless:

- death is synchronous with the extinction of consciousness (although it is more important that exposure leads immediately to unconsciousness, and that consciousness is not regained), or
- death occurs immediately, or
- vital functions are reduced gradually without signs of obvious suffering.

The crucial aspects are the degree and length of suffering prior to unconsciousness and subsequent death. Therefore, the time necessary to obtain the death of the target vertebrate and the conditions under which death occurs shall be evaluated (Annex VI, para 48).

Annex VI also states that for an authorisation of a repellent product, the intended effect shall be obtained without unnecessary suffering and pain for the target vertebrate.

Suffering can be thought of as a specific state of "mind" which can be caused by pain or distress of sufficient intensity and/or duration. Pain can be defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage." In order to experience pain an animal has to be conscious, i.e. it must have an alert cerebral cortex. Distress can be defined as "a state where the animal has to put substantial efforts or resources into adaptive responses to challenges in the environment, and is failing to cope." It is usually caused by extremes in the animal's physical and social environment (e.g. heat or social aggression), and the degree of distress varies with the ability of the animal to cope with these. Some clear criteria for defining when changes indicate severe distress have been published (e.g. Anon, 1994).

Pain and distress are states of adverse subjective experience and cannot be measured directly. However, an assessment can be made based on an animal's overall pattern of physiological and behavioural responses, a knowledge of the mode of action of the active substance, and post-mortem reports.

6.3.2 Types and availability of data

6.3.2.1 General requirements

No internationally agreed test guidelines exist. However, it is recommended that the competent authority makes decisions on humaneness based on existing data wherever possible, including:

- any information relating to the experiences of humans clinically treated with, or otherwise exposed to (e.g. at the workplace), the candidate product or other products containing either the same active substance or ones with similar chemical structures and/or suspected modes of action (it is assumed that conditions which are known to cause pain in humans do so in other vertebrates unless convincing evidence is available to the contrary); and
- any information on the humaneness, toxicity and efficacy of the candidate product or its active substance, or of active substances with similar chemical structures and/or suspected modes of action, in the target species or any related species, which may be of use in assessing the humaneness of the product. In this respect, emphasis should be placed on using **the existing data set** for the active substance and the product, and literature searches. Humaneness information should, where possible, be obtained from the acute mammalian toxicity tests, acute ecotoxicity tests and/or efficacy studies on the product using laboratory strains of the target species.

The competent authority must assess the relevance of this information for the candidate product, particularly where the data do not directly concern the candidate product or its active substance, or

the proposed target species. If a decision can be made on the likely suffering of wild animals based on data obtained using laboratory strains, the competent authority may decide that no further testing is required. Similarly, if the need for the product is fully justified, further testing would not be appropriate (see section 6.3.5).

Confirmatory humaneness testing of the product on the target species should therefore **not normally be required**. If, following a review of the data, the competent authority decides that further confirmatory testing is required, it should provide a full justification. Such testing should only involve small scale experiments using wild caught animals, or wild animals bred in captivity, housed in environments that approximate in important respects (e.g. temperature, lighting, food, social grouping, etc.) to the natural habitat. Procedures should initially involve low doses, in order to minimise the likely severity of suffering, and doses should not go beyond that on the proposed label for commercial use. The competent authority must inform the applicant of its decision, and if further testing is necessary, agree on an acceptable programme with them. The test programme should comply with European and national legislation on animal welfare (i.e. Directive 86/609/EEC).

6.3.2.2 Details to be included in a test report

No formal guidelines for studies to investigate humaneness exist. It is recommended that the competent authority should expect the test report to contain the following details, where relevant (this list is not exhaustive):

- details of species, genetic strain, age, sex, weight, reproductive history and origin (whether wild-caught or hand-reared, etc.) for each experimental animal;
- a description of the environmental conditions (and uncontrolled external influences) before and during trials, including diet and stocking details;
- dose levels and method of delivery (with vehicle used, if applicable, and concentration in the units expressed on the proposed product label);
- the time to death (and conditions under which death occurs, including clinical observations) after dosing for each animal, where the intended effect is to kill the target vertebrate;
- the time to insensibility after dosing for each animal, where the intended effect is to make the target vertebrate unconscious, and the time to regain sensibility prior to death or full recovery as appropriate;
- **a range of appropriate observations concerning the degree and duration of suffering while the animal is conscious prior to either death or full recovery** (e.g. for repellents and sub-lethal exposure). The circumstances, appearance, performance and behaviour patterns of test animals should be recorded as objectively as possible at regular intervals before, during and after dosing, using appropriate scales with accompanying descriptive information where relevant;
- reasons and criteria used for killing of test organisms in order to avoid unacceptable suffering (e.g. when an animal develops grossly abnormal behaviour such as self-mutilation); and
- the training and experience of personnel conducting the experiments, with details of precautions taken against observer influence.

6.3.3 Evaluation

The applicant's data submission should include all information necessary to allow an evaluation of the humaneness of the biocidal product to the target organism (including the mechanism by which the effect is obtained) at the recommended dose/application rate, when used in accordance with the label instructions. The competent authority will evaluate the data and consider the duration and severity of any symptoms caused by the proposed normal use of the product, and whether they demonstrate that (where relevant):

- death is synchronous with the extinction of consciousness[3], or
- death occurs immediately, or
- vital functions are reduced gradually without signs of obvious suffering.

Suitable criteria must be used to judge the severity of symptoms (e.g. Anon, 1994)). It should be assumed that increased severity or duration of symptoms increase the degree of distress which in turn decrease the degree of humaneness. In addition, it is essential that physiological data are assessed in the light of behavioural information because some phenomena frequently associated with pain (such as dilation of the pupils) can occur in animals after the cerebral cortex has been destroyed.

The competent authority should perform the evaluation with regard to:

- test objective;
- study content and methodology (including use of controls and reference products, test procedures, results and analysis, etc.);
- acceptability of the method;
- robustness;
- quality assurance;
- completeness; and
- adequacy (i.e. its reliability and relevance to the proposed use of the candidate product).

Expert judgment is needed for proper interpretation of humaneness data in view of the complexity of the issues. Examples of complicating factors include:

- products with analgesic properties (a target organism rendered insensitive to pain may still suffer through high levels of stress or discomfort);
- palatability (target organisms which find a product unpalatable may only receive a sub-lethal dose in the field situation, and consequently they experience different degrees of suffering than if they had taken a lethal dose);
- misleading symptoms (e.g. a decrease in blood pressure through blood loss may result in symptoms which appear to indicate sedation whereas in fact the animal may still be conscious and experiencing pain); and
- behaviour (this may be affected by factors that are not product-related, such as human disturbance or social stress, and there are differences between species, strains and individuals).

In addition, the humaneness of the entire control procedure may need to be considered on occasion, e.g. for methods that involve capture of the animal before administration of the biocidal product. In these cases, the method and competence of capture and the transfer of the animal to the application container will have at least as great an influence on the humaneness of the technique as the effects of the biocidal product itself.

Conclusions as to the performance of the product must be valid for all areas of the Member State in which it is to be authorised and must hold for all conditions under which its use is proposed. Decisions may also need to be made regarding read-across of humaneness data for similar species, especially where the intention is to extend the label claim.

6.3.4 Examples

Humaneness needs to be considered for all products used against vertebrates:

- *Product type 14:* Rodenticides
- *Product type 15:* Avicides
- *Product type 17:* Piscicides

[3] It is in fact more important that exposure leads immediately to unconsciousness, and that consciousness is not regained.

- *Product type 19:* Repellents and attractants
- *Product type 23:* Biocidal products used to control other vertebrates (e.g. moles and rabbits)

In addition, humaneness must be considered for vertebrates that are treated with biocidal products to control non-vertebrate target organisms:

- *Product type 3:* Veterinary hygiene biocidal products
- *Product type 19:* Repellents and attractants

6.3.5 Decision making

The competent authority must determine whether any suffering caused by the biocidal product is unavoidable (including any considerations for replacing the product or refusing an authorisation) and therefore "necessary" (see section 6.3.1).

For products that are intended to harm the target animal, the consideration of the humaneness data must take account of

- the type of product and its mode of action;
- the availability of alternative treatments;
- the scale of usage of the material;
- the significance of the pest;
- the presence of resistance; and
- any special factors.

For products not intended to harm the target animal (e.g. repellents), a case must be made to justify the acceptability of the humaneness data for each product.

Based on this assessment the competent authority will decide which of the following will apply:

- authorisation/registration can be granted without specific conditions, because the data demonstrate a level of vertebrate suffering which is justified by the intended use;
- authorisation/registration can be granted with conditions of use, because the data demonstrate a level of vertebrate suffering which is justified provided the conditions are met (e.g. specific methods of bait delivery to ensure that a lethal dose is administered);
- a decision on authorisation/registration cannot be given until additional data/information are available to resolve a particular point or item of concern; or
- the biocidal product cannot be authorised/registered because the level of vertebrate suffering is unjustified and cannot be reduced to an acceptable level by restrictions on use.

This decision must be a reasoned balance between the benefits of using a product and the level of humaneness, taking into account the availability of other control methods and more humane alternatives, and the implications of the loss of the product through refusal of authorisation/registration.

6.4 OTHER EFFECTS

6.4.1 Introduction

Annex VI of the Directive requires the competent authority to evaluate the possibility of any other unacceptable effects occurring if there are indications that they may do so. This section is therefore concerned with those unacceptable effects that may affect performance but do not involve target organisms. It should be noted that many possible effects that could be included in this category (such

as tainting of foodstuffs and discolouration of surfaces), whilst undesirable, are not related to product safety and so should not be considered as part of the authorisation process.

The competent authority should therefore evaluate other effects only if they are directly linked to human, animal or environmental safety, and there are indications that they may occur. It is the duty of the applicant to provide all relevant information on hazards that are not obvious from use of the product. **For most products it is expected that 'other' effects will not need to be considered.**

6.4.2 Types and availability of data

Due to the types of effects which may occur the requirements supporting data generation must be flexible. Effects data may arise from specific tests, or may be inferred indirectly from non-specific tests, but it is expected that data will often only arise from experience in use. The effects considered must be relevant to the intended use of the product when applied as directed by the label. Evidence of effects may come from:

- laboratory studies (including simulated use tests), e.g. from product development trials or tests required for either Annex I/IA inclusion of the active substance or product authorisation;
- field studies (in which data are generated in the actual service conditions and in the manner described on the product label); or
- other sources, e.g. information in industry codes of practice or safety data sheets.

When a particular effect is suspected from circumstantial evidence, a confirmatory test may be desirable. Relevant data may be available for individual product components (including the active substance), and specific information may also be available for either the candidate product or products containing similar ingredients.

6.4.3 Evaluation

The applicant's data submission should be sufficient to allow the competent authority to perform a reasonable evaluation of the likelihood of the occurrence of relevant effects at the recommended dose/application rate, when the product is used in accordance with the label instructions. In general, the competent authority should expect the applicant to have shown that they have considered all relevant effects which can reasonably be expected from the nature of the product. In addition, particularly when the effect is inferred indirectly from other data, the competent authority must assess whether it is likely to occur in real-life situations.

It is expected that expert judgment will play a large part in the proper interpretation of data. For example, some biocidal products are highly surface-specific and will not move into another material in close proximity. Where there is doubt, the competent authority may need either corroborating data, or evidence to show that other possible causes of the effect have been excluded. Conclusions as to the performance of the product must be valid for all areas of the Member State in which it is to be authorised and must hold for all conditions under which its use is proposed.

6.4.4 Example

An example of the type of effect that needs to be considered is the increased risk of corrosion of certain types of metal fixings in timber on exposure to some wood preservatives when applied wet (e.g. copper/chromium/arsenic wood preservatives can affect both ferrous metal and uncoated aluminium fittings - see BS 4072: Part 2: 1987 and BS 5268: Part 5: 1989 for further information).

6.4.5 Decision making

The acceptability of the effect depends to a large extent on the likelihood of its occurrence and its significance. Based on the assessment the competent authority will decide which of the following will apply:

- authorisation can be granted without specific conditions, because the data demonstrate that all identified undesirable effects will have little impact on product safety in practice due to their low significance and/or their low probability of occurrence;
- the undesirable effects may affect product safety, but the biocidal product can be authorised subject to specific conditions;
- a decision on authorisation cannot be given until additional data/information are available to resolve a particular point or item of concern; or
- the biocidal product cannot be authorised because product performance will be unacceptably affected even with restrictions on use.

This decision must be a reasoned balance between the benefits of using a product and the lowering of safety (real or potential) caused by the effect(s), taking into account the availability of other control methods (see Chapter 8).

In practice it is expected that no authorisation would be refused on the basis of such undesirable effects alone. Instead, authorisation is more likely to be subject to specific conditions (e.g. label warnings) which may be tied in with controls for other effects. For the wood preservative example given above:

- the label may need to include advice to avoid fitting fixings for a certain time period after treatment until the fixation of these preservatives is complete, or until the moisture content of the timber has fallen below a certain level (depending on the intended service life of the component and likelihood of dampness).

CHAPTER 7 EFFICACY ASSESSMENT

7.1 INTRODUCTION

7.1.1 Background

Efficacy data are a fundamental component in the regulatory management and decision making process for biocidal products. Efficacy data are required to establish the benefit arising from the use of biocidal products and must be balanced against the risks their use poses to man and the environment.

Under Article 5(1)(b) of the Directive the authorisation of a biocidal product will only be granted if that product is shown to be sufficiently effective.

Efficacy is not definied specifically in the BPD, but it may be defined as 'the power to produce an effect'. Efficacy is described in the Directive (Annex IIB [5.10], and Annex VI, paragraph 51) as the ability of a biocidal product to fulfil the label claims made for it on the proposed label. Section 7.2 of this document outlines that evaluation is based upon substantiation of efficacy claims and sets out the information that makes up an efficacy claim.

These guidelines provide general guidance only and as such are designed to be flexible and are intended to provide advice as to the nature and extent of efficacy data required to support a positive authorisation. They do not set out a checklist or rigid criteria and consequently expert scientific judgement should be exercised in using them in either conducting tests and/or evaluation of the data.

The information and data required relevant to the effectiveness of the active substance(s) to be employed in biocidal products are outlined in Annex IIA. For biocidal products the data required are set out in Annex IIB. The exact data requirements for both active substances and biocidal products for the 23 product types are amplified in the TNsG on Data Requirements.

7.1.2 Objective of the guidance

The general objectives of this guidance document have been presented in Chapter 1. However, compared with the assessment of risks for humans and the environment, assessment of efficacy has a number of important differences:

- There is, at present, no international consensus as to what data are needed to provide sufficient evidence of efficacy in support of label claims. However, for product type 8 (wood preservatives), a fast track procedure (based on the Vienna agreement between CEN and ISO) was initiated by CEN from 1995 to 1997 to ISO, with the objective of internationalisation of standards. Agreements also exist in the EU for disinfectants established by CEN/TC 216. There is a wide diversity of product types and use patterns encompassed within substances intended for use in biocidal products and consequently the nature and extent of data required to demonstrate efficacy and the fulfillment of label claims will vary from one product to another;
- Only a few internationally agreed test guidelines for use in efficacy testing across the range of product types under scope of the Directive are available. CEN has already issued pass-fail criteria for biocide type 8 efficacy in EN 599 and is planning to issue 15 guidelines in 2002 for disinfectant products used in veterinary and public food hygiene and medical situations;
- The lack of harmonisation or written guidance on efficacy requirements for biocidal products can potentially result in uncertainty, confusion, inconsistency or misunderstanding regarding the nature and extent of efficacy data required by regulatory authorities. This includes a lack of guidance on study design, complexity, conduct or;

- As efficacy testing does not consider testing for safety (with respect to human or animal health or the environment), the application of the principles of Good Laboratory Practice (GLP) is not required in the legislation. However, this guidance indicates that the spirit of such principles should be applied to the testing for efficacy at least regarding documentation of the conduction of tests and the results.

- The assessment of efficacy is only part of an overall performance evaluation, which itself is highly complex and involves many diverse contributory factors including the potential for resistance and unacceptable effects. Examples of other common factors that contribute to performance include viscosity, solubility, heat stability, UV stability, colour, odour, compatibility with process, compatibility with the final matrix, selection of formulants.

This chapter gives guidance in these areas, to both applicants and competent authorities, such that competent authorities can evaluate data to determine their completeness and adequacy with respect to the application. In particular, it addresses:

- what information is needed to make up a 'label claim';
- the robustness of a study, e.g. in terms of the types of study that may be available, use of controls, replication, statistics, etc., and the detail to be recorded in a study report;
- the Quality Assurance procedures which should be adopted (cf. ISO 17025 for testing and certification);
- the overall evaluation of the data package when the completeness and adequacy of the data is compared with the label claim; and
- the decision making process.

The competent authority will be undertaking the efficacy assessment in order to consider authorisation in their territory. This will require consideration of the appropriateness of the use of a biocidal product and the relevance of the proposed use patterns and target organisms in their territory. CEN standards allow the possibility of “national declarations” concerning the occurrence of the various biological agents; such declarations have an informative status; they allow e.g. the suppliers of wood preservatives and treated wood to recognise the main challenges and requirements in the countries of use of treated wood; this facilitates the necessary amendments to provide by the applicants who may import treated wood from one country, while the wood preservative has already been imported from somewhere else. The same process of bio agents identification occurs in member states where the regions are scattered in different continents and islands (case of Caribbean isles, la Reunion, Corsica and continental France, even without considering other overseas territories).

The principles in this document, including the generic nature of the examples, are valid for all countries in the European Union. However, situations within certain territories may vary due to different working practices, environmental, geographic and climatic conditions and relevance and/or breeding period of target species. For wood preservatives, the evaluation of the efficacy should take into consideration the expected service life of the treated wood (short term for temporary (sapstain) treatment, long term (structural/building)), and anti-termite treatment (preventive or remedial treatment for soil and walls).

There is a wide diversity of product types and potential use patterns covered under the scope of the Directive. Thus, the nature and extent of data required to demonstrate efficacy and the fulfilment of label claims will vary from one product type to another and as for instance in wood preservatives within a given product type. Consequently, technical detail giving advice concerning the nature and extent of data available for evaluation appropriate to specific product types is presented in the relevant technical annexes. This chapter provides a general guidance only and should be used alongside expert judgment.

7.2 EVALUATION OF LABEL CLAIMS

7.2.1 Substantiation of label claims

The Directive (Annex VI paragraph 51) requires that test data be submitted and evaluated to ascertain that the efficacy claims of the biocidal product can be substantiated.

The competent authority will evaluate these data and consider whether they demonstrate the efficacy of the biocidal product against the target organisms when used normally in accordance with the conditions of authorisation. If the competent authority is not satisfied then the product will not be authorised or the label claims will be amended.

The competent authority efficacy assessment will be made against the claims made on the product label or other statements on associated product literature for the effectiveness of the product.

7.2.2 What information makes up a 'label claim'?

Efficacy claims for biocidal products will be highly variable and will depend largely on the type of product, use pattern and desired effect.

Biocidal products are used in a diverse range of industries and therefore products, processes and the type/extent of biological challenge can vary enormously even within the same application area. Efficacy claims within a particular product type may often be very specific in nature with respect to target organisms and use patterns or alternatively they can also be very broad. In the case of broad label claims it will not be appropriate or realistic to include the entire range of target organisms. Instead suitable principal organisms should be identified. Occasionally an application to broaden a label claim will be made. In these circumstances the final decision will depend largely on the extent of the data submitted and the relevance of the representative target organisms selected (with respect to morphology, biology and behaviour, as appropriate) to the proposed use of the candidate product.

An efficacy claim can be considered to be a matrix of information that, depending on the particular product type, will normally comprise the following parameters: target organism(s)/spectrum of activity/effect/duration/area of use or site of application/application method/dose rate/directions for use the efficacy/inefficacy of the product under certain conditions (nature of the infestation, density of micro-organisms, application temperature.

For substances, a label claim prescribes a range of doses, which fits with the nature of treatment (preventive, curative, temporary, maintenance) in compliance with existing standards for efficacy. The entire range of organisms against which the biocide is intended to be used, is not necessarily included on the label. It may be a simple matrix of dose/efficacy per main categories of biological agencies, sometimes in direct relation with the type of use (use classes in relation with exposure to biological agents; typically the case of wood preservatives, product type 8).

For biocidal products, as combination of substances, the same type of matrix dose/efficacy may be used.

The following information (outlined in Annex IIB) is likely (for most of the product types under scope) to form the basis of a label claim on the efficacy of a biocidal product:

- product type
- spectrum of biological activity (including the (complexes of) target organisms and their development stage) and function (preventive, curative, maintenance, temporary)
- its mode of action (e.g. destroy, deter, render harmless, prevent the action of or otherwise exert a controlling effect on harmful organisms)

- area of use/site of application; geographical variability, limits and provisions concerning non-dominant targets and their tolerance for biocides
- duration of control/effect
- directions for use (including method(s) of application and application rate(s), time and duration of application); some products may be segmented in types of intended users: industrial, professional, amateur of the public at large
- other relevant information pertinent to the efficacy of the product (e.g. target dose rate, its variability and the application method), cf. Section 7.2.2.6

Table 7.1 provides examples of the parameters that should constitute a label claim for a few of the product types under scope of the Directive. **This table is not intended to be exhaustive with respect to use patterns and claims or prescriptive with respect to data generation.** Amplification of the type of information required from the parameters that make up the matrix of a label claim are presented in the remainder of this section.

Annexes 7.1-7.23 provide amplification of these points for individual product types.

7.2.2.1 Product type

This should be identified by reference to the inclusion and accompanying descriptors in Annex V of the Directive.

7.2.2.2 Target organisms/Spectrum of activity

The range of target organisms for which claims are made and from which principal organisms representative of the biological challenge can be selected should be identified on the product label or associated literature. In the case of broad label claims it will not be appropriate or realistic to include the entire range of target organisms to which the product will be applied in practice; instead suitable principal organisms representative of the biological challenge should be identified. Where the consideration of the broadening of a label claim is required the final decision will depend largely on the extent of the data submitted and the relevance of the representative target organisms selected (with respect to morphology, biology and behaviour as appropriate) to the proposed use of the candidate product (Annexes 7.1-7.23 give further clarification for the individual product types).

Some generic examples of target organisms attributed for some of the product types under scope are given below **(N.B. these examples are not intended to be either exhaustive or prescriptive)**.

Table 7.1: ***Example(s) of the parameters that should constitute a 'label claim'.***

Product type	Area of use/site of application	Spectrum of activity[1]	Mode of action/Duration of effect	Application method	Expression of Application /dose rates
Wood preservative	Timber Out of ground contact	Fungi (wood rotting Basidiomycetes) Insects (including termites)	preventive	Vacuum/pressure impregnation brush/spray/injection dip	kg /m^3 g/m^2 dilution rate %
	Timber Out of ground contact	Fungi (wood disfiguring)	preventive	brush /spray dip	g/m^2 dilution rate %
	Timber In ground contact	Fungi (soft rot and soil inhabiting micro-organisms) Insects (including termites)	preventive	Vacuum/pressure impregnation	kg/m^3
	Building	Termites	Preventive curative	Injection/spray	Dilution rate Number of liters/m2 for soil. At refusal for walls.
Insecticide	Surface spray	Insects (cockroaches)	kill repellents, IGR[2]	Spray	mg/m^2
	Space spray	Insects (house flies)	knockdown kill	Aerosol/fog	mg/m^3
Slimicide	Paper/pulp	Fungi Bacteria	kill	Manual/Automatic feed	[Unknown]
Disinfectants	Public health area disinfectants	Bacteria Fungi Virus	kill	Spray	v/v w/v
	Swimming pools	Bacteria Fungi Virus	kill	Direct dosing	v/v w/v
Metal working fluid	Concentrate	Bacteria Fungi Slime	kill inhibition of growth	Manual/Automatic feed	% w/w
In-can preservatives	Wet paint (in can) preservation	Bacteria Fungi Yeasts	kill inhibition of growth	In-can	% w/w

[1] May be wide ranging or very specific

2 Insect Growth Regulator

Product type 2

If a biocidal product is intended to be used as a disinfectant in the area of public hygiene and claims use as a disinfectant with a broad spectrum of activity against micro-organisms, then applicants should indicate that efficacy against Gram-negative bacteria (such as *Salmonella choleraesuis*) and Gram-positive bacteria (such as *Staphylococcus aereus*).

If claims for disinfectant products are more expansive then efficacy testing requirements and representative test organisms will be increased as appropriate; for example:

If the product is intended to destroy tuberculosis bacteria (such claims are often used by medical users of disinfectants as an indicator of product strength as tuberculosis bacteria are more difficult to kill than most other types of bacteria) then claims against *Mycobacterium tuberculosis* will need to be substantiated.

Product type 8

If a product is intended to be used as a wood preservative then applicants should indicate if activity is to be claimed against fungal and/or insect species. It will not be necessary to identify an exhaustive range of deteriogens but instead broad target organisms are usually named on a label to reflect those that are common in practice (or representative of those that are). These species or groups of species will also be those that when used in a test study can be easily handled in the laboratory, are aggressive and consistent in their behaviour and response.

For product type 8, the references are EN 599, EN 351 for preventive wood preservatives and prEN 14128 for curative products. The matrix shall provide critical values (doses) per use classes of EN 335, plus fungi and options concerning non-universal target organisms (half a dozen, termites, *Anobium punctatum, Lyctus brunneus, Hylotrupes bajulus*, stains, moulds, where the dose is specific and defined in EN 599 as the biological reference value of the target) and the type of application (surface or impregnation) because the units are different as well as tests (g/m2 for surface and kg/m3 for impregnation). The concept of curative action is mainly linked to insects and total killing: curative action on decayed wood is not documented in EN standards, except for the replacement in case of failure. In this category is as well the temporary treatment (sapstain) and the antitermite products (chemical barriers, physical-chemical barriers, baits) employed to protect wooden structural elements in buildings.

Product type 12

If a product is intended to be used as a slimicide in industrial processes, e.g. on wood and paper pulp, then applicants should indicate whether efficacy is to be considered against bacterial slime (such as *Enterobacter aerogenes* and *Pseudomonas aeruginosa*) and/or fungal slime (such as *Aspergillus niger* and *Chaetomium globosum*).

Product type 18

If a product is intended to be used as a pest control product then applicants should clearly indicate which test organisms the product is intended to control. For example, for products intended for use as insecticides and acaricides, claims may be very specific or very broad in nature.

For products claiming use against specific pests where only activity against one insect/arachnid order or a certain family within that order is claimed, then a limited number of pest species will be required. For example:

- a claim stating "for use against dust mites..." - this may only require testing against a *Dermatophagoides* spp.
- a claim stating "for use against cockroaches..." - this may only require testing against species such as *Blattella germanica* and *Blatta orientalis*.

If, however, the product is claiming a broader spectrum of activity, e.g. use against "crawling insects" (such as cockroaches, ants, fleas, etc.) or for use against "flying insect pests" (such as flies, mosquitoes, wasps, etc.) then a qualification of the ranges of pests against which the product is intended to be used should be provided. When broad claims are made, tests on representative pest species will need to be provided for the ranges of pest orders against which efficacy is claimed. Where such a claim covers a diverse range of pest habitats and pest morphology and biology, a greater number of representative test species will be required.

7.2.2.3 Mode of action/Effect(s) on target organism

Information or actual studies on the chemical/biochemical mode of action of a biocide is required to demonstrate the nature and extent of its biocidal control properties. Mode of action data is also used in the evaluation of the potential and existing pest resistance.

The data supplied must be relevant to the claimed mode of action or intended effect on the target organism. For example:

If the claim is associated with a killing effect on bacteria then the data must cover the killing action against bacteria.

If the claim is associated with the inhibition of growth, respiration or exoskeleton polymer production of an organism, then the test data must cover these parameters.

If the claim states specific effects such as knockdown, flushing or repellency the data must address these parameters.

If a claim indicates an element of residual activity (e.g. "...control of cockroaches for up to 3 months...") the data must adequately demonstrate the effect for the time period stated in order for the claim to be fully substantiated.

Product types 1,2,3,4,5

Typical use patterns for disinfectant products may include use as health care disinfectants for use on hard surfaces in hospitals, clinics, dental offices or medical equipment, or use in the public health area to reduce pathogenic or nuisance organisms and algae to an acceptable level (e.g. use in swimming pools to prevent the spread of communicable microbial diseases or algal growth, use on hard surfaces in domestic, commercial and public premises, use in air conditioning systems to significantly reduce levels of air-borne micro-organisms, etc.)

Other disinfectant products could be intended for use in veterinary situations or other animal accommodation areas to prevent or control the outbreak of infectious diseases such as tuberculosis, foot-and-mouth disease and fowl pestilences.

Alternatively antimicrobial biocidal products could be intended for use in public health areas as bacteriostats against micro-organisms identified as causing economic or aesthetic problems (e.g. odour-causing bacteria) in the presence of moisture.

Product type 8

In considering a wood preservative product possible use patterns may include preventive and/or remedial (curative) use. Additionally data submitted should represent the service environments in which the timber, following treatment, is likely to encounter (i.e. grouped in Use classes according to the severity of exposure, degree of wetting and biological challenge, e.g. equivalent to those Use classes as defined in EN 335-1).

Product type 18

For insecticides/acaricide products examples of typical use patterns may include application via surface treatments (i.e. for the control of crawling insects by products applied directly to the surfaces), space treatments (i.e. for the control of insects in flight by products dispersed into the atmosphere e.g. via fogs, mists, aerosols) or baits (i.e. for the control of pests by attraction to a point where they will pick up the biocidal product by feeding or contact). These typically utilise a palatable foodbase and sometimes incorporate an attractant (pheromone - Product type 19) which may draw the pest to the bait over some distance.

7.2.2.4 Areas of use/Site of application

The product label should clearly indicate the intended areas of use/site of application of the product. The data submitted must reflect the intended use pattern/area of use for the candidate product.

Whatever the intended use the competent authority should ensure that the nature and extent of testing is appropriate to that particular area of use and associated microbial challenge and desired effect.

7.2.2.5 Directions for use

The label will also include the information that defines the way in which the biocidal product is handled and applied and typically will encompass some or all of the following:

- preparation of the formulation for use;
- application method/delivery technique;
- application rate/dose rate/treatment frequency/treatment time; and
- other information/limitations pertinent to the efficacy of the candidate product.

For product type 8, application rate is very important. Differences exist between the different countries in Europe, depending on the process of application, the chemical nature of the products and the treatment time.

The competent authority should ensure that the appropriate information relevant to the application is provided.

7.2.2.6 Other information/limitations pertinent to evaluation of the efficacy of a biocidal product

The information highlighted in Sections 7.2.2.1 – 7.2.2.5 is likely to form the basis of data required for the assessment of the efficacy of most biocidal product types. However, it is not exhaustive and other factors may need to be considered when designing or selecting appropriate efficacy test methods and evaluating the data generated from them.

For example with regard to antimicrobial biocides one or more of the following parameters may play an important role (either positively or negatively) in the determination of their efficacy – these are illustrated in the example box on the following page

N.B. Whilst the parameters indicated overleaf are examples of factors that can influence the efficacy of certain types of antimicrobial biocidal products some of these factors (or alternatively additional factors) may influence the efficacy of other biocidal products.

7.3 GUIDANCE ON EVALUATION OF AN EFFICACY STUDY

7.3.1 Types of study

In order to support a product authorisation, it is necessary to demonstrate either through testing of the candidate product, or by presenting data generated on a very similar product formulation, that the product is efficacious when used in accordance with the label instructions.

As the label claims for biocidal products can differ widely, the requirements on generation of supporting data must be equally flexible. Data requirements are presented in the TNsG on Data Requirements. Sections 7.3-7.6 below provide guidance to competent authorities evaluating these data on areas of completeness, quality and adequacy of the data and also on testing strategies that may be adopted in order to address the flexibility required.

7.3.1.1 Test guidelines

Testing should be carried out according to Community guidelines whenever these are available and applicable (Par. 52 of Annex VI of the Directive). Where appropriate, other methods may be used as shown in the following list of testing methodology :

- CEN, ISOor other international standard method
- National standard method
- Industry standard method (accepted by competent authority)
- Individual producer standard (accepted by competent authority)
- Data from the actual development of the biocidal product (accepted by the competent authority)

Examples of additional factors that may contribute to the efficacy of disinfectant biocides – these and other factors are often incorporated into standard efficacy test methods for these biocidal products

- ***Hard water claims***

The degree of hardness of the water (i.e. the presence of Ca^{2+} and Mg^{2+}) used to dilute the disinfectant may affect its performance. Generally the harder the water the less effective is the diluted disinfectant. Any product that carries label claims for effectiveness in hard water must be tested by the appropriate method in synthetic hard water at the level claimed. It is noted that many current test standards require that products tested for dilution with potable water must, for the purpose of efficacy testing, be diluted in water of 'standard hardness'.

- ***Presence of interfering substances***

Where disinfectants are applied to either inanimate surfaces, any number of substances may be present which may affect the activity of the products.

- ***Organic and inorganic contaminants***

The nature, degree and condition of the contaminant present will affect the efficacy of a disinfectant. Hard compacted contaminants are more difficult to disinfect than loose friable ones, and solid contaminants generally have a greater adverse effect on efficacy than liquid contaminants.

In many cases, however, residual contamination must be anticipated, and in some situations (e.g. in the treatment of blood spillages) disinfectants are used specifically to decontaminate 'soil' and to prevent infection transfer and to assist in safe disposal.

Blood, urine, faeces, food debris, fats and oils, dust and proteinaceous materials are the most likely organic contaminants to be encountered. Lime scale, milk stone and earth are the most common inorganic contaminants.

Where claims are made for use under 'soiled' or 'dirty' conditions, use concentrations must be determined from tests carried out in the presence of a suitable contaminant. Contaminant materials commonly used in efficacy tests include albumin, serum, blood, yeast and yeast extract.

N.B. The interfering substance(s) used in a test method should be selected according to the conditions and intended use pattern for the product.

- ***Temperature***

Generally disinfection performance increases with temperature. This applies to disinfection against all microorganisms though the effect on individual species differs, some being more affected than others. However, excessively high temperatures can result in poorer disinfection if the biocide is not stable at elevated temperatures. In balance, temperature may also raise the aggressiveness of targets, generally up to their optimum of survival.

- ***Contact time***

Within limits, the longer the contact time the more effective is the disinfectant. Some disinfectants act very quickly, whereas others require an extended contact time to achieve adequate performance. Mycobacteria take longer to kill than most vegetative microorganisms.

- ***pH***

The prevailing degree of acidity or alkalinity during disinfection can affect the performance and choice of disinfectant. Generally, biocides are more active as undissociated molecules than when in an ionised form.

- ***Surfaces***

Smooth impervious surfaces are easier to disinfect (and also to clean) than rough or pitted ones. In some circumstances the microorganisms might be protected from the action of disinfectants being protected in porous surfaces. Clumps of microorganisms may also be more difficult to kill, as cells inside are protected by dead microorganisms on the outside. Bacteria and fungi can adhere to surfaces forming biofilms in which the cell surface properties are altered and this makes them more difficult to kill, as biocide penetration can be difficult to achieve.

When a product is to be recommended for certain patterns of use and where contaminants are present, more potent products, longer contact times, higher concentrations, pre-cleaning or a combination of these parameters may be necessary for the product to be effective.

However, most standard testing methodologies concern laboratory tests and as such are not always useful predictors of performance under actual conditions of use stated on the product label. For certain biocidal product types, field data is considered to be highly relevant and in some cases they may be essential to assessment of a label claim. Consequently these data, where available, should be submitted (Annex VI (paragraph 52) recognises that where relevant, field data can also be submitted) and the competent authority should take these into account when assessing its adequacy in supporting the product label claims.

An OECD Overview of Efficacy Testing Methods for Biocides has been prepared in order to improve knowledge on what methods are available for efficacy testing of the different biocidal product types, on their validity and on any problems they may have. The publication is available at the OECD web site (www.oecd.org). Available standard test methods for individual product types are presented in the Annexes 7.1-7.23.

With the exception of wood preservatives and disinfectant products, there are at present very few ISO, CEN or other international/national standard methods available covering the product types within scope of the Directive. Whilst this may be addressed in the long term, for the foreseeable future data submitted for evaluation will have been generated using industry/individual producer standards or via product development studies.

7.3.1.2 Experimental design

Efficacy test data submitted for evaluation by a competent authority will usually be one or more of three types. These are:

Screening tests

These usually include laboratory studies of the active substance, or relatively simple formulations containing the active substance to establish the innate or intrinsic biocidal effect on the test organisms. These studies may also include dose-response tests.

Laboratory test methods need to be rapid, reliable, reproducible and relevant to the field of use. Whilst some laboratory test methods for evaluating activity against some specific use patterns exist as national standards or draft development standards, many relevant non-standard methods are also available.

Laboratory tests are designed and intended to establish the innate activity of the product against specific organisms in procedures designed to control and optimise the test under carefully controlled and reproducible conditions. Furthermore, the spectrum of activity (e.g. bactericide) of the active substance can be determined with laboratory screening tests. Laboratory tests are often conducted using the active substance(s) in a carrier solvent or on products based on simple formulations. Unfortunately, this approach is not recommended when speciation occurs: substances may show activity in homogeneous media and none in practical conditions (case of wood as substrate).

Data obtained from laboratory tests often do not lend themselves directly to prediction of actual treatment levels or effectiveness in service under actual conditions of use.

Simulation tests

These may include laboratory studies generated from test systems which are designed to reconstruct artificially the environment in which the product will be used. Whereas the formulations used in screening studies may often be simple solutions of the active substance those used in simulation studies should mirror the type of formulation for which authorisation is sought or may be the actual product formulation. These studies may often be designed to evaluate substrate/organism/biocide interactions to determine the efficacy of a product against a range of substrates. Laboratory screening studies or simulation tests should be performed, if possible, before field studies are performed.

Field studies

These are studies in which data are generated when the biocidal product is used in the actual situation and in the manner prescribed on the product label.

Field studies are conducted under conditions representative of those expected in service e.g. the interactions of the natural factors which influence efficacy to be tested including the natural, mixed populations of biological agencies. Since field studies involve exposure to practical conditions they can be regarded as in use/practical tests and as such any field data generated in support of an application should be conducted on products that closely resemble the fully formulated commercial product. It is considered that evidence of effectiveness based on field studies will be more convincing owing to the difficulties of representing the conditions of service through laboratory testing.

However, even data generated from field studies must be interpreted with caution since often it is not possible to simulate in individual studies the full range of factors, which will influence the efficacy of the product in all uses. Field studies are often typical or representative of conditions of use, e.g. with respect to application technology, level of pest pressure, etc, but may on occasion maximise the severity and realism of the challenge to the product in a particular treatment situation.

Not all of these methods will be relevant to every product type under scope. A common aspect to all types of testing is the need for traceability of the tests. One key issue is the necessity for the applicant to provide the non ambiguous identification of the product submitted to testing, with reference to the product designed to be put on the market.

A further distinction which can be made between these three types of studies is the nature of the formulation, application method and application rate used in these tests in relation to those of the product(s) for which authorisation is sought. For example, all of these parameters are likely to be the same for the candidate product under field study conditions. These distinctions are outlined in Table 7.2.

This table illustrates the principle that efficacy studies generated before the final product formulation has been developed have a part to play in an evaluation of an active substance in a biocidal product and emphasises that each study submitted in a data package will be assessed on its own merit.

Table 7.2: *Examples of the variability between efficacy study conditions conducted on a product containing a biocidal active substance and actual use of the product (target organism(s), application method etc.) should authorisation be granted.*

Nature of the study	Resemblance to product application					
	Active substance source	Formu-lation	Appli-cation method	Appli-cation rate	Organism tested	Comments
Screening tests	✓	×/✓	×/✓	×/✓	× /✓	These tests should give an indication of the inherent biocidal activity and/or the range of concentrations over which such activity would be expected.
Simu-lation tests	✓	× /✓	× /✓	✓	✓	These tests should introduce elements of choice for the target organism to reflect the environment in which the proposed product will be used.
Field studies	✓	✓	✓	✓	✓	These studies should involve the use of the proposed product, formulated, applied and targeted as described on the product application form and draft label.

✓ - the same as that proposed in the product application

× - not always necessary to resemble/mirror that proposed in the product application

The competent authority should evaluate all available and relevant data, considering the overall adequacy of the data package in coming to a view on the acceptability.

7.4 PERFORMANCE STANDARDS

The term 'performance standard' refers to the pre-determined efficacy that is required by Regulatory Authorities for authorisation of a biocidal product for a particular use. The term is synonymous with 'pass/fail' criteria and 'acceptability criteria'.

Biocidal products should be evaluated against performance standards in accordance with the following general principles:

- The performance standard for a biocidal product should be the same within all Member States unless there is compelling scientific, or social, cultural, historical or economic reason to deviate. Meeting a sufficient yet practical performance standard across the community should eliminate the potential concern that ineffective biocidal products are marketed in some parts of the community.
- The performance standard reflects a defensible hypothesis that biocidal product performance, supported by practical and logical usage instructions, can be expected to deliver a product type related benefit to end-users (e.g. reduce risk of exposure to pathogenic organisms, reduce odour-causing germs, control of disease vectors etc.).
- The performance standard is demonstrated using scientifically valid and robust laboratory or field testing methods. These methods will offer a reasonable prediction of the real-world benefit to end-users when the product is used in accordance with biocidal label instructions.
- The performance standard being sought will guide test method selection, particularly with respect to some or all of the technical parameters as appropriate to the type of biocidal product under test
  - Contact time
  - Duration of effect (e.g. kill or residual effect)
  - Spectrum of activity (efficacy against specific target organisms, representative groups of targets such as bacteria, fungi, and/or viruses etc.)
  - Presence of interfering substances (e.g. organic matter)
  - Climatic factors (e.g. temperature or relative humidity)

  Other performance assessment parameters may be appropriate for other biocidal product types and label claims.
- A performance standard can be stated and measured in either quantitative or qualitative units. For example, efficacy standards can be expressed in terms of particular level of control, percentage kill, degree of inhibition, minimum number of organisms to be killed etc. Alternatively, product performance may be expressed in the measurement of the pest problem and the resulting secondary or qualitative effects e.g. the amount of biofilm/slime, odour etc. For certain product categories, the performance standard is a combination of qualitative and quantitative units, reflecting expected scientific and practical results. For the setting of a performance standard all important sources of statistical variability should be taken into account.
- Performance standards may be stated in the efficacy test method itself, but more commonly they are not. Performance standards are often established as a result of expected results and outcomes that are not necessarily directly related to the level of reduction of the target species.

Efficacy standards (does it work, at what concentration, to what degree and for how long etc.) assist manufacturers and formulators in deciding whether a candidate biocidal product would be effective in a consistent and cost-effective manner. This assessment ultimately results in a proposed label to reflect what they have determined to be reliable performance results.

The biocidal product's purpose and level of effectiveness may have a bearing on the type of product designation. For example, levels of performance for some public health antimicrobial biocidal products require more extensive testing, i.e. larger number of tested organisms may be required than for a non-public health biocidal product. The product's purpose and level of effectiveness may have a bearing on

the type of product or its use pattern designation. Normally, the performance standard shall always be met.

7.5 GENERAL CONSIDERATIONS FOR THE DEVELOPMENT AND REPORTING OF EFFICACY DATA

7.5.1 General Comments

To facilitate the critical evaluation of an efficacy package submitted in support of the authorisation of a biocidal product it is important that the data be presented in an ordered manner and that the submission contains studies reported in sufficient detail.

7.5.2 Sources of information

Efficacy data from studies where method and results are well documented should be considered. Efficacy data submitted for evaluation may originate from several sources, e.g.:

(i) Well conducted and documented studies which are either laboratory tests of biocidal effectiveness, semi-field or small scale field trials of products carried out under simulated service conditions or actual field/operational trials (such field trials must have been running for a period sufficient to demonstrate effectiveness).

(ii) Evidence relevant to the product from published work in reputable journals. It is recognised that published data provided in support of an application may often lack important detail. The applicant must document that the formulation(s) referred to in a published paper are equivalent to those for which approval is sought.

(iii) Field data generated from outside the territory of the Member State in which product authorisation is sought may be considered provided a justification of the relevance of the data is made. The extent of the information required will be dependent on the type of biocidal product, its proposed use pattern and the similarity of conditions in the two countries. Justification may include, as relevant and appropriate, information on the target organism (e.g. comparison of genera/species and its relevance and importance in the country in which authorisation is sought) and environmental parameters such as details of location and mean temperatures and rainfall.

An applicant might also provide anecdotal evidence or testimonials from individuals for some end points. Although these are a potential source of additional information, they are unlikely to be sufficiently reliable for the scientific evaluation of efficacy, and should never be accepted in lieu of data.

7.5.3 Quality Assurance Procedures

Although there is no requirement for efficacy data to be subject to the requirements of GLP, the tests (and data generated) should be based on sound scientific principles and practice.

Competent authorities should ensure that satisfactory Quality Assurance procedures (e.g. with respect to study personnel, methods, procedures, documentation, archive storage and retrieval of raw data) are given in the test report (cf. ISO 17025).

7.5.4 Reporting

Details to be included in an efficacy test report are schematically described in Appendix 7.

7.6 GUIDANCE ON OVERALL EVALUATION WITH RESPECT TO COMPLETENESS AND ADEQUACY OF DATA COMPARED TO PROPOSED LABEL CLAIMS

7.6.1 Objective

The purpose of the efficacy assessment is to ensure that the proposed use of a biocidal product is supported by adequate scientific information.

7.6.2 Overall evaluation

The data package should include all information necessary to provide a complete evaluation of the effectiveness of a biocidal product. The competent authority will evaluate this with respect to both its completeness and adequacy (here covering both the reliability of the data and also its relevance to the proposed use of the candidate product).

The competent authority should ensure that:

a) the data package is complete: i.e. there are no apparent major data gaps which would prevent a meaningful evaluation of the submission.
b) adequacy: the appropriateness of the submission, i.e. the intended use pattern and adequacy of the data that have been supplied.

Finely balanced decisions can be influenced by the overall confidence in the available data; low confidence may result in a refusal of an authorisation or a request for further information whereas a high degree of confidence in the data may result in the granting of an authorisation.

7.6.2.1 Completeness of data

For the active substance(s) present in the biocidal product, as they should be listed on Annex I/IA for the use pattern envisaged, the data required by Annex IIA should be complete. For biocidal products the competent authority should ensure that all data required by Annex IIB are available.

The competent authority should examine the data package and form a judgment as to whether any data omissions are significant and adversely affect the assessment. Those so identified should be communicated back to the applicant for supplemental data submission before the evaluation can be undertaken.

7.6.2.2 Adequacy of data

The adequacy of an efficacy test study is evaluated on the basis of the usefulness of the data i.e. whether it is designed and conducted following appropriate test procedures. Elements for consideration should include:

- the method(s) adopted should measure a response and, as appropriate an end point relevant to the label claim;
- the method(s) should employ chemical/physical/biological conditions relevant to the application; and
- the method should include appropriate control(s).

In many situations data based on either single studies or based upon simple laboratory screening studies alone will not be comprehensive enough to support the commercial authorisation of a product, whereas the provision of other types (e.g. simulated use or actual field studies) are more likely to lead to a successful application. Often, therefore, conclusions will be drawn on the efficacy of a biocidal product based on the results of a series of studies submitted in support of a label claim for a biocidal product.

Specific guidance on the nature of data required to support label claims for individual product types are presented in Annexes 7.1-7.23.

The adequacy of a test is defined by two basic elements: reliability and relevance.

Reliability

This covers the inherent quality of a test relating to test methodology and the way in which the results of the test are described. The reliability will be determined by the overall confidence that a competent authority has in individual studies and data packages.

In general, the more details provided on methodology, test procedures and results and analysis, the easier an evaluation of their reliability should be. The amount of information presented will thus provide the basis for a decision by a competent authority on the reliability of the data reported.

Data judged to be reliable will usually include well documented studies or reports which were carried out following the guidance and criteria outlined in Section 7.3, and conducted using quality assurance procedures. In principle the same criteria apply to test data reported in the published literature. The amount of information presented will provide the basis to decide on the reliability of the data reported. In general, publications in peer reviewed journals are preferable. High quality reviews may also be used as supporting information.

Data judged to be unreliable will usually include studies or data from the literature which do not provide sufficient experimental detail and which are only listed in short abstracts or secondary literature (books, reviews, etc.). Additionally anecdotal evidence or testimonials without supporting scientific data are unlikely to be of much value in substantiation of label claims.

Relevance

The relevance of the test data covers the extent to which data and/or tests are appropriate for assessment against the label claim(s) and will therefore need to be contrasted against the elements that make up the label claim for the candidate product.

The competent authority will assess the efficacy in order to grant authorisation in their territory. Data generated from outside the territory in which authorisation is sought may be provided. In this situation the competent authority should consider the relevance of the proposed use of a biocidal product with respect to the climatic conditions, target organisms and/or breeding periods of the target species in the territories where the product is intended to be used.

If satisfied as to the relevance of the use of the proposed biocidal product in their territory the competent authority should then examine the relevance of the data supplied with respect to, as appropriate, the following parameters of the label claim:

- product type
- target organisms/spectrum of activity
- mode of action/effect(s) on target organism
- areas of use/site of application
- application method
- application rate/dose rate/treatment time
- other conditions affecting product performance, e.g. pH, presence of organic matter

7.6.3 Assessment of the effectiveness of the biocidal product

Having considered the reliability of the data and its relevance against each of the points above (as appropriate) the competent authority will consider the overall efficacy evaluation.

The data should demonstrate that, when used in accordance with the label instructions, the use of the biocidal product will result in a measurable beneficial effect in relation to a performance standard. The data supplied should demonstrate that an acceptable level, duration of control or protection or other intended effect is likely to result from use of the biocidal product at the recommended dose/application rate (the evaluation should determine a dose rate that is considered to be effective but not excessive).

The acceptable level of control or performance standard may vary depending on the intended purpose of the proposed use and the label claims.

For broad label claims, the competent authority should ensure that the data available are on organisms representative of the claim as a whole. These data should be relevant to the challenge posed by all organisms likely to be within the broad claim and should include a full consideration of the biology, morphology and behaviour as appropriate. Therefore, due to the variability of label claims and intended effects, expert judgment will have an important place in all evaluations.

Conclusions as to the performance of the product must be valid for all areas of the Member State in which it is to be authorised and must hold for all conditions under which its use is proposed, except where the proposed label specifies that the preparation is intended for use in certain specified circumstances or geographic areas.

CHAPTER 8 INTEGRATION AND DECISION MAKING

This chapter provides guidance on:

- integrating the conclusions from the assessments of effects on humans, animals, the environment, efficacy and unacceptable effects; and
- considering the benefits of using the biocidal product.

8.1 OVERALL CONCLUSIONS FOR HUMAN HEALTH, ANIMALS, THE ENVIRONMENT, EFFICACY AND UNACCEPTABLE EFFECTS

Competent authorities must ensure that all relevant data are considered and properly evaluated with respect to both completeness and adequacy in reaching separate conclusions for the risks to humans, animals, and the environment, efficacy and unacceptable effects.

Where, despite availability of the common core data and additional data according to Annexes IIB and IIIB to the Directive, competent authorities come to the conclusion that scientific evidence is insufficient, inconclusive or uncertain and the high level of protection chosen by the EU can therefore not be ensured, the Precautionary Principle should be applied according to the guidance given by the European Commission (Commission of the European Communities, Communication from the Commission on the precautionary principle, Brussels, 2.2.2000 COM(2000) 1 final).

The conclusion of the risk characterisation for each considered product will be one of the following for each product type and for each field of use of the biocidal product for which application has been made:

- the biocidal product is unlikely to pose a risk under the proposed use and realistic worst case scenario;
- there may be a risk, but it can be reduced to an acceptable level by application of conditions or restrictions on use, etc.;
- further data are required before a decision on the risk can be made; or
- the product poses an unacceptable risk, which cannot be reduced to an acceptable level by application of conditions.

The decision based on the risk assessment for each use pattern and for each of these areas will be one (or more) of the following:

- the biocidal product can be authorised or registered for the use as applied for, subject to specific conditions/restrictions (risk management measures);
- more data are required before a decision on authorisation/registration (or a particular aspect, e.g. a specific use or application method) can be made; or
- the biocidal product cannot be authorised/registered, even after careful consideration of all possible conditions which could be applied.

8.1.1 Risk management measures

In considering that an authorisation can be granted, conditions or restrictions will usually be required. The competent authority will need to consider which risk management measures are appropriate. The nature and severity of these will depend on the nature and extent of the expected advantages and risks likely to arise from the use of the biocidal product. Conditions and restrictions may include:

- restriction of category of user, e.g. to professional use only;
- restriction of application methods, e.g. enclosed instead of open processes, brushing instead of spraying;
- restriction in the field of use, e.g. indoor use only;
- modification of formulation, e.g. ready-for-use rather than concentrate, replacement of substances of concern with less dangerous ones, etc.;
- modification of packaging, labelling and measures for the protection of people and/or the environment, e.g. reduced pack size or use of automated transfer systems; and/or
- adjustment of dose or application rate to suit particular circumstances.

8.1.2 Requirement for further data

If the competent authority considers that additional information or data are required before an authorisation decision can be made, **then the need must be justified**. This additional information or data shall be the minimum necessary to carry out a further appropriate risk assessment.

8.2 INTEGRATION OF CONCLUSIONS

The integrated conclusion is the combination of the conclusions for humans, animals, the environment, unacceptable effects and efficacy.

Where the integrated conclusion is that the biocidal product can be authorised with conditions, the competent authority should ensure that all conditions are compatible and practical. For example:

- there may be occasions where application methods proposed by the applicant need to be modified to allow safe use, but where they are not practical for the proposed use pattern;
- the conditions required for safe use for humans may not be compatible with those required for safe use for the environment; and
- there may be occasions when application of a single general condition can enable a number of specific conditions to be replaced.

It is likely that the integrated conclusion will be a mixture of outcomes. For example, authorisation may be refused for certain uses, more data may be required before other uses can be considered and, simultaneously, further uses may be authorised subject to conditions.

8.3 RISK/BENEFIT CONSIDERATIONS

Biocidal products are necessary to control organisms that are harmful to humans, animals or the environment, that cause damage to natural and manufactured materials or that might be useful to control unwanted organisms. For example their use helps to:

- prevent the outbreak and spread of communicable diseases between humans, from animals to humans and between animals;
- prevent microbial spoilage of food and foodstuffs and otherwise protect consumers from contaminated products;
- save valuable resources by extending the life of materials and structures and ensuring the efficient operation of industrial processes.

Annex VI (paragraphs 63 and 96) requires competent authorities to take into account the benefits of using biocidal products in coming to a decision on an application for authorisation. If there is no concern over a particular product, consideration of benefits is not necessary for the product to be authorised. Similarly, if the risks can be controlled by measures that are typical for products of that

type used in that way, there should not usually be a need for a formal analysis. If there is an existing product authorisation that has previously proved the need for a biocidal product (particularly with reference to Article 3(7) of the Directive) in the use area then the assessment can be short, perhaps referring to the original. However, if it is a new use area the argument should be made working through the issues in full.

There may be exceptional cases where the increased level of protection afforded to people, animals or the environment from the use of a biocidal product may justify the acceptance of the risk from its use. The competent authority must therefore perform a risk-benefit analysis on a case by case basis in relation to requests for further data, imposition of conditions and refusal of an authorisation. For example, the public health benefits of using a particular disinfectant product to treat drinking water may far outweigh the risks arising from the disinfectant and its by-products and the alternative of using a disinfectant that is less efficacious. Some biocidal products may also have a very specific, essential, use for which there are no alternative products or methods of control. The competent authority may, in such circumstances, overrule the integrated conclusion from the risk assessment, and grant an authorisation subject to very tightly controlled conditions (e.g. local permits to work). In all cases a full justification of the decision of the competent authority must be given. This justification has to be added to the authorisation or has to be outlined within the authorisation which the competent authority issues to the applicant.

This information is especially important for reasons of transparency if the owner of such an authorisation applies for a subsequent authorisation in another Member State. As the second Member State has to decide on this authorisation by the procedure according to Article 4 para 1 of Directive 98/8/EC (mutual recognition) it should be aware about the considerations of the first Member State. Within the procedure of mutual recognition the time constraints are difficult to cope with as a decision has to be taken within 120d (authorisation) or 60 days (registration). It should be immediately obvious to the competent authority of the second Member State whether the first authorisation had been granted by a “normal” decision or whether risk/benefit considerations had overruled the conclusions from the risk assessment. As risk/benefit-considerations may be strongly influenced by national peculiarities the second Member State should have the possibility to take a decision according to Article 4 para 4 of Directive 98/8/EC.

It is strongly recommended that an authorisation having been granted by risk/benefit considerations will be reviewed according to the procedure according to Article 6 Directive 98/8/EC.

When a risk/benefit analysis is necessary, the competent authority should list the advantages and disadvantages to the user (and where necessary bystanders and the environment) of the proposed course of action (possibly ranking them in a qualitative way to determine their significance). This should include (where relevant) consideration of the consequences of not allowing the product on the market. In considering benefits, the competent authority should also bear in mind the need to have a range of biocidal products available for a particular end-use, to avoid resistance problems as much as possible.

8.4 FINAL DECISION

Having considered the proposed conclusions from each of the effects on humans, animals and the environment the possibility of unacceptable effects and the efficacy, the overall conditions to be applied to the authorisation and the risk/benefit factors, the competent authority will come to an overall balanced view for the product. This will be one of three possible overall decisions as follows:

- the biocidal product can be authorised or registered for the use as applied for, subject to specific conditions/restrictions;
- more data are required before a decision on authorisation or registration can be made; or
- the biocidal product cannot be authorised or registered for the use as applied for.

In coming to a decision permitting the authorisation or registration of a biocidal product, the competent authority will have established that:

- it contains only active substances listed on Annex I or IA for use in such biocidal products and any requirements laid down in these Annexes are fulfilled;
- it does not present an unacceptable risk to humans, animals or the environment, has no other unacceptable effects and is efficacious when used in accordance with its conditions of authorisation or registration;
- the nature and quantity of its active substances and, where appropriate, any toxicologically or ecotoxicologically significant impurities and co-formulants, and its residues of toxicological or environmental significance, which result from authorised uses, can be determined according to the relevant requirements in Annex IIA, IIB, IIIA or IIIB;
- it is designed in such a way and comes with such information that it can be properly used, including application at an efficacious dose and at the minimum dose level required to exert the desired effect;
- the requirements for labelling and, where relevant, the safety data sheet (according to Articles 20 and 21 of the Directive) are fulfilled, and the particular conditions or restrictions under which the biocidal product may or may not be used have been specified; and
- the requirements for packaging and, if appropriate, procedures for destruction or decontamination of the biocidal product or any other relevant material associated with the biocidal product which conforms with the relevant regulatory provisions are fulfilled.

CHAPTER 9 POST EVALUATION PROCEDURES

9.1 GENERAL INTRODUCTION

Post evaluation procedures are required to ensure that following the evaluation of an active substance and/or product dossier the competent authority is able to:

- prepare an authorisation/registration summary;
- establish which data should be granted protection from access by other applicants;
- establish which data should remain confidential with no access by other applicants; and
- establish what information may be released under other legislation.

Linked to these issues is the use of letters of access as introduced in section 2.3 of Chapter 2.

The Directive makes it clear that the issues of data protection and confidentiality must be considered. This chapter gives further explanation of the distinction between these two terms and how the competent authority can implement each in practice. In addition, it provides further guidance on the establishment and use of frame formulations and the release of information on active substances and products.

Once the evaluation is completed and a decision has been reached on whether a product may be authorised/registered, the competent authority will need to inform the applicant of its decision and the conditions under which the authorisation/registration is granted. In all cases, the competent authority must provide sufficient information to explain how the decision was reached, particularly when the conditions initially proposed by the applicant are amended. If the decision is that further information is required before authorisation can be granted, the competent authority should agree with the applicant on a timetable for submission.

9.2 PREPARATION OF SUMMARY OF AUTHORISATION OR REGISTRATION

Article 8(10) of the Directive requires competent authorities to keep:

- a file containing a copy of the application;
- a copy of the summary of the dossiers submitted; and
- details of the administrative decisions taken for each application.

The summary produced should contain sufficient information to allow other Member States to trace how the decision to authorise or not to authorise a product was reached. In any case other Member States may require to receive the full information both on the product and the active substance(s), cf. Article 8(10) of the Directive.

The summary for each product evaluated should contain information to such detail to prove that the data requirements according to Annex II and III have been fulfilled. At least the following information is required:

1. Details of the applicant (authorisation/registration holder) and the formulator company, e.g. names, addresses and telephone numbers, etc.
2. Identity of the biocidal product, e.g. product name, name and percentage of active substance(s), formulation details, etc.
3. Identity of the product type to which the product belongs.
4. Procedure for evaluation (authorisation or registration) and date on which authorisation/registration were granted.
5. Summary of both the physical and chemical properties of the product and the methods of identification and analysis.
6. Summary of the risk assessment for human health including specific toxicological endpoints, potential for exposure and an overall integration of human health risk characterisation.

7. Summary of the risk assessment for the environment including effects assessment, exposure assessment and risk characterisation.
8. Unacceptable effects of the biocidal product e.g. resistance, unacceptable suffering of the target organisms, other effects.
9. Summary of the efficacy of the biocidal product including function of the product, evaluation of label claims, pests controlled, effects on target organisms, known limitations.
10. Summary of the final decision taken; in case of a negative decision a summary of the justifications leading to the decision must be taken.

In addition, on each product authorised/registered, the following information is required:

- Classification, packaging and labelling for the biocidal product, e.g. hazard symbols, indications of danger, proposals for safety data sheets.
- Conditions of authorisation of the biocidal product, e.g. method of application, application rate, product type, field of use, user, proposed limits on residues (where appropriate), any other restrictions.

Where letters of access and/or reasoned cases are used to satisfy data requirements or specific data are not provided for a justifiable reason, sufficient explanation must presented in the summary to ensure that Member States can fully comprehend the decisions made with respect to the application.

9.3 DATA PROTECTION, CONFIDENTIALITY AND RELEASE OF INFORMATION

9.3.1 Distinctions between data protection and confidentiality

Data protection is a system of protecting data such that only those companies who have paid for the data or are granted access to them can use the data to support Annex I/IA inclusion or product authorisation/registration. Data protection is only given for a fixed period of time. After this the data are no longer protected and can be used by any applicant in support of an Annex I/IA inclusion or a product authorisation/registration.

There is an important distinction between "ownership" and "granted access". The owner(s) has access to the whole data package including the raw data, whereas the company that has been granted access (through a letter of access) does not necessarily have access to other data than the data available to the general public, but the competent authority can use the data package on behalf of the authorising company to evaluate the biocidal product.

Confidentiality refers to the system whereby competent authorities do not release certain items of the data, necessary for annex I/IA entry of an active substance or authorisation/registration of a product, to other parties. The information which is confidential is commercially sensitive. Confidentiality is for an indefinite period or until the owner of this information informs the competent authority that it is no longer confidential.

There is therefore no link between data protection and confidentiality. Data which are protected are not necessarily confidential, and conversely confidential data are not necessarily protected. When the time period of data protection has ended confidentiality will still apply. The differences between data protection and confidentiality are illustrated in Figure 9.1.

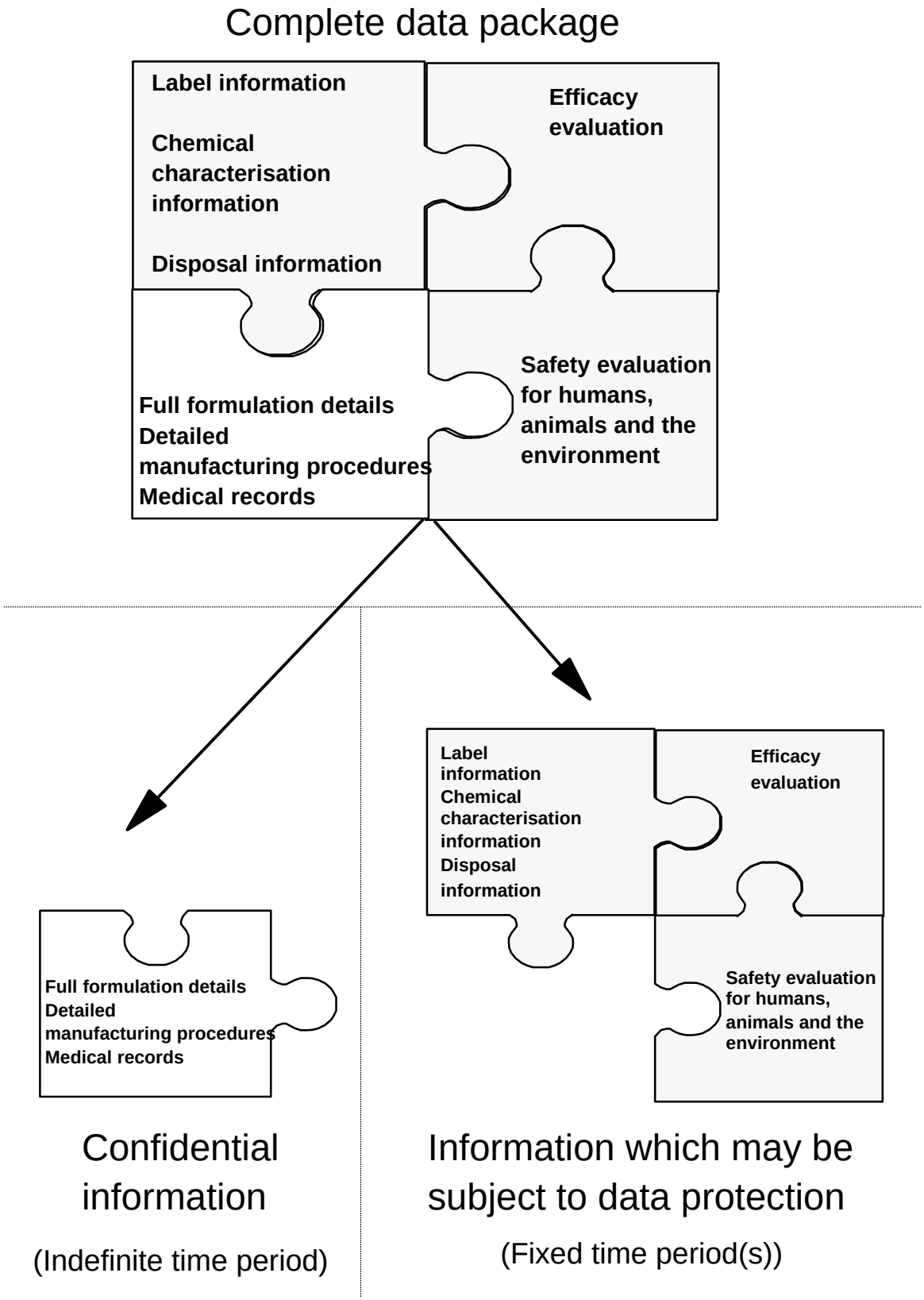


Figure 9.1 ***Data protection and confidentiality within a data package***
Note: Aspects of the release of information are different for protected and confidential information. Protected data can be released but confidential information can not.

9.3.2 Data protection

[The subchapters 9.3.2 and 9.3.3 will be revised when the data protection document which is discussed at CA level is adopted.]
Article 12 of the Directive establishes conditions including time limits for the protection of those data referred to in Article 8 of the Directive. This protection of data ensures that:

- only those companies who own these data, or
- those given permission to access these data by the data owner through a letter of access,

may use these data to support their applications for registration/authorisation.

The system of data protection:

- allows industry to recover the cost of producing these data for both the Annex I/IA entry of the active substance and the authorisation of the biocidal product;
- gives data protection for a specified period of time as laid down in Article 12, and once this period has expired these data are no longer subject to protection; and
- does not give protection to data which are already publicly available, for example published studies.

9.3.3 Periods of data protection

Article 12 establishes conditions for data protection for both new and existing active substances and biocidal products, and distinguishes between new and existing data. A new active substance is one which was not on the European market on the date of implementation of the Directive. Table 9.1 gives details of the periods of protection which apply to data.

Table 9.1 ***Summary of data protection periods***

Data on	Purpose of submission	Time period
New active substance	First entry to Annex I/IA	15 years
Existing active substance	Following its entry onto Annex I/IA	Up to 10 years
Additional data on existing or new active substance	To maintain/vary the active substance's Annex I/IA entry	At least 5 years
New biocidal product	For the first authorisation of a biocidal product	10 years
Existing biocidal product	Following the product's authorisation	Up to 10 years
Additional data on existing and new biocidal product	To vary the conditions of a biocidal product's authorisation	At least 5 years

From Table 9.1 it can be seen that the period of protection depends on whether the data are for the active substance or the biocidal product. It also depends on whether or not the data are new or existing.

When an applicant has been successful in gaining or altering entry on Annex I/IA for an active substance or the authorisation/registration of a biocidal product, it will be necessary for the competent authority to identify, for each individual item of data (i.e. complete reports or documents) used to support the application/review:

- the data owner;
- any other companies which have the right to use these data on their behalf (through letters of access);
- if the data are new or existing; and
- if any data protection already applies under existing national rules in their territory.

The periods of data protection, as shown in Table 9.1, should be assigned to each piece of data (e.g. each study report). Different items of data in a data package may have different periods of data protection. For example, a data package may include a mixture of new and existing data.

To ensure that competent authorities can monitor data protection, accurate records should be kept. Once the period of data protection has expired, the data are no longer protected and any applicant can instruct a competent authority to use these data on their behalf without requiring a letter of access from the original data owner.

Data protection under Article 12 does not prejudice the use of data on either an active substance or a biocidal product by the European Commission, the Scientific Committees (as referred to in Article 27) and the Member States for the purposes of carrying out the instructions of the Directive.

9.4 CONFIDENTIALITY

Article 19 of the Directive establishes conditions for the confidentiality of information which an applicant considers to be commercially sensitive (i.e. disclosure of which might harm the applicant industrially or commercially). This information should only be made known to the competent authorities and the European Commission. A system of confidentiality is necessary to protect the results of the research and development of individual companies by not allowing third parties to use the information for their own commercial benefit. The Article also lists items which can not be claimed to be confidential.

The applicant must indicate, with full justification, which information is considered to be confidential (details of the full product formulation will always be confidential). The competent authority will then decide whether the justification is sufficient. Information which may be considered as confidential includes the following:

- technical details of the manufacturing process;
- names and addresses of test laboratories, sites and personnel; and
- individual medical details.

Such confidentiality is normally for an indefinite period, and is independent of data protection. Therefore, even after a period of data protection expires, confidential information will continue to be confidential.

Confidentiality operates independently of the patent protection requirements, and without prejudice to Council Directive 90/313/EEC on the freedom of access to information on the environment, or to the provisions of Directives 67/548/EEC, 1999/45/EC and 95/46/EC.

9.5 RELEASE OF INFORMATION

There is no clear statement within the Directive about the release of information other than that the conditions of other directives concerning such release must be fulfilled, specifically 90/313/EC on the freedom of access to information on the environment. Release of information by the competent authority does not affect the data protection status of this information.

Release of information can be considered as falling into one of two groups. Either it is "reactive release" where information is requested from an individual or interested party, or it is "active release" where the competent authority actively releases information, e.g. by official publications. Such forms of release are likely to be driven by national legislation in each Member State as long as these do not prejudice current or future Directives covering this issue.

Anyone may request to see data, submitted for the purposes of this Directive to a competent authority, for example under Directive 90/313/EEC on the freedom of access to information on the environment. Therefore, competent authorities will need to keep formal archives of all data submitted to them which can be accessed by individuals if required. The competent authority should

ensure that any confidential information is not released. This may involve removing such information from data held in these archives prior to it being released.

9.6 FRAME FORMULATIONS

Frame formulations are a specific tool for use by the competent authority to establish efficient systems of work for authorising and registering biocidal products. Frame formulations are defined in Article 2 as follows:

> "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 lower risk, and which do not decrease its efficacy."

In addition, the use of frame formulations is referred to in Annex VI, paragraph 9:

> "It is known that many biocidal products present only minor differences in composition and this should be taken into account when evaluating dossiers. The concept of "frame formulations" is relevant here."

They should also be considered in the context of Annex VI, paragraph 12:

> ".....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, animals and the environment."

The use of frame formulations:

- reduces the complexity of the authorisation system by permitting products to be authorised in ranges of colours and fragrances without the need for specific data on every formulation variation. This reduces the amount of data needed and the need for multiple assessments on virtually identical products; and
- does not compromise human or environmental safety or the efficacy of a product resulting from their use. This is because there will have been an assessment completed on a dossier of one formulation within this frame and all other formulation variations only represent minor differences from that which the dossier supported.

A product which has been assigned to a frame formulation:

- must be used in the same way as other products in the frame formulation; and
- be able to satisfy the label claims made for this frame.

In addition:

- products from different applicants may fall within an existing frame formulation; and
- the use of frame formulations introduces the concept that a range of formulations (which are similar but not identical) can be supported by a single data set.

Examples of the use of frame formulations are presented in Appendix 9.1.

In addition to frame formulations being used by the competent authority there is provision in the Directive for the communication of frame formulations to applicants under Article 3 which states that:

"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."

However, a detailed frame formulation may only be communicated to the party(ies) whose products originally established the frame formulation so that issues of confidentiality and data protection are not compromised.

9.7 PROVISION OF NEW INFORMATION

Article 14 of the Directive requires Member States to introduce procedures to ensure that the holder of an authorisation for a biocidal product shall notify the competent authority immediately of any information on either the active substance or the biocidal product which may affect its continued authorisation. For example:

- Active substance(s)
  - changes in source/composition, including impurities
  - new information on effects, for example
    - effects not reported in the evaluation of the active substance agreed by the Standing Committee on Biocides (SCB)
    - effects reported in previous evaluations at higher concentrations but subsequently found to occur at significantly lower concentrations
- Biocidal product
  - new information on effects (of product, coformulants)
  - changes in composition including impurities
  - development of resistance or other unacceptable effects
  - changes in the level of residues
  - administrative changes (e.g. company name)
  - packaging

In addition, the information may be provided to satisfy a data requirement from a previous authorisation decision, or it may be in an effort to change a decision (e.g. the applicant may be able to scientifically demonstrate that under relevant field conditions the risk of concern is not expressed, either directly or indirectly, by the biocidal product according to the proposed conditions of use). In such circumstances the competent authority must decide on a case by case basis whether to consider the new information as part of the original application, or as a new submission.

If new information is received on the active substance(s), the competent authority must immediately inform the European Commission. The European Commission must then determine whether the new information is such that a review of the Annex I inclusion of the active substance(s) is necessary. If this is the case, the European Commission will appoint a rapporteur to undertake the work and make recommendations to the SCB.

If the new information is on the biocidal product or a coformulant, the competent authority must assess the data and review the authorisation of the product. Once the competent authority has completed its assessment and review, it will amend the authorisation if necessary and then inform the European Commission and other competent authorities of its actions. In accordance with Article 7(3) of the Directive, if the decision is that an existing authorisation should be cancelled, the competent authority must also inform and hear the authorisation holder before reaching a final decision.

The timetable for such procedures will depend on the type of data provided, but should be no longer than that required to consider an application.

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GLOSSARY

Anecdotal evidence

A report based on personal experience or observation with no validated data to support it.

Animals

Animals belonging to species which are normally fed and kept or consumed by people. This includes companion animals (pets) and livestock. It does not refer to wild species of fauna in the context of this document.

Antagonism

The combined effect of two or more substances that is lower than the sum of their individual effects.

Article

A product in which a substance is integrated and is not meant or designed to escape from, or does not easily do so, during normal use (excluding consideration of accidents, waste or eventual recycling).

Biological agent

Any micro-organism or endoparasite which may cause any infection, allergy or toxicity, or otherwise create a hazard to humans, animals or the environment.

Default value

An agreed number that is used when real data for a particular parameter are not available (e.g. in exposure modelling).

Disposal

The removal of excess product, the container or material containing the biocide via normal waste-treatment systems.

Hazard

An inherent source of harm.

LC_{50}

Lethal Concentration 50% - usually expressed as mg/l or ng/m^3. A measure of acute toxicity being the concentration of a substance in air expected to kill 50% of a population of test animals exposed for a specified period.

LD_{50}

Lethal dose 50% - usually expressed as mg/kg. A measure of acute toxicity, being the dose of a substance expected to kill 50% of a population of test animals exposed for a specified period.

Letter of access

A letter of authorisation from a data holder that allows the competent authority to use their data package on behalf of a third party in support of that party's application. The third party does not physically receive the data package itself.

Normal use

This is use which is intended by the producer of the product. Exposure as a result of accidents (e.g. release during transport) or abuse (e.g. suicide attempts) is not addressed in this document.

OECD

Organisation of Economic Co-operation and Development

Product

A chemical preparation (formulation).

Proofing

The creation of a barrier to prevent an organism's access to an item or space.

Read across

The use of data in support of an application which has not been obtained using the chemical (product or active substance) to which the application refers. Usually this means data obtained from studies using a similar, but not identical, chemical. This is only permissible if a reasoned case can be given for such an action which is acceptable to the competent authority.

Realistic worst case

The reasonable unfavourable but not unrealistic situation. It includes cases where populations are exposed to a product from minor spills during normal use, upper estimates of extreme use, and reasonably foreseeable misuse.

Reasonably foreseeable misuse

Use which is not intended by the producer of a product, but which could occur when a reasonable person uses the product in the absence of any indications to the contrary. It should also take account of the behaviour of the elderly and children (e.g. accidental swallowing of a product). It does not refer to product abuse.

Risk

The possibility that a harmful event arising from exposure to a chemical or physical agent may occur under specific conditions.

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 normally be classified as dangerous according to Directive 67/548/EEC and be present in the biocidal product at a concentration leading the product to be regarded as dangerous within the meaning of Article 3 of Directive 1999/45/EC. Other grounds for concern include, for example, effects for which classification criteria have not yet been developed, or other undesirable effects such as significant persistence.

Synergism

The combined effect of two or more substances that is greater than the sum of their individual effects.

Systemic effect

The non-localised effect of a chemical.

Treated material

A product or article to which a biocidal product has been intentionally applied.

Use

See 'Normal' use and 'Reasonably foreseeable misuse'.

Appendices to chapter 4

Appendix 4.1 ACUTE TOXICITY

A4.1.1 Data available

a) Biocidal product

i) There should be animal data from acute oral, dermal and possibly inhalation studies.

ii) If studies have not been conducted, information can be derived from:
- product component data (see b) and c) below), leading to classification under Directive 1999/45/EC; and
- similar products (e.g. classification based on a frame formulation).

iii) Human data may be available for either the biocidal product itself or a similar one (particularly those containing existing active substances). Examples include:
- reports on the effects of accidents or abuse; and

b) Active substance

i) Use the acute toxicity profile and classification (via oral, dermal and possibly inhalation exposure) agreed at Annex I (of Directive 98/8/EC) inclusion.

ii) Relevant information may also be available from other studies

c) Substance(s) of concern

i) Check Annex I of Directive 67/548/EEC for classification for acute toxicity.

ii) Check the data required according to chapter 2 Part B point 6.5 and Chapter 4.3 of the TNsG on Data Requirements.

Experimental human toxicity studies must not be conducted specifically for the purposes of biocidal product authorisation.

A4.1.2 Assessment

a) **Classify the biocidal product for acute toxicity**, taking care to ensure that, for dermal and inhalation studies, the duration of exposure is relevant to the classification criteria specified in Annex VI of Directive 67/548/EEC.

b) If the product <u>is</u> classified, **determine which component(s) contribute to this classification** (where possible). The risk characterisation is performed on these components.

c) If the product is not classified, determine whether acute toxicity is still a ground for concern.

d) **Determine dose-response relationships** for all the components contributing to the classification, where possible. For the active substance(s), this will have been done during consideration of the Annex I listing.

<u>Note</u>: Numerical values derived for acute toxicity in animals may be an $LD(C)_{50}$ value or a discriminating dose. If NOAELs or 'no-mortality' levels are available, then these should be identified.

A4.1.3 Risk characterisation

a) Risk characterisation is necessary when there is a possibility of discrete single exposures (by ingestion, dermal contact or inhalation). For example:
- maintenance operations;
- occasional use by both professionals and non-professionals, e.g. once a month to humans;
- risks from foreseeable misuse (e.g. where a child might swallow the product)

If exposure can be by more than one route simultaneously, then total exposure should be determined.

N.B. Biocidal products classified as Toxic or Very Toxic cannot be authorised for use by non-professionals.

b) Compare the predicted exposure with the effects assessment for acute toxicity, using:
- a no-effect level from human or animal studies, if available; or
- the $LD(C)_{50}$ from animal studies (this is more usual); or
- a discriminating dose from a Fixed Dose Procedure study.

A4.1.4 Conclusions

a) If the ratio of the likely exposure and the relevant concentration in the acute study is not of concern then authorisation can be granted.

b) If the difference is of concern then authorisation is likely to be refused. The applicant should be consulted to see if the reliability of the risk assessment can be improved, through revision of either the exposure assessment (e.g. data from monitoring) or the effects assessment (e.g. studies indicating no-effect levels in animals).

A4.1.5 Risk management options

Risk management conditions to consider include:

i) For professionals:
- engineering controls; and
- use of personal protective equipment.

ii) For non-professionals:
- child resistant closures.

Appendix 4.2 IRRITATION AND CORROSIVITY

A4.2.1 Data available

a) Biocidal product

i) There should be animal test data from skin and eye irritation studies.

ii) If studies have not been conducted, information can be derived from:
- the product has been shown to have potential corrosive properties (and is classified)
- product component data (see b) and c) below), leading to classification under Directive 1999/45/EC; and
- similar products (e.g. classification based on a frame formulation).

b) Active substance

i) Use the skin and eye irritation profile and classification agreed at Annex I inclusion.

ii) Relevant information may also be available from other studies in which local responses of the skin, eye, mucous membranes and/or respiratory system were reported.

c) Substance(s) of concern

i) Check Annex I of Directive 67/548/EEC for classification for irritancy or corrosivity.

ii) Check the data required according to chapter 2 Part B point 6.5 and Chapter 4.3 of the TNsG on Data Requirements.

d) **Experimental human toxicity studies must not be conducted specifically for the purposes of biocidal product authorisation.** However, useful human data from well-documented case-reports or epidemiological studies (on either the active substance(s) or the biocidal product or a closely related one) can provide very useful information on skin and/or respiratory irritation, sometimes for a range of exposure levels. Often the only useful information on respiratory irritation, which can be a threshold effect in the workplace, is obtained from human experience. The usefulness of all human data on irritation will depend on the extent to which the effect, and its magnitude, can be reliably attributed to the active substance(s) or biocidal product. Experience has shown that it is difficult to obtain useful data on active substance-induced eye irritation, but data may be available on human ocular responses to certain biocidal products.

A4.2.2 Assessment

a) **Classify the biocidal product for skin, eye and, where appropriate, respiratory irritation**, taking care to ensure that the studies used are relevant to the classification criteria specified in Annex VI of Directive 67/548/EEC.

b) If the product is classified, **determine which component(s) contribute to this classification** (where possible). The risk characterisation is performed on these components.

c) If the product is not classified, determine whether irritation or corrosivity is still a ground for concern (see section 4.4.1).

d) **Determine dose-response relationships** for all the components contributing to the classification, where possible. For the active substance(s), this will have been done during consideration of the Annex I inclusion.

Note:

i) Usually, it is not possible to derive non-irritating concentrations from standard skin and eye irritation studies. Values may, however, be derived from studies in which a range of concentrations were used.

ii) For respiratory irritation, non-irritating concentrations may be derived from studies using inhalation exposure in which respiratory system irritation was observed.

iii) It may be possible to derive reliable non-irritating concentrations from human studies. However, data may only show that a substance is irritant, or causes transient irritation or (by inference) is not irritating.

A4.2.3 Risk characterisation

a) Risk characterisation is necessary:
   - if populations can be exposed to the biocidal product through skin or eye contact; or
   - if there is potential for inhalation exposure.

b) Skin and eye irritation and corrosivity
   Given the nature, likelihood, and duration of potential exposure, consider whether such reactions would occur in practice. Make use of any available information from studies where non-irritating concentrations have been determined.

c) Respiratory irritation
   - If information on non-irritating concentrations is available, compare the effects assessment with the predicted exposure.
   - If there is no information on non-irritating concentrations, adopt a pragmatic approach taking into account the pattern and extent of human exposure.

A4.2.4 Conclusions

a) If the likely exposures indicate that corrosivity/irritation are unlikely to occur, then authorisation can be granted.

b) Particular attention should be given to biocidal products classified under 99/45/EC as severely irritant or corrosive to skin, or severely damaging to eyes or as irritant to the respiratory tract. Exposure during all stages of use of typical products should be described for prescribed conditions of use taking into account the presentation and/or delivery of the product. Data from Poison Control Centers could also be used in the assessment process. The full range of risk management procedures should be used to reduce the possible risk arising from the use of biocidal products classified as severely irritant or corrosive to an acceptable level, bearing in mind for non-professional use paragraph 73 of Annex VI of the Biocidal Products Directive. Risk management could play a key role for the final acceptability of the use of products and would, therefore, be influential in the decision as to whether the risk from use of the biocidal product is acceptable. Consequently, the risk from these effects of particular concern will have to be considered on a case-by-case basis. Authorisation of a product with these effects for use by the general public should not be allowed unless safe use can be demonstrated.

A4.2.5 Risk management options

Risk management conditions to consider include:

i) For professionals:
   - engineering controls; and
   - use of personal protective equipment.

ii) For non-professionals:
   - closed transfer systems for diluting concentrates; and
   - ready-for-use formulations.

Appendix 4.3 SENSITISATION

A4.3.1 Data available

a) Biocidal product

i) There should be a skin sensitisation study in animals.

ii) If a study has not been conducted, information can be derived from:
- product component data (see b) and c) below), leading to classification under Directive 1999/45/EC; and
- similar products (e.g. classification based on a frame formulation).

b) Active substance

Use the information from the skin sensitisation study and classification agreed at Annex I inclusion.

c) Substance(s) of concern

i) Check Annex I of Directive 67/548/EEC for classification for sensitisation.

ii) Check the data required according to chapter 2 Part B point 6.5 and Chapter 4.3 of the TNsG on Data Requirements.

d) **Experimental human toxicity studies must not be conducted specifically for the purposes of biocidal product authorisation.** However, human data may be available on both older active substances and biocidal products. These may include case reports or epidemiology studies from human exposure. Those which report on cutaneous (allergic dermatitis, eczema) or respiratory (allergic rhinitis, alveolitis, asthma) reactions are of particular significance. Studies indicating negative results should also be evaluated.

Data from dermatologic tests (e.g. Human Repeated Insult Patch test, skin prick test) and also from bronchial challenge provocation tests will sometimes be available. Immunological tests (e.g. RAST) may be helpful. Structural similarities with known sensitisers should be considered.

Note: Respiratory sensitisation
Some data (usually from studies on the active substance(s) or individual components of the biocidal product) may be available from animals on the respiratory sensitisation potential of the biocidal product. No methods are yet fully validated.

A.4.3.2 Assessment

a) **Classify the biocidal product for skin and respiratory sensitisation**, taking care to ensure that the studies used are relevant to the classification criteria specified in Annex VI of Directive 67/548/EEC.

b) If the product is classified, **determine which component(s) contribute to this classification** (where possible). The risk characterisation is performed on these components.

c) If the product is not classified, determine whether sensitisation is still a ground for concern (see section 4.4.1). For example, consider:
- the severity of the sensitisation reactions;
- whether classified components can increase in concentration (e.g. if a liquid product dries out);
- the test protocols used (e.g. a positive maximisation test for the active substance(s) but a negative Buehler test for the product); and
- when a well-conducted animal study is negative, whether there are reports in humans of responses to components at concentrations similar to that in the product. In this case the positive human data would override the negative product data.

d) **Determine dose-response relationships and NOAELs** (see Notes) when it is decided a risk characterisation is necessary. For the active substance(s), this will have been done during consideration of the Annex I inclusion.

Note:

i) It is not usually possible to derive non-sensitising concentrations from standard skin sensitisation studies.

ii) For respiratory sensitisation data on non-sensitising concentrations may be available.

iii) Some physico-chemical characteristics and biological properties (e.g. reactivity with proteins) appear to be important correlates. It is probable that most, if not all, substances which are respiratory allergens also have the potential to cause skin sensitisation in experimental models. The converse is not necessarily true, however, since there are substances which elicit positive responses in predictive tests for skin sensitisation that have not been found to induce respiratory sensitisation in humans.

iv) In general, positive results from human studies will override negative results from animal tests. However, particular attention should be paid to:
- the number of well-documented cases in relation to the size of the exposed population;
- the existence of two types of population: individuals previously sensitised to other active substances or biocidal products and individuals not previously sensitised;
- the type of exposure: e.g. adequate identification of test article, multiple exposure, physical state, and concentration/quantity of the active substance or biocidal product, frequency and duration of exposures; and
- reports of sensitisation to substances with structural analogues.

A.4.3.3 Risk characterisation

a) Risk characterisation is necessary:
- if populations can be exposed to the biocidal product through skin contact; or
- if there is potential for inhalation exposure.

b) Skin sensitisation
Given the nature, likelihood, and duration and frequency of potential exposure, consider whether such reactions would occur in practice. Make use of any available information from studies where non-irritating concentrations have been determined.

c) Respiratory sensitisation
- If information on non-sensitising concentrations is available, compare the effects assessment with the predicted exposure.
- If no information is available on non-sensitising concentrations, adopt a pragmatic approach, taking into account the pattern and extent of human exposure.

A4.3.4 Conclusions

a) If the likely exposures indicate that sensitisation is unlikely to occur, then authorisation can be granted.

b) If a reaction in humans could occur, then consider the severity of the effects and whether there are ways potential exposure could be reduced. If following this it is still considered that sensitisation reactions in humans are likely to occur, then authorisation is likely to be refused. The applicant should be consulted to see if the reliability of the risk assessment can be improved, through revision of either the exposure assessment (e.g. data from monitoring) or the effects assessment (e.g. studies on modified formulations with a lower concentration of the sensitising substance(s), or studies on the original formulation indicating no-effect levels).

A4.3.5 Risk management options

Risk management conditions to consider include:

i) For professionals:
- engineering controls;
- use of personal protective equipment; and
- improved packaging, e.g. the use of water soluble packaging.

ii) For non-professionals:
- closed transfer systems for diluting concentrates; and

Appendix 4.4 REPEATED DOSE TOXICITY

Repeated dose toxicity comprises the adverse general toxicological effects (i.e. excluding reproductive, genotoxic or carcinogenic effects) occurring as a result of repeated daily dosing with, or exposure to, a substance for a part of the expected lifespan (sub-acute or sub-chronic) or for the whole, or major part of, the lifespan (chronic exposure).

A4.4.1 Data available

a) Biocidal product

   i) There are no specific data requirements. The hazardous properties of the biocidal product are normally determined by reference to those of the active substance(s) and substance(s) of concern.

   ii) Data on dermal penetration

   Such data, usually determined from studies using a single application, may be derived from studies on the specific formulation, similar formulations (i.e. based on the frame formulation concept) or simple formulations based on similar solvents (e.g. water or organic based).

b) Active substance

   Use the repeated dose toxicity profile and classification agreed at Annex I inclusion.

c) Substance(s) of concern

   i) Check Annex I of Directive 67/548/EEC for classification for repeated dose toxicity.

   ii) Check the data required according to chapter 2 Part B point 6.5 and Chapter 4.3 of the TNsG on Data Requirements.

d) There may be human data including epidemiology studies and other human experience although experimental human toxicity studies must not be conducted specifically for the purposes of biocidal product authorisation.

A.4.4.2 Assessment

a) **Classify the biocidal product for repeated dose toxicity.** b) If the product <u>is</u> classified, **determine which component(s) contribute to this classification** (where possible). The risk characterisation is performed on these components.

c) If the product is not classified, determine whether repeated dose toxicity is still a ground for concern.

d) **Determine dose-response relationships and NOAELs**. For the active substance(s), this will have been done during consideration of the Annex I inclusion.

   <u>Notes</u>:

   i) In selecting the most appropriate N(L)OAEL when considering data on the biocidal product, active substance or a substance of concern, give preference to:
      - In the absence of a species that is clearly most relevant for humans, tests on the most sensitive animal species are used. However, do not choose an N(L)OAEL on the basis of animals that are known not to be extrapolated to humans or are adaptive in nature;
      - tests using the most appropriate route, duration and frequency of exposure in relation to the expected route(s), frequency and duration of human exposure to the biocidal product during normal and realistic worst case exposure scenarios. This may mean that several N(L)OAELs from studies of different durations and routes of exposure are identified for use in the risk assessments for different populations exposed to the biocidal product.

   ii) Sometimes a critical effect can be identified and be the subject of specific investigation(s). In these cases greater weight should be given to specific tests investigating this effect in the identification of the N(L)OAEL.

iii) When reliable and relevant human data are available, they can be very useful for hazard identification and even preferred over animal data. However, human data adequate to serve as the sole basis for the dose-response assessment are rare because for many studies:

- the circumstances of exposure and the exposure levels themselves are not well known;
- exposures may have occurred to several substances;
- the incidence of effects is low;
- the number of exposed individuals is small; and
- the latency period between exposure and disease may be long.

In addition, the exposed population may be mixed with respect to age, sex, diet, environment, activity patterns, physical fitness and genetic constitution. Such studies require careful interpretation.

iv) Neurotoxicity and other special properties

There may be occasions where specific organ/system toxicity is identified in repeated dose toxicity studies. Such effects may be subject to specific investigations. The protocols used for such investigations may be internationally agreed guidelines (e.g. delayed neurotoxicity study in the adult hen) or be specific for the effect under investigation. For further guidance in the areas of neurotoxicity, immunotoxicity (there are strategies currently being agreed internationally for both of these) and lung overload and fibrosis, see the publication of the European Commission, 1996.

All these effects are usually considered to have an underlying dose threshold mechanism. When possible, a N(L)OAEL value for the adverse effect should therefore be identified for use in risk characterisation. In addition, the dose-response relationship should be assessed. For active substances this will have been done during consideration of the Annex I inclusion.

In selecting the most appropriate N(L)OAEL when considering data on the biocidal product or substance of concern, give preference to:

- studies conducted according to international guidelines and/or strategies where these exist;
- tests using a species which is an accepted model for humans.

In all other respects, the data available and their evaluation are considered in the same way as typical repeated dose studies.

A.4.4.3 Risk characterisation

a) Risk characterisation is necessary where there is potential for frequent, repeated exposure.

N.B. Biocidal products classified as Toxic with the risk phrase 'Danger of serious damage to health on prolonged exposure' cannot be authorised for use by non-professionals.

b) Choose N(L)OAELs appropriate to the exposure pattern in terms of:
- frequency (daily/weekly/seasonal);
- duration (continuous, whole working day, small part of day); and
- routes (inhalation, dermal, ingestion or a combination).

For example, where exposure:
- is repeated but only on a very small number of days during the year (e.g. in batches), choose the N(L)OAEL from a 28 day study;
- is repeated over longer periods of the year for a working life (e.g. seasonal work or certain types of shift work), choose the N(L)OAEL from a 90 day study; and
- is life-long (e.g. continuous daily exposure over a working life, or long-term exposure to non-professionals or populations that are indirectly exposed via the environment), choose the N(L)OAEL from a study with a duration of at least 12 months.

Notes:

i) Appropriate use of toxicokinetic information and data on dermal penetration may be needed when undertaking route:route extrapolations and when converting from, for example, an oral dose to a systemic N(L)OAEL.
ii) If the major route of exposure is dermal or inhalation and appropriate studies using such routes are available, the N(L)OAEL from such studies may be more appropriate. This is particularly the case if the same systemic effect is identified as the critical effect from a range of studies by different routes.
iii) In choosing the most relevant study for the N(L)OAEL, the competent authority must consider the toxicokinetics of the substance in question (e.g. whether bioaccumulation is possible, etc.).

c) Compare the predicted exposure with the appropriate N(L)OAEL to give a margin of exposure (MOE).

If exposure can be by more than one route simultaneously, use the total exposure.

d) A same type of evaluation has to be undertaken using the AOEL value.

A4.4.4 Conclusions

a) If the MOE between the likely exposures and the N(L)OAEL are satisfactory then authorisation can be granted.

b) If the MOE is not satisfactory then consider whether there are ways potential exposure could be reduced. If following this it is still considered that repeated dose effects are likely to occur, then authorisation is likely to be refused. The applicant should be consulted to see if the reliability of the risk assessment can be improved, through revision of either the exposure assessment (e.g. data from monitoring) or the effects assessment (e.g. studies indicating no-effect levels in animals).

c) A same type of evaluation has to be undertaken using the AOEL value.

A4.4.5 Risk management options

Risk management conditions to consider include:

i) For professionals:
- engineering controls;
- use of personal protective equipment; and
- a warning not to use the product in situations where bystander exposure could be continuous.

ii) For non-professionals:
- authorisation for occasional use only.

Appendix 4.5 GENOTOXICITY

A4.5.1 Data available

a) Biocidal product

There are no specific data requirements. The genotoxic (mutagenic) properties of the biocidal product are normally determined by reference to those of the active substance(s) and substance(s) of concern.

b) Active substance

i) Use the genotoxicity profile and classification agreed at Annex I inclusion (Annex I relating to both Directive 98/8/EC and 67/548/EEC).

ii) For older active substances there may be additional data available from animal studies. Some of these studies may have been conducted according to recent international guidelines. However, others may have been conducted to older protocols.

c) Substance(s) of concern

i) Check Annex I of Directive 67/548/EEC for classification for mutagenicity (genotoxicity).

ii) Check the data required according to chapter 2 Part B point 6.5 and Chapter 4.3 of the TNsG on Data Requirements.

d) It is very rare for data from studies in humans to be available.

A.4.5.2 Assessment

a) **Classify the biocidal product for mutagenicity (genotoxicity)**.

b) If the product is classified, **determine which component(s) contribute to this classification** (where possible). The risk characterisation is performed on these components.

c) If the product is not classified, determine whether genotoxicity is still a cause for concern

Note: It is prudent to assume that, with the possible exception of aneuploidy, a threshold does not exist for genotoxicity.

A.4.5.3 Risk characterisation

Risk characterisation is necessary where exposure is expected or can be predicted.

A4.5.4 Conclusions

a) It is prudent to assume that there is no safe level of exposure. Nevertheless, if there is an outstanding benefit for the product (e.g. for the treatment of infectious organisms) consider whether all available opportunities have been taken to reduce exposure to a very low level. If this is the case, it is possible that authorisation may be granted.

b) If there is still concern over exposure and quantitative data are not available, then these should be obtained. If there is likely to be exposure to unprotected people then it is likely that authorisation will be refused.

N.B. Biocidal products classified as Mutagens in Categories 1 or 2 cannot be authorised for use by non-professionals.

A4.5.5 Risk management options

Risk management conditions to consider include:

For professionals:

- engineering controls;
- use of personal protective equipment; and
- a warning not to use the product in situations where bystander exposure may occur.

Appendix 4.6 CARCINOGENICITY

A4.6.1 Data available

a) Biocidal product

There are no specific data requirements. The carcinogenic properties of the biocidal product are normally determined by reference to those of the active substance(s) and substance(s) of concern.

b) Active substance

i) Use the carcinogenicity profile and classification agreed at Annex I inclusion.

ii) For older active substances there may be additional data available from animal studies. Some of these studies may have been conducted according to recent international guidelines. However, others may have been conducted to older protocols (some of which may have been individually designed).

c) Substance(s) of concern

i) Check Annex I of Directive 67/548/EEC for classification for both carcinogenicity and mutagenicity (genotoxicity).

ii) Check the data required according to chapter 2 Part B point 6.5 and Chapter 4.3 of the TNsG on Data Requirements.

d) Human data (usually epidemiology studies) may provide direct information on the carcinogenicity of older active substances. Such data will not normally be available for newer active substances.

A.4.6.2 Assessment

a) **Classify the biocidal product for carcinogenicity.**

b) If the product <u>is</u> classified, **determine which component(s) contribute to this classification** (where possible). The risk characterisation is performed on these components.

c) If the product is not classified, determine whether carcinogenicity is still a ground for concern.

d) For genotoxic carcinogens, it is prudent to assume that a threshold does not exist for carcinogenicity.

For non-genotoxic carcinogens of relevance to humans, with identifiable thresholds for the primary toxic effects of concern (e.g. sustained cell proliferation induced by cytotoxicity, or interference with cellular growth control), it may be possible to define a no-effect level for the underlying toxicity. In these cases **determine the dose-response relationship and N(L)OAEL**. For the active substance(s), this will have been done during consideration of the Annex I inclusion.

<u>Notes</u>:

i) In selecting the most appropriate N(L)OAEL for a substance of concern, give preference to:
- tests using a species which is an accepted model for humans.
- tests using the most appropriate route, duration and frequency of exposure in relation to the expected route(s), frequency and duration of human exposure to the biocidal product during normal and realistic worst case exposure scenarios.

ii) Sometimes a critical effect can be identified and be the subject of specific investigation(s). In these cases greater weight should be given to specific tests investigating this effect in the identification of the N(L)OAEL.

A.4.6.3 Risk characterisation

a) Risk characterisation is necessary where exposure is expected or can be predicted.

b) It is prudent to assume that there is no safe level of exposure for genotoxic carcinogens.

c) Non-genotoxic carcinogens can act by route-specific mechanisms (i.e. only following contact with the skin, gastro-intestinal tract or respiratory system).

   i) Consider whether exposure by such routes is likely to occur, and whether this is significant and prolonged.

   ii) In addition to the exposure <u>levels</u>, consider the exposure <u>pattern</u> in terms of:
   - frequency (daily/weekly/seasonal);
   - duration (continuous, whole working day, small part of day); and
   - routes (inhalation, dermal, ingestion or a combination).

   If exposure can be by more than one route simultaneously and carcinogenicity is not due to a route-specific mechanism, use the total exposure.

   iii) Determine the appropriate N(L)OAEL (usually from animal studies). Consider other data (e.g. N(L)OAELs from studies investigating the underlying mechanism(s) of toxicity), if these are available.

   iv) Compare the predicted exposure with the appropriate N(L)OAEL to give a margin of exposure (MOE).

   v) A same type of evaluation has to be undertaken using the AOEL value.

A4.6.4 Conclusions

N.B. Biocidal products classified as Carcinogens in Categories 1 or 2 cannot be authorised for use by non-professionals.

a) <u>Genotoxic carcinogens</u>

   i) Consider whether all available opportunities have been taken to reduce exposure to low level and that there is an outstanding benefit for the product. If this is the case, authorisation may be granted.

   ii) If there is still concern over exposure and quantitative data are not available, then these should be obtained. If exposure of unprotected people is likely, then authorisation will be refused.

b) <u>Non-genotoxic carcinogens</u>

   i) If the MOE between the likely exposures and the N(L)OAEL are satisfactory then authorisation can be granted.

   ii) If the MOE is not satisfactory then consider whether there are ways potential exposure could be reduced. If following this it is still considered that carcinogenic effects are likely to occur, then authorisation is likely to be refused. The applicant should be consulted to see if the reliability of the risk assessment can be improved, through revision of either the exposure assessment (e.g. data from monitoring) or the effects assessment (e.g. studies indicating no-effect levels in animals).

   iii) A same type of evaluation has to be undertaken using the AOEL value.

A4.6.5 Risk management options

Risk management conditions to consider include:

a) <u>Genotoxic carcinogens</u>

For professionals:
- engineering controls.

b) Non-genotoxic carcinogens

i) For professionals:
- engineering controls;
- use of personal protective equipment; and
- a warning not to use the product in situations where bystander exposure may occur.

ii) For non-professionals:
- authorisation for occasional use only.

Appendix 4.7 REPRODUCTIVE TOXICITY

A4.7.1 Data available

a) Biocidal product

There are no specific data requirements. The effects of the biocidal product on reproduction are normally determined by reference to those of the active substance(s) and substance(s) of concern.

b) Active substance

i) Use the reproductive toxicity profile and classification agreed at Annex I inclusion.

ii) For older active substances there may be additional data available from animal studies. Some of these studies may have been conducted according to recent international guidelines. However, others may have been conducted to older protocols (some of which may have been individually designed).

c) Substance(s) of concern

i) Check Annex I of Directive 67/548/EEC for classification for reproductive toxicity.

ii) Check the data required according to chapter 2 Part B point 6.5 and Chapter 4.3 of the TNsG on Data Requirements.

d) Human data will rarely be available.

A.4.7.2 Assessment

a) **Classify the biocidal product for toxicity to reproduction**.

b) If the product is classified, **determine which component(s) contribute to this classification** (where possible). The risk characterisation is performed on these components.

c) If the product is not classified, determine whether reproductive toxicity is still a ground for concern.

d) **Determine dose-response relationships and NOAELs** (reproductive toxicity is usually considered to be an effect with an underlying dose threshold mechanism). For the active substance(s), this will have been done during consideration of the Annex I inclusion. In selecting the most appropriate N(L)OAEL for a substance of concern, give preference to studies conducted according to international guidelines.

Detailed guidance on evaluation of effects with respect to single and multiple exposures and to other issues such as the relationship between developmental effects and maternal toxicity is provided in the Technical Guidance Document on Risk Assessment [EC 2002].

A.4.7.3 Risk characterisation

a) Risk characterisation is necessary where exposure is expected or can be predicted.

b) Underlying mechanisms of reproductive toxicity are usually considered to have a threshold for effects. Therefore carry out risk characterisation as for repeated dose toxicity. Particular attention should be given to the relationship between dose/concentration and both adverse effects on reproduction and other systemic toxicity. A higher MOE may be appropriate if the N(L)OAEL is based on serious developmental effects (e.g. major irreversible malformations).

c) In addition to the exposure levels, consider the exposure pattern in terms of:
- frequency (daily/weekly/seasonal);
- duration (continuous, whole working day, small part of day); and
- routes (inhalation, dermal, ingestion or a combination).

If exposure can be by more than one route simultaneously, use the total exposure. As developmental toxicity could occur as a consequence of a single exposure, exposures during a foreseeable misuse situation should also be assessed.

A4.7.4 Conclusions

N.B. Biocidal products classified as Toxic to Reproduction in Categories 1 and 2 cannot be authorised for use by non-professionals.

a) If the MOE between the likely exposures and the N(L)OAEL are satisfactory then authorisation can be granted.

b) If the MOE is not satisfactory then consider whether there are ways potential exposure could be reduced. If following this it is still considered that effects on reproduction are likely to occur, then authorisation is likely to be refused. The applicant should be consulted to see if the reliability of the risk assessment can be improved, through revision of either the exposure assessment (e.g. data from monitoring) or the effects assessment (e.g. studies indicating no-effect levels in animals).

c) A same type of evaluation has to be undertaken using the AOEL value.

A4.7.5 Risk management options

Risk management conditions to consider include:

i) For professionals:
- engineering controls;
- use of personal protective equipment; and
- a warning not to use the product in situations where bystander exposure may occur.

ii) For non-professionals:
- authorisation for occasional use only; and
- reduction in pack size.

[*These do not address the differences between single and multiple dose effects - Member States may need to agree on appropriate measures in each case.*]

Appendices to chapter 7

7.1 Details to be included in an efficacy test report

Properly designed studies should enable the results to be interpreted with confidence. In this respect appropriate attention should be given to items such as test substance, identity of organisms used, objectives of study, number of treated groups, appropriate controls, environment, replication and where relevant statistical analysis, etc. (cf. the requirements of ISO 17025)

In evaluating test reports, competent authorities should ensure that there is sufficient detail presented with respect to product identification, study methodology, test procedures, results and analysis, etc.

In evaluating data competent authorities should consider the following points:

1 Test objective

The objective of the test method(s) together with the criteria by which they are to be judged should be clearly defined. A clear description of the test procedure should be available.

2 Test substances

The test substance should ideally be the formulated product (or one very similar in formulation to the candidate product) for which authorisation is sought.

3 Use of controls and reference products

There should be appropriate inclusion of a negative (untreated) control wherever possible. In this case the experimental design of the study is identical to that of the biocidal challenge except that the biocidal agent is not applied in the control study. A biocidal agent may be considered as the formulation or as the actual biocidal active substance itself.

In situations where this is not practical (i.e. as is the case with certain field studies) suitable baseline conditions established before use of the product may be used. Use may also be made of suitable reference products (where one exists) as a control. A suitable reference product is a biocidal product that is authorised for the same use pattern as the candidate product and has proven efficacy. In general, formulation type, effects on the target organisms, working spectrum and method of application should be similar to those of the candidate product for which authorisation is sought.

Alternatively some standard test protocols cite certain materials as a reference compound. These materials will tend to be based on formulations of whose efficacy under the situations of the particular test has been demonstrated over a long period of time (for example in some EN tests for wood preservatives, reference materials are cited depending on the particular test situation and biological challenge).

4 Organisms used in the study

The scientific names (and where relevant strains) and numbers of the organisms used in the test should be reported. Additionally, where appropriate, the stage of the life cycle, age and sex of the organisms, should also be reported. The organisms tested should be representative of those for which a biocidal effect is claimed on the label for the biocidal product.

5 Application/dosage rate(s)

The biocide product should ideally be tested at a variety of application rates including rates below those suggested for commercial use (in accordance with paragraph 93 of Annex VI of the Directive, in order to assess if the recommended dose is the minimum necessary to achieve the desired effect). Such dose response data must include an untreated control. These data, if appropriate, can be used to indicate that the use rate is effective but not excessive.

In the absence of dose ranging data being available and appropriate then the product must be tested in accordance with the rate proposed on the label for the intended use.

The application/dosage rate should be expressed in a manner consistent with that on the proposed product label.

6 Application/delivery method

The effectiveness of a biocidal product can often be influenced by the way the treatment is applied. Therefore, particularly in those test methods using either field or simulated use data the methods of application used in the efficacy test(s) and those given in the label claim
directions must be in agreement (i.e. the same or equivalent).

7 Study environment

Full details of the study environment should be provided with any test results. These could include, as appropriate, temperature, humidity, lighting conditions, construction and dimensions of any test chambers and the addition of any nutrients and water to such chambers. In addition appropriate observations, monitoring and recording of changes that might affect populations of target organisms should be reported.

8 Biocidal exposure details

All periods of exposure and methods of introducing the target organisms into the exposure scenario should be documented. In addition methods of recording/scoring the effect of exposure on the target organism(s) should be given. In field studies, details of the monitoring regime adopted and any procedures to reduce human bias, e.g. reducing sampling bias from different operators during monitoring work, should be given.

9 Assessment of effectiveness

In the assessment of the efficacy of a candidate product, observations should be scored using convenient quantitative and qualitative methods such as percent kill or control, extent of remaining population, greatest dilution of product (v/v or m/v) producing desired antimicrobial effect, etc.

Whatever the type of assessment chosen, it should be clearly described.

The effectiveness of the product should be measured against an untreated control. The untreated control provides a reference point and a measure of the degree of pest infestation or development of microbial problem that would occur in the absence of treatment.

In those few cases where inclusion of an untreated control is not practical (e.g. to avoid spread of certain diseases in disease control trials) the biocidal product must be tested against some other base, such as another product of known efficacy used as a reference standard or conditions measured before the start of the test.

10 Data analysis and interpretation

Test data should be analysed against the objectives and criteria established prior to conducting the experiment. Based on the analysis of the results, conclusions on the performance of the test material including interpretation and discussion should be made.

In addition, the competent authority should ensure that individual data sets usually presented in appendices, together with summary tables/graphs and, if appropriate, statistical analysis assessed in accordance with predetermined criteria, are available. Examples of statistics that could be included, where relevant include simple statistics such as mean and range, regression analysis for graphical presentations or analyses of variance.

11 *Summary*

The following table summarises the general information that should be included in an efficacy test report.

Table: *Summary of details that should be included in an efficacy study report*

The test Study/method

- The objective of the particular efficacy study
- The name, number and reference of any standard protocol used (if appropriate)
- Any deviations from standard protocols (if standard protocols were used)
- Validity criteria of the test
- Quality assurance

Test Organism(s)

- The names (and where relevant, the strains and national collection numbers), origin and culture conditions of the organism(s) used
- Stage of the life cycle
- Age of the stadia (where relevant)
- Any selection pressure
- Numbers used in the test
- Sex of those used in the test (where appropriate)

Active Substance and Formulation

- The identity, nature and full details of the formulation(s) used (where relevant)
- The solvent or diluent used
- The identity and concentration(s) of the active substance(s) present in the material tested
- Control and reference substance/product

Study details

- Pre-conditioning of test species
- Application/delivery method used
- Application/dosage rate
- Test chamber construction/measurements
- Temperature, relative humidity and lighting during the test
- Number of replicates
- Controls
- Nutrient supply conditions
- Any additions or alterations to the test environment during the study
- Duration of the exposure to the biocide (contact time)
- Post monitoring of the test organism

Results

- Dates of assessment
- Scoring or other assessment system used in the test
- Presentation of all results data including tabulation or graphical presentation of the summarised results
- Performance evaluation including fulfilment of validity criteria, interpretation, discussion and conclusions that relate to label claims

Test reference

- Test reference including author(s), title, test house, test study number, year of publication/report, location of raw data and a statement on whether these results have been published (if so a full journal reference should be included where possible)

N.B. The checklist is not exhaustive and the items necessary will vary between product types and types of test as appropriate.

PRODUCT TYPES 1 TO 5 - DISINFECTANT PRODUCTS

N.B. This technical annex provides general guidance only and is not exhaustive to these product types with respect to use patterns and label claims. The UK together with other EU Member states and industry experts are involved in international activities aimed at developing a harmonised approach to the regulation of disinfectant and other antimicrobial biocides. Specifically, the OECD Biocides programme has included activities related to the development of harmonised guidance in the development of efficacy data (reference: http://www1.oecd.org/ehs/Biocides/efficacy-overview.htm). Through discussions within the EU and the OECD arenas with other international agencies responsible for the regulation of antimicrobial biocides there will be opportunities to share knowledge and experience related with the requirements and assessment of efficacy. In this regard the guidance in this document should be considered to be draft only and subject to adaptation arising from such discussions

INTRODUCTION

This technical annex amplifies the nature and extent of data that should be available to support the label claims for the following groups of biocidal product types.

- **Product type 1 - Human hygiene biocidal products**

  Products in this group are biocidal products used for human hygiene purposes.

- **Product type 2 - Private area and public health area disinfectants and other biocidal products**

  Products used for the disinfection of air, surfaces, materials, equipment and furniture which are not used for direct food or feed contact in private, public and industrial areas, including hospitals, as well as products used as algaecides.

  Usage areas include, *inter alia* swimming pools, aquariums, bathing and other waters; air-conditioning systems; walls and floors in health and other institutions; chemical toilets, waste water, hospital waste, soil or other substrates (in playgrounds).

- **Product type 3 - Veterinary hygiene biocidal products**

  Products in this group are biocidal products used for veterinary hygiene purposes including products used in areas in which animals are housed, kept or transported.

- **Product type 4 - Food and feed area disinfectants**

  Products used for the disinfection of equipment, containers, consumption utensils, surfaces or pipework associated with the production, transport, storage or consumption of food, feed or drink (including drinking water) for humans and animals.

- **Product type 5 - Drinking water Disinfectants**

  Products used for the disinfection of drinking water (for both humans and animals).

These product types exclude cleaning products that are not intended to have a biocidal effect, including washing liquids, powders and similar products.

1. LABEL CLAIMS

1.1 Spectrum of biological activity (including target organisms)

A disinfectant product may claim one or more of a number of types of efficacy. The types of efficacy claims that a disinfectant may make depend upon, among other things, the types of microorganisms, the disinfectant targets (e.g. vegetative bacteria, tuberculosis or a specific virus) and the disinfectant's intended level of activity (e.g. a reduction in the level of the microorganism or kill). Label claims and recommendations must be supported by the results of bactericidal, fungicidal, etc. tests appropriate to the area of application.

Applicants must clearly indicate on the product label the spectrum of activity claimed for the proposed product.

Examples of *some* of the common claims are presented in Table 1.

Table 1: Examples of *some* common types of effectiveness claimed for disinfectant products (see also Glossary of Terms at the end of this Annex 1 for further descriptors)

"claim"	**Descriptor**
Sterilants	Sterilants are intended to destroy or eliminate viruses and all living bacteria, fungi and their spores. The claim denotes killing all microorganisms including the highly resistant spore forms.
Disinfectant	Disinfectants are used on inanimate surfaces and objects to destroy infectious fungi, viruses and bacteria, but not necessarily their spores. Disinfectant products can be divided in to a number of broad categories which include, hospital (medical), veterinary; and general use disinfectants. Hospital disinfectants are primarily used on floors, walls bed linens, toilet seats and other hospital surfaces and some medical and instruments. Some hospital disinfectants are also effective against the organism that causes tuberculosis. General use disinfectants are used in households, swimming pools and water purifiers.
Bactericide	A product that kills vegetative bacteria.
Bactericidal Activity	The capability of a product to produce a reduction in the number of viable bacterial cells of relevant test organisms under defined conditions.
Bacteriostat	A product which inhibits growth or spreading of bacteria under defined conditions
Fungicide	A product which kills fungi (vegetative mycelia, budding yeats and/or their spores) under defined conditions.
Fungicidal activity	The capability of a product to produce a reduction in the number of viable vegetative yeast cells and mould spores of relevant test organisms under

	defined conditions.
Fungistatic	A product which inhibits the growth of fungi under defined conditions
Mycobactericide	A product which kills mycobacteria under defined conditions
Tuberculocide	A product which kills *Mycobacterium tuberculosis* under defined conditions
Sporicide	A product which kills dormant bacterial spores under defined conditions
Virucidal	The disinfectant is intended to destroy or inactivate one or more specific viruses under defined conditions.

1.1.1 Target organisms

The range of target organisms for which claims are made and from which principal organisms representative of the microbial challenge can be selected should be identified on the product label.

Since the claimed microbial efficacy for disinfectant products will encompass a large spectrum of potential target organisms it is not necessary or indeed feasible to include all the possible microorganisms in an efficacy test designed to support a label claim. Instead for each type of claim one or more indicator(s) or surrogate microorganism(s) relevant to the intended use and claim is recommended.

Efficacy tests usually include strains from the main bacterial groups, bacilli, gram-positive and gram-negative, and mycobacteria in certain standards. Yeast and fungi have to be usedfor fungicidal efficacy testing. It may be useful to include microorganisms of different species involved in specific applications.

Wherever possible strains should be selected from international collections (their genetic stability is checked regularly). The media for preservation procedures must be described with precision. *In the case of large-scale use of disinfectant (e.g. in hospitals), it may be necessary to evaluate the sensitivity of bacterial species causing nosocomial infections. These species are often different from the proposed reference species.*

When a disinfectant is used against a specific group of microorganisms for example, viruses, bacteria or fungi, a virucidal, bactericidal or fungicidal disinfectant should be used. If the types of microorganisms are unknown, a disinfectant that has broad spectrum of activity (i.e. one that is capable of effective microbial action against all or the majority of classes of microorganisms) should be used.

The choice of disinfectant therefore depends upon:

- The spectrum of organisms it is required to kill
- The conditions under which it will be used

Currently available test methods (See Section 2.5) utilise a range of microbial species which are representative species that take into account their relevance to practical use.

1.2 Areas of Use/Sites of Application

1.2.1 Areas of Use

Disinfectants are used almost everywhere people want to kill disease-causing microorganisms. They are used to kill or inactivate bacteria, fungi and viruses in households, hospitals, schools, restaurants, offices, kitchens, bathrooms, dairy farms, on medical and dental instruments, eating utensils and at many other locations.

Although the role of the inanimate environment in transmitting infections has not been completely defined, the use of disinfectants is considered an important part of infection control programmes.

Applicants should clearly indicate on the label the intended area of use for the product e.g. areas of use could include (not exhaustive):

Domestic and institutional use
Food industry
Veterinary/animal health use
Hospital or medical areas
Breweries
Recreational areas

1.2.2 Sites of Application

In addition to the types of efficacy claimed (e.g. bactericidal, fungicidal, tuberculoidal) and the intended area of use, the applicant must specify on the label the use patterns for which the disinfectant is recommended.

Broad examples of use patterns (not exhaustive) could include areas such as:

Use against microorganisms on hard surfaces, work surfaces, cutting boards etc.
Use against microorganisms on fabrics or textiles
Use on toilets, bathroooms, sinks, etc.
Use in operating theatres, isolation wards, use on medical instruments etc
Use in food manufacturing, retailing, processing areas etc.
Use in animal housing and equipment, e.g. pigs, sheep, poultry etc.
Use against microorganisms associated with human or animal wastes
Use in air conditioning systems
Use in swimming pools, spas, aquariums, bathing and other waters
Use in tanks, pipelines, equipment soak or bottle wash

1.3 Directions for use (Methods of application)

Efficacy data must be developed to substantiate label directions (which should include reference to concentration of the use solution and contact time) and claims in regard to the number of times a prepared use solution of an antimicrobial product can be applied (or re-applied) before a fresh solution must be prepared. Such data must show retention of the claimed level(s) of antimicrobial activity in the use solution after repeated microbial and other appropriate challenges for the period of time or the number of times specified in the directions for use.

2. AVAILABLE DATA

2.1 Laboratory tests

In laboratory testing of disinfectants the ultimate purpose is to establish whether products meet specified requirements under “in use” conditions.

Various laboratory methods have been developed for biocide efficacy testing. Although these experiments differ in their design and experimental detail, all are based on the principle of adding a test inoculum to disinfectant and removing samples at specified times. The biocide in each sample is neutralised and levels of survival of the organisms assessed. In practice the methods can be classified into 3 groups according to how the end-point of the test is determined:

- **End-point tests**

The sample of biocide treated cells is transferred to nutrient medium and incubated to determine the presence or absence of survivors. The result is expressed as the concentration of biocide producing kill (i.e. no detectable survivors) within a specified contact period, or the time required to achieve kill using a given concentration.

- **Quantitative tests**

Samples of untreated and biocide-treated cells are plated on nutrient medium. After incubation the number of colony forming units is determined and the log reduction in viable counts determined.

- **Capacity tests**

The biocide is challenged successively with bacteria at defined time intervals. Following each inoculation, samples are taken after a suitable contact period has elapsed, the biocide is neutralised and the suspension incubated in the medium to determine the presence or absence of detectable survivors. The result is expressed as magnitude of the accumulated inoculum that was required to produce the “failure”.

2.2 Simulated use/Practical tests

Simulated use or practical tests mimicking real-life conditions belong to the second testing stage. After measuring the time-concentration relationship of the disinfectant in an *in-vitro* test, these practical tests are performed to verify if the proposed use dilution is likely to be adequate in real life conditions.

2.3 Field or in use tests

In use testing involves the antimicrobial evaluation of the product under actual conditions of use on specified surfaces or materials in a designated environment. As with standard and non-standard laboratory methods, representative organisms or actual organisms of concern may be used.

2.4 Other considerations and factors

2.4.1 Neutralisation

In trials where the testing organisms are taken from treated samples for further analysis, such as plate count following biocidal treatment, appropriate neutralisers must be used to inactivate the active ingredient. Evidence supporting the effectiveness of the neutraliser against the active ingredient and

showing that the neutraliser itself does not have antimicrobial activity must be included in a test report. In such cases:

- An effective neutraliser for the test product should be identified and effective neutralisation without toxic effects on surviving organisms should be demonstrated.

- Appropriate controls for determining the efficacy of the neutraliser should be performed. This is to provide evidence to eliminate the potential for false-negative results caused by static or microbicidal activity of disinfectant carried over onto the recovery medium.

In lieu of chemical neutralisation it must be documented that appropriate subculture techniques have been employed that preclude residual carry over of active substances.

2.4.2 Hard Water Claims

The degree of hardness of the water used to dilute the disinfectant may affect its performance. Generally the harder the water the less effective is the diluted disinfectant. Therefore it follows that any product that carries label claims for effectiveness in hard water must be tested by the appropriate method in synthetic hard water at the level claimed.

2.4.3 Presence of Interfering Substances

Where disinfectants are applied to either inanimate surfaces *or the hands*, any number of substances may be present which may affect the disinfectants activity.

Water of Standard Hardness (WSH)
Since there is evidence that the activity of some disinfectants may be affected by the presence of metal ions such as Ca^{2+} and Mg^{2+}, current test programmes require that products destined for dilution with potable water must, for the purpose of efficacy testing, be diluted in water of standard hardness.

Organic and Inorganic Soiling
The nature, degree and condition of the soiling present will affect the efficacy of a disinfectant. Hard compacted soils are more difficult to disinfect than loose friable soils, and solid soils generally have a greater adverse effect on disinfection than liquid soils.

In many cases, however, residual contamination must be anticipated, and in some situations (e.g. in the treatment of blood spillages) disinfectants are used specifically to decontaminate soil and to prevent infection transfer and to assist in safe disposal.

Blood, urine, faeces, food debris, fats and oils, dust and proteinaceous materials are the most likely organic soils to be encountered. Limescale, milkstone and earth are the most common inorganic soils.

Where claims are made for use under soiled conditions, use concentrations must be determined from tests carried out in the presence of suitable soil. Soiling materials commonly used in efficacy test methods include albumin, serum, blood, yeast and yeast extract.

When a product is to be recommended for certain patterns of use where the soiling is of a specific type (such as soap film residue or hard water scum), the product must be tested in the presence of that specific soil.

In all cases, soiling will reduce the efficacy of the disinfectant, and where soiling is present, longer contact times, higher concentrations, precleaning or a combination of these parameters may be necessary.

2.4.4 Temperature

Generally disinfection performance increases with temperature. This applies to disinfection against all microorganisms though the effect on individual species differs, some being more affected by others.

2.4.5 Contact Time

Within limits, the longer the contact time the more effective is the disinfectant. Some disinfectants act very quickly, whereas others require an extended contact time to achieve adequate performance. Mycobacteria take longer to kill than most vegetative microorganisms.

2.4.6 pH

The prevailing degree of acidity or alkalinity during disinfection can also affect the performance and choice of disinfectant.

2.4.7 Surfaces

Smooth impervious surfaces are easier to disinfectant (and also to clean) than rough or pitted ones. In some circumstances the microorganisms might be protected from the action of disinfectants by being protected in porous surfaces. Clumps of microorganisms may also be more difficult to kill, as cells inside are protected by dead microorganisms on the outside.

Bacteria and fungi can adhere to surfaces forming biofilms in which the cell surface properties are altered and this makes them more difficult to kill, as penetration can be difficult to achieve.

2.5. Standard Test Methods

Standard test methods have been produced (or are in preparation) by CEN in Europe and by AOAC and ASTM in North America (US EPA and Canada) that address the efficacy testing of disinfectant products.

Whilst the use of CEN standards {as available and appropriate} are highly recommended for assessment of efficacy of disinfectant products, use of these standards is not mandatory.

It is recognised that some products may be developed for very specific applications and may not pass standard tests that are general in nature. In these instances applicants should present appropriate, repeatable and reproducible data to support their applications.

Competent authorities will consider alternative testing strategies either based on other national or international standard test methods (e.g. BSI, AFNOR, DGHM, EPA etc.) or alternatively non-standard test data provided they are relevant and robust.

A list of available efficacy test methods for biocidal products has been collated and referenced by the OECD and this list is available on its website.

Reference: http://www1.oecd.org/ehs/Biocides/efficacy-overview.htm).

2.5.1 European Standard Test Methods

In Europe the European Committee for Standardisation (CEN) Technical Committee (TC 216) was established to produce harmonised European methods for the efficacy testing of disinfectants and

antiseptics used in food hygiene, medicine, agriculture and veterinary practices. The standards are largely based on suspension tests (i.e. quantitative tests) although some surface test methods are also included.

Use of these standards in testing to support claims for microbiocidal activity is proposed to follow a matrix of testing ranging from simple innate activity, through simulated use tests to field tests under practical conditions. Three levels of testing are described. Phase 1 tests determine whether the product diluted in distilled water has a basic level of activity in the absence of any organic or inorganic soiling. Phase 2 tests determine activity in simulated use conditions with an organic load and several test microorganisms, either as a suspension test (step 1) or on surfaces (step 2). Phase 3 tests consist of "in-use" (field) trials.

A summary of this modular approach to testing using EN test methodology is outlined below:

PHASE 1	Quantitative Suspension tests for the basic activity of the product to define minimum standards for bactericidal, fungicidal and sporicidal activity. (No specific test conditions).
PHASE 2, STEP 1	Quantitative Suspension tests under conditions representative of practical use. (Specific test conditions related to intended use).
PHASE 2, STEP 2	Other laboratory tests, e.g. handwash, handrub and surface tests simulating practical conditions.
PHASE 3	Field tests under practical conditions.

CEN are currently preparing a guidance document [CEN/TC 216 N 127] which outlines the application and interpretation of European Standards for chemical disinfectants. This document outlines the various EN standards currently available and provides guidance as to the choice of available standards that may be used to verify the effectiveness of disinfectants in particular situations (such as medical, veterinary and food hygiene) and gives guidance for the interpretation of results from such tests in making and supporting efficacy claims.

Whilst the CEN test standards cover the methodology to test for disinfectant products likely to be encompassed within product types 1, 2, 3 and 4 of the Directive, the application areas for disinfectants to water systems such as swimming pools, spas, and drinking water has yet to be addressed. Therefore claims for efficacy of such products will need to be demonstrated through testing using other test methods where available.

A list of current EN standards and those in preparation is given in Annex 2.

2.5.2 North American standard test methods

In the United States, the standard methods for the evaluation of chemical disinfectants are predominately those of the Association of Official Analytical Chemists (AOAC). These tests are, in the main, end-point tests and are used to determine the *optimum use-dilution* of a disinfectant product to be used for a specific application and they are also used to satisfy the US EPA requirements for the registration of antimicrobial products. With the use of specified test organisms and, in some instances, representative environmental surfaces, the AOAC methods form the core of the EPA's efficacy data requirements. Some non-AOAC methods are specified by the EPA to demonstrate efficacy against specific microorganisms. These include the EPA virucidal method, or a recently accepted alternative method for the quantitative assessment of tuberculoidal activity.

A list of AOAC test methods is provided in Annex 3 and additionally some ASTM methods in Annex 4.

2.6 Specific Data to Support Label Claims

2.6.1 Basic bactericidal activity

Available data
No chemical substance or preparation can be regarded as a disinfectant if it is not active against vegetative bacteria. Therefore, disinfectant testing should always start with the determination of antibacterial activity.

Of the currently available CEN standards, EN 1040 (a Phase 1 test), based on a quantitative suspension test, addresses claims for basic bactericidal activity.

Test species
EN 1040, addresses the activity of a test material against *Staphylococcus aureus* (ATCC 6538) and *Pseudomonas aeruginosa.* (ATCC 15442).

Test method and requirements
A test suspension of bacteria is added to a prepared sample of the product under test. The mixture is maintained at 20 ^{o}C. At a specified contact time chosen from one of the following: 1 , 5, 15 , 30 , 45 or 60 minutes, an aliquot is taken. The bactericidal action of this aliquot is immediately neutralised or suppressed by a validated method. The method of choice is dilution-neutralisation. If a suitable neutraliser cannot be found, membrane filtration is used. The number of surviving bacteria in each sample is determined and the reduction in viable counts calculated.

A criterion for activity by this test method is that the test material should demonstrate at least a 5-log reduction in viable counts of the test organisms in 60 minutes.

2.6.2 Basic Fungicidal activity

Available data
Of the currently available CEN standards, EN 1275 (a Phase 1 test) addresses basic claims for fungicidal activity.

Test species
EN 1275 addresses the activity of a test material against *Candida albicans* (ATCC 10231) and *Aspergillus niger* (ATCC 16404).

Test method and requirements
A test suspension of yeast cells or mould spores is added to a prepared sample of the product under test. The mixture is maintained at 20 ^{o}C. At a specified contact time chosen from one of the following 5, 15, 30 or 60 minutes, an aliquot is taken; the fungicide action in this portion is immediately neutralised or suppressed by a validated method. The method of choice is dilution-neutralisation. If a suitable neutraliser cannot be found, membrane filtration is used. The number of surviving yeast cells or mould spores in each sample is determined and the reduction in viable counts calculated.

The criterion for activity by this test is that the test material should demonstrate at least a 4-log reduction in viable counts of the test organisms in 60 minutes.

2.6.3 Basic sporicidal activity

Available data
Of the currently available CEN tests, Pr EN 216003 (a Phase 1 test) addresses claims for basic sporicidal activity.

Test organisms
Pr EN 216003 addresses the activity of a test material against dormant spores of *Bacillus subtilis* (ATCC 6633) and *Bacillus cereus* (ATCC 12826).

Test method and requirements
A prepared sample of the product under test is added to a test suspension of bacterial spores. The mixture is maintained at 20 ^{o}C or any other temperature to be defined. At a specified contact time chosen from one of the following: 30, 60 and 120 minutes, an aliquot portion is taken and the sporicidal as well as sporistatic action in this portion is neutralised. The method of choice is dilution-neutralisation. The number of surviving bacterial spores is determined in parallel and the reduction in viable counts calculated. The effectiveness of neutralisation is controlled in the test.

The criterion for activity by this test is that the test material should demonstrate at least a 4-log reduction in viable counts of the test organisms in 120 minutes.

2.6.4 Virucidal action

A basic test is not considered to be appropriate.

2.6.5 Claims for disinfectants intended for specified or defined purposes

Disinfectant products to be recommended for a defined purpose will require a further level of testing which is more complex and extensive in design and is intended to simulate conditions more relevant to practical conditions.

Using the CEN methodology as an example this would include testing by **Phase 2** suspension and surface tests, selected to be relevant to the area of intended product use.

Suspension tests (PHASE 2, Step 1)
The suspension tests in this situation would follow the procedure of the basic Phase 1 tests but include additional test strains (e.g. *Proteus mirabilis* and *Enterococcus faecium*), product diluents (water of standard hardness), organic soil (e.g. 0.3 % or 1 % w/v albumin), contact times (5, 30 or 60 minutes) and temperatures as appropriate to intended use.

Surface tests (PHASE 2, Step 2)

Currently CEN are drafting a series of quantitative surface tests for the evaluation of disinfectants used in the medical and veterinary fields and in food, industrial, domestic and institutional areas.

Surface tests in this situation consider a test suspension of bacteria or fungi in a solution of interfering substances which is inoculated onto a test stainless steel surface and dried. A prepared sample of the product under test is applied in a manner which covers the dried film. The surface is maintained at a specified temperature for a defined period of time. The surface is transferred to a previously validated neutralisation medium so that the action of the disinfectant is immediately neutralised. The number of surviving organisms which can be recovered from the surface is determined quantitatively.

The number of bacteria, fungi etc. on a surface treated with hard water in place of the disinfectant is also determined and the reduction in viable counts calculated by difference.

Each treated surface is transferred into the counting medium in order to check the efficiency of the recovery of the test organisms.

Additional Phase 2, Step 2 test methods

Additional Phase 2, Step 2 test methods have been prepared (or are in preparation) to consider the efficacy of disinfectants in the medical areas for use on instruments, for use as surgical hand disinfectants, hygienic hand washes and hygienic hand rubs.

2.6.6 Claims against specific named organisms

Where label claims for antimicrobial activity against specific target organisms (e.g. a specific virus such as poliovirus 1) are made then such claims must be supported by efficacy data generated using tests that include the specific organism(s). Where available, strains from cultured collections should be used for these tests. The nature and extent of laboratory testing should be equivalent to that of the Phase 1 and Phase 2 suspension and surface tests, wherever possible.

2.6.7 Phase 3 tests

In-use or field testing involves the antimicrobial evaluation of the disinfectant under actual conditions of use on specified surfaces or materials. As with standard and non-standard laboratory methods, representative or the actual organisms of concern are employed.

Such tests can be performed by a variety of procedures. A convenient method involves the sampling of a disinfectant solution following actual use on surfaces by membrane filtration. The recovery of any viable non-spore forming bacteria from these solutions after an appropriate recovery time indicates failure of disinfection.

Another example of a practical or field test involves contact sampling of items after they have been treated with the disinfectant. Again, no vegetative organisms should be recovered.

N.B. CEN TC 216 are intending to prepare a standard "protocol" which specifies how a field trial shall be conducted. This standard is intended to give guidelines on the factors to be taken into account and controlled when carrying out a field trial.

2.7 SUMMARY OF CEN EFFICACY TESTING STRATEGIES FOR DISINFECTANTS

- Label claims and recommendations must be supported by the results of bactericidal, fungicidal, etc. tests appropriate to the area of application

- Ordinarily products should be subjected to a programme of Phase 1 and Phase 2 tests (a number of caveats exist with respect to the modular approach to testing in this way.)

- Label claims and recommendations may be supported by results of Phase 3 (field/in-use tests) as appropriate to the intended area of application

For certain situations it may be that certain tests are considered to be inappropriate for the particular application, e.g. the data available to the Competent Authority may indicate that:

> Phase 2 suspension tests and surface tests are adequate and that further Phase 1 tests are not relevant
>
> Phase 2 suspension tests provide sufficient information and additional Phase 2 surface tests are not relevant
>
> Phase 2 surface tests provide sufficient information and additional Phase 2 suspension tests are not relevant

A schematic representation of the modular approach to standard efficacy testing proposed by CEN is depicted in Figure 1

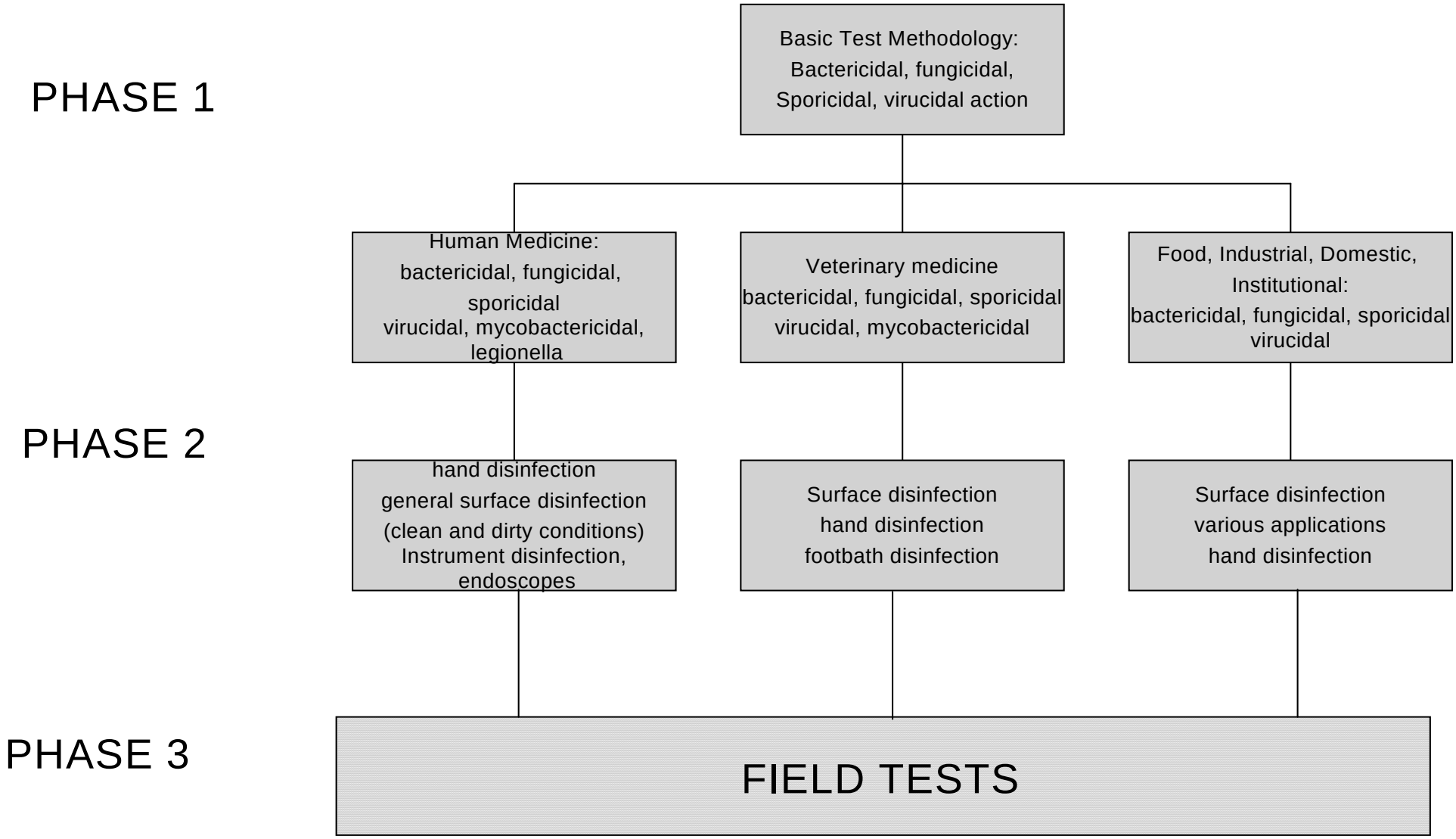


FIGURE 1: SCHEMATIC REPRESENTATION OF EFFICACY TESTING STRATEGY FOR DISINFECTANT PRODUCTS

ANNEX 1

ABBREVIATIONS

AFNOR	Association Francaise de Normalisation
AOAC	Association of Official Analytical Chemists
ASTM	American Society for Testing and Materials
ATTC	American Type Culture Collection
BSI	British Standards Institute
CEN	Committee de Normalisation
DGHM	Deutsche Gesellschaft Fur Hygiene und Mikrobiologie
EN	European Standard
EPA	United States Environmental Protection Agency
HWG	Horizontal Working Group
ISO	International Standards Organisation
MAFF	Ministry of Agriculture, Fisheries and Foods
OECD	Organisation for Economic Co-operation and Development
PrEN	draft European Standard
TC	Technical Committee
WG	Working Group

GLOSSARY OF TERMS

Antimicrobial product
A product which prevents the growth of/reduces the number of/mitigates the growth of/…….

Bactericide
A product which kills vegetative bacteria under defined conditions

Bactericidal activity
The capability of a product to produce a reduction in the number of viable bacterial cells of relevant test-organisms under defined conditions

Bacteriostat
A product which inhibits the growth or spreading of bacteria under defined conditions

Biofilm
An accumulation of microbial cells immobilised on a substratum and embedded in an organic polymer matrix of microbial origin

Fungicide
A product which kills fungi (vegetative mycelia, budding yeasts and/or their spores) under defined conditions

Fungicidal Activity
The capability of a product to produce a reduction in the number of viable vegetative yeast cells and mould spores of relevant test organisms under defined conditions

Fungiostatic activity
The capability of a product to inhibit the growth of fungi under defined conditions

Microbes/microorganisms
Vegetative bacteria (including bacterial spores) or fungi (including fungal spores) or viruses

Mycobactericide
A product which kills mycobacteria under defined conditions

Mycobactericidal activity
The capability of a product to produce a reduction in the number of viable mycobacterial cells of relevant test organisms under defined conditions

Neutraliser
A chemical agent or formulation which suppresses the residual activity of an disinfectant within a test but does not inhibit or inactivate microorganisms

Performance standard
Regulatory or scientific standard for biocides that is either quantitative or qualitative (that may also be specified in the test method) by which a decision is taken on the acceptability of a claim.

Sporicide
A product which kills dormant bacterial spores under defined conditions

Sporicidal Activity
The capability of a product to produce a reduction in the number of viable bacterial spores of relevant test organisms under defined conditions

Sporistatic activity
The capability of a product to inhibit the germination of dormant bacterial spores under defined conditions

Sterilant
A product that destroys or inactivates all forms of microbial life in the inanimate environment, including all forms of vegetative bacteria, bacterial spores, fungi, fungal spores and viruses.

Tuberculocide
A product which kills *Mycobacterium tuberculosis* under defined conditions

Tuberculocidal activity
The capability of a product to kill Mycobacterium tuberculosis, demonstrated by the capability to produce a reduction in the number of viable cells of the test organism *Mycobacterium terrae* under defined conditions

Virucide
A product which inactivates virus under defined conditions

Virucidal activity
The capability of a product to produce a reduction in the number of infectious virus particles of relevant test organisms under defined conditions

ANNEX 2

RECOGNISED STANDARD METHODS FOR EFFICACY TESTING OF DISINFECTANTS **(For a fuller list see the OECD collated list of efficacy standards)**

ISO STANDARDS

ISO 7218 (1996) E
Microbiology of food and animal feeding stuffs - General rules for microbiological examinations.

CEN STANDARDS

GENERAL GUIDANCE

CEN/TC 216 HWG N 113 (February 1998)
Terminology.

EN 12353 (2000). Chemical disinfectants and antiseptics - Preservation of microbial strains used for the determination of bactericidal and fungicidal activity.

CEN/TC 216 N 127 (June 2001)
Antiseptics and disinfectants - Guidelines for the application of European Standards for Chemical disinfectants.

Phase 1 tests

1. CEN 1040 (1997)
Chemical disinfectants and antiseptics - Basic bactericidal activity - Test Method and requirement (Phase 1).

2. CEN 1275 (1997)
Chemical disinfectants and antiseptics - Basic fungicidal activity - Test Method and requirement (Phase 1).

3. CEN: WI 216003 (under development)
Chemical disinfectants and antiseptics - Basic sporicidal activity - Test Method and requirement (Phase 1).

Medical Area Disinfectants - {BPD Product type 1}

Phase 2 Step 1 tests

1. **prEN 13713**
Chemical disinfectants and antiseptics - Surface disinfectants used in human medicine. Bactericidal activity - Test method and requirements (Phase 2, Step 1).

2. **prEN 13727** Chemical disinfectants and antiseptics – Quantitative suspension test for the evaluation of bactericidal activity for instruments in the medical area – Test method and requirements

3. **prEN 13624** Chemical disinfectants and antiseptics – Quantitative suspension test for the evaluation of fungicidal activity for instruments used in the medical area – test method and requirements

4. CEN WI: 216038 and WI 216031 (under development)
Quantitative suspension test for evaluation of mycobactericidal activity of chemical disinfectants in the medical area including instrument disinfectants- Test Method and requirements (Phase 2, Step 1).

5. CEN WI: 216022 (Under development)
Chemical Disinfectants and antiseptics in the medical field – Virucidal activity – test method and requirements (Phase 2, Step 1).

6. **Pr EN 13727** Chemical disinfectants and antiseptics - Water treatment products against *Legionella pneumophila*, Bactericidal activity - Test Method and Requirements (Phase 2, Step 1).

7. CEN: WI 216032 (under development) Chemical disinfectants and antiseptics: Sporicidal activity – test methods and requirements (Phase 2, Step 1).

8. **prEN 12054** Chemical disinfectants and antiseptics – Quantitative suspension test for the evaluation of bactericidal activity of products for hygienic and surgical handrub and handwash used in human medicine – test method and requirements

9. CEN WI 216039
Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of fungicidal activity of products for hygienic and surgical handrub and handwash used in human medicine - Test methods and requirements (Phase 2, Step 1).

10. CEN WI: 216023 (under development) Chemical disinfectants and antiseptics in the medical field – Fungicidal activity – Test methods and requirements (Phase 2, Step 1)

Phase 2, Step 2 tests

1. CEN WI 216019 Chemical disinfectants and antiseptics – Bactericidal surface disinfection – test methods and requirements

2. CEN WI 216033 – Chemical disinfectants and antiseptics – quantitative carrier test for the evaluation of bactericidal activity of chemical disinfectants for instruments used in medical area – test methods and requirements

3. CEN WI 216034 – Chemical disinfectants and antiseptics – quantitative carrier test for the evaluation of mycobactericidal activity of chemical disinfectants for instruments used in medical area – test methods and requirements

4. CEN Pr EN... (WI 216035) –Chemical disinfectants and antiseptics - Quantitative carrier test for evaluation of mycobactericidal activity of chemical disinfectants for instruments used in the medical area - Test Method and requirements (Phase 2, Step 2).

5. CEN WI 216037 (under development)
Chemical disinfectants and antiseptics – quantitative carrier test for the evaluation of virucidal activity of chemical disinfectants and antiseptics for instruments used in medical area

6. CEN WI 216036 (under development)

Chemical disinfectants and antiseptics – quantitative carrier test for the evaluation of sporicidal activity of chemical disinfectants for instruments used in medical area – Test methods and requirements

7. **Pr EN 1499 (1997)** Chemical disinfectants and antiseptics: Hygienic handwash - Test Methods and requirements (Phase 2, Step 2).

8. EN 1500 (1997)
Chemical disinfectants and antiseptics: Hygienic handrub - Test Methods and requirements (Phase 2, Step 2).

9. Pr EN 12791
Chemical disinfectants and antiseptics: Surgical hand disinfection - Test Methods and requirements (Phase 2, Step 2).

Veterinary Area Disinfectants - {BPD Product type 3}

Phase 2, Step 1 tests

1. EN 1656 (2000)
Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of bactericidal activity of chemical disinfectants and antiseptics for use in the veterinary field - test method and requirements.

2. EN 1657 (2000)
Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of fungicidal activity of chemical disinfectants and antiseptics for use in the veterinary field - test method and requirements.

3. PrEN 14204
Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of mycobactericidal activity of chemical disinfectants and antiseptics used in the veterinary field - Test method and requirements (Phase 2, Step 1).

4 CEN WI: 216040 (under development)
Chemical disinfectants and antiseptics in the veterinary field - Sporicidal activity - Test method and requirements (Phase 2, Step 1).

5. CEN WI: 216026 (under development)
Chemical disinfectants and antiseptics in the veterinary field - virucidal activity - Test method and requirements (Phase 2, Step 1).

Phase 2, Step 2 Tests

1. **prEN 14349**
Chemical Disinfectants and antiseptics - Quantitative surface test for the evaluation of bactericidal activity of chemical disinfectants and antiseptics used in the veterinary field on non-porous surfaces without mechanical action - Test method and requirements (Phase 2, Step 2).

2. CEN WI 216041
Chemical disinfectants and antiseptics – Quantitative surface test for the evaluation of bactericidal activity of chemical disinfectants and antiseptics for use in the veterinary field on porous surfaces without mechanical action. Test method and requirements

Other National (UK) Veterinary Disinfectant tests specific to Disease outbreak/Control: include

MAFF 1969

Disinfectants for use specifically against

a) Anthrax, brucellosis, contagious bovine pleuro-pneumonia and glanders
b) For use against tuberculosis
c) For use against foot-and-mouth disease
d) For use against fowl pest (Newcastle disease fowl plague)

Food, Industrial, Domestic and Institutional Hygiene - {BPD Product type 2}

Phase 2, Step 1 tests

1. CEN 1276 (1997)
Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of bactericidal activity of chemical disinfectants for use in food, industrial, domestic and institutional areas - Test method and requirements (Phase 2, Step 1).

2. CEN 1650 (1998)
Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of fungicidal activity of chemical disinfectants for use in food, industrial, domestic and institutional areas - Test method and requirements (Phase 2, Step 1).

3. **EN 13704 (2002)**
Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of sporicidal activity of chemical disinfectants used in food, industrial, domestic and institutional areas - Test method and requirements (Phase 2, Step 1).

4. **prEN 13610**
Chemical disinfectants - Quantitative suspension test for the evaluation of virucidal activity against bacteriophages of chemical disinfectants used in food and industrial areas - Test method and requirements. (Phase 2, Step 1).

Phase 2, Step 2 Tests

1. **prEN 13697 (2001)**
Chemical disinfectants and antiseptics - Quantitative surface test for the evaluation of bactericidal and/or fungicidal activity of chemical disinfectants used in food, industrial, domestic and institutional areas - Test Method without mechanical action and requirements (Phase 2, Step 2).

Food and Feed Sector Disinfectants - {BPD Product type 4}

Phase 2, Step 1 tests

1. CEN 1276 (1997)

Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of bactericidal activity of chemical disinfectants for use in food, industrial, domestic and institutional areas - Test method and requirements (Phase 2, Step 1).

2. CEN 1650 (1998)
Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of fungicidal activity of chemical disinfectants for use in food, industrial, domestic and institutional areas - Test method and requirements (Phase 2, Step 1).

3. **EN 13704 (2002)**
Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of sporicidal activity of chemical disinfectants used in food, industrial, domestic and institutional areas - Test method and requirements (Phase 2, Step 1).

4. **prEN 13610**. Chemical disinfectants - Quantitative suspension test for the evaluation of virucidal activity against bacteriophages of chemical disinfectants used in food and industrial areas - Test method and requirements. (Phase 2, Step 1).

Phase 2, Step 2 Tests

1. **EN 13697 (2001).** Chemical disinfectants and antiseptics - Quantitative surface test for the evaluation of bactericidal and/or fungicidal activity of chemical disinfectants used in food, industrial, domestic and institutional areas - Test Method without mechanical action and requirements (Phase 2, Step 2).

Water treatment Products - {BPD Product type 5}

1. **PrEN 13727.** Chemical disinfectants and antiseptics - Water treatment products against *Legionella pneumophila*, Bactericidal activity - Test Method and Requirements (Phase 2, Step 1).

ANNEX III
EPA RECOMMENDED METHODS FOR TESTING DISINFECTANTS

Efficacy level claimed	**Use pattern**	**Test required**	**Old Guide Ref No.**	**New Guideline Reference No.**
Steriliser	Any site/application	AOAC Sporicidal test	91-2(a)	810.2100 (b)
	Hard inanimate surfaces	AOAC Use Dilution test (hard water and organic soil) **or** AOAC Germicidal Spray test **or** AOAC Hard Surface Carrier Test (Distilled water only)	91-2 (b), (c), (d)	810.2100 (c), (d), (e)
	Toilet bowl, urinal surfaces	AOAC Use Dilution test (hard water and organic soil) **or** AOAC Germicidal Spray test **or** AOAC Hard Surface Carrier Test	91-7 (a) (l)	810.2600 (b) (l)
	Swimming pool, spa, hot tub, jacuzzi, whirlpool water	AOAC method for water disinfectants for swimming pools: lab test **and** Field in-use test	91-8 (c)	810.2700 (d)
Disinfectant	Human drinking water: emergency water supplies	EPA Guide Standard and Protocol for testing microbiological Water Purifiers or controlled or simulated In-use study	91-8 (a) (2)	810.2700 (b) (l)
	Laundry additives: pre-soak treatment	AOAC Hard Surface Carrier Test (Distilled water only) **or** AOAC Use-Dilution Test Method modified to include organic soil (Hard water)	91-4 (a) (1)	810.2300 (b) (2)
	Laundry additives: (non-residual)	Petrocci and Clarke Laundry Additives (disinfectant level) or actual in-use study	91-4 (a) (2)	810.2300 (b) (3)
Efficacy level claimed	**Use Pattern**	**Test Required**	**Old guide Ref No.**	**New Guideline Ref No.**
Disinfectant	Pre-saturated/impregnated towlettes	Simulated in-use study	-	810.2100 (i)
Water Purification Claim	Water treatment units including emergency water supplies	EPA Guide Standard and Protocol for testing Microbiological water purifiers	91-1 (a)(2), (a)(3),	810.2700 (b)(2), (b)(3)

			91-8 (a)(2)	
Tuberculoidal claim	Any site/application	AOAC Tuberculoidal Activity Test Method (standard) **or** AOAC Tuberculoidal Activity of Disinfectants Test Method (modified) **or** Quantitative Tuberculoidal Activity Test Method **or** AOAC Germicidal Spray Products Test (modified for spray products)	91-2 (g)	810.2100 (h)
Virucidal claim in conjunction with disinfectant claim	Any site/application	Virucidal Activity Method used in conjunction with modifications of: AOAC Hard Surface Carrier Test (Distilled water only) **or** AOAC Germicidal Spray test	91-2 (f)	810.2100 (g)
Fungicidal claim	Any site/application	AOAC Fungicidal test **or** AOAC Hard Surface Carrier Test (Distilled water only) **or** AOAC Germicidal Spray Products test	91-2 (e)	810.2100 (f)
Sanitising claim	Non-food contact surfaces (non-residual)	Sanitiser Test for Hard Inanimate Non-Food contact surfaces	91-2 (j)	810.2100 (l)
Efficacy Level Claimed	**Use Pattern**	**Test Required**	**Old Guide Ref No**.	**New Guideline Ref No**.
	Previously cleaned food-contact surfaces (non-residual)	*Halide chemical products*: AOAC Available Chlorine Germicidal Equivalent Concentration Method *All other chemical products* AOAC Germicidal and Detergent Sanitisers Method	91-2 (k)(1), (2) 91-2 (l)(2)	810.2100 (m) (1) 810.2100 (m)(2)
	Laundry additives: Sanitising pre-soak	Sanitiser Test for Hard, Inanimate Non-Food Contact Surfaces modified to include organic soil	-	810.2100 (b)(2)
Sanitising Claim	Laundry additives (non-residual)	Petrocci and Clarke Laundry Additives Method (Sanitising level)	91-4 (a)(3)	810.2100 (b)(4)
	Fabrics and textiles: impregnated self-sanitising	Simulated in-use study	91-4 (d)	810.2300 (e)
	Carpets	EPA Carpet Sanitiser Protocol	91-4 (b)	810.2300 (c)
	Air	*Glycol-containing*	91-5	810.2400

		Chemical analysis *Non-Glycol containing* Quantitative Microbiological Assay	(b)(1) 91-5 (b)(2)	(b)(1) 810.2400 (c)(2)
	Toilet Bowl and Urinal surfaces	Sanitiser Test for Hard Inanimate Non-food Contact Surfaces	91-7 (a)(2)	810.2600 (b)(2)
	Toilet and Urinal bowl water	Simulated use study	91-7 (b)(1)	810.2600 (c)(1)
	Toilet in-tank sanitisers	Simulated use study	-	810.2600 (d)(1)
Efficacy Level Claimed	**Use Pattern**	**Test Required**	**Old Guide Ref No.**	**New Guideline Ref No**.
	Hard surfaces (residual self-sanitising activity of dried chemical residues on hard inanimate surfaces)	Controlled in-use study **or** Simulated in-use study	91-2 (m)	810.2100 (o)
Residual Self-Sanitising Claim	Laundry additives: (Residual self-sanitising)	Petrocci and Clarke Laundry Additives **or** AATCC Test Method 100-1974	91-4 (a)(4)	810.2300 (b)(5)
Sterilant, Disinfectant or Sanitising Claim	Mattresses, upholstered furniture, pillows	Simulated in-use test	91-4 (c)	810.2300 (d)

ANNEX 4 -
OTHER AVAILABLE STANDARD TEST METHODS

ASTM TEST METHODS

ASTM E 1052-85 (Re-approved 1990)
Standard Test Method for Efficacy of Virucidal Agents Intended for Special Applications.

ASTM 1053-91
Standard Test Method for Efficacy of Virucidal Agents Intended for Inanimate Environmental Surfaces.

ASTM 1054-91
Standard Practices for Evaluating Inactivators of Antimicrobial Agents Used in Disinfectant, Sanitiser, Antiseptic, or Preserved Products.

ASTM E 1115-91
Standard Test Method for Evaluation of Surgical Hand Scrub Formulations.

ASTM E 1153-94
Standard Test Method for Efficacy of Sanitisers Recommended for Inanimate Non-food Contact Surfaces.

ASTM E 1173-93
Standard Test Method for Evaluation of a Pre-Operative Skin Preparation.

ASTM E 1174-94
Standard Test Method for Evaluation of Health Care Personnel Handwash Formulation.

ASTM E 1326-90
Standard Guide for Evaluating Nonconventional Microbiological Tests used for Enumerating Bacteria.

ASTM E 1327-90 (1995)
Standard Test Method for Evaluation of Health care Personnel Handwash Formulations by Utilising Fingernail Regions.

ASTM E 1482-92
Standard Test Method for Neutralisation of Virucidal Agents in Virucidal Efficacy Evaluations.

ASTM E 1589-94
Standard Test Method for Evaluation of First Aid Antiseptic Drug Products.

ASTM E 1766-95
Standard Test Method For Determination of Effectiveness of Sterilisation Processes for Reusable Medical Devices.

PRODUCT TYPE 6 – IN-CAN-PRESERVATIVES

1 INTRODUCTION

This technical annex provides background information regarding in-can (and in-tank) preservative use, and amplifies the nature and extent of data that should be available to support efficacy claims relating to these substances.

1.1 USE OF IN-CAN PRESERVATIVES

In-can preservatives are included in many manufactured products, including paints, adhesives and binders. They are used to control micro-organisms that may be present in the product and which may cause deterioration prior to use. They therefore help to ensure product integrity during normal shelf life. For example, food preservatives and cosmetics preservatives, which are used exclusively in these two product types are not included in Product Type 6.

1.2 THE NEED FOR IN-CAN PRESERVATIVES

In order to grow in a manufactured product, a micro-organism must have access to both moisture (water) and a nutrient source.

Water may be an integral part of a particular manufactured product. However it may be present in a product as a result of the moisture content of various components, and not added separately.

An extremely wide range of substances can act as a source of nutrition. These substances may be utilised by micro-organisms as they are, or following some form of conversion or degradation.

Utilisation of nutrition sources by micro-organisms results in the loss from the product of one or more components, leading to reduced integrity and spoilage. By-products of microbial growth also contribute to spoilage. Thus vulnerable products require an in-can preservative content for protection during the wet state, prior to use.

1.3 NATURE OF THE MICROBIAL PROBLEM

Bacteria are the major group of spoilage organisms, but other causes of problems are yeasts and moulds. The consequences of uncontrolled microbial growth in the wet state are varied, but include:

Discolouration (many bacterial cells are pigmented)
Gassing
Malodour
Loss in viscosity*
Ropiness (certain bacteria produce slime)
Phase separation

> *Liquefaction of cellulosic thicken agents can be caused by enzymes which are produced by bacteria and fungi. Such enzymes (cellulases) are capable of exhibiting their bio-catalytical activity at concentrations as low as 10-5 units ml-1. Since enzymes cannot be inactivated by subsequently adding preservatives in the usual doses, it is recommended that preventative measures are taken at an early stage in production.

Such microbial damage is irreversible and therefore steps to control microbial growth/spoilage must be taken at the earliest opportunity.

Examples of some spoilage micro-organisms are presented in Table 1:

Table 1. Common spoilage micro-organisms associated with in-can products

Bacteria	Fungi	Yeast
Alcagenes species		Candida albicans
Micrococcus luteus	Aspergillus spp.	Rhodotorula rubra
Escherichia coli	Geotrichium candidium	Saccharomyces cerevisiae
Proteus vulgaris	Penicillium spp.	-

1.4 EFFICACY TESTING OF IN-CAN PRESERVATIVES

1.4.1 LABORATORY TEST METHODS

1.4.1.1 MIC determinations

MIC (Minimal Inhibitory Concentration) determinations are conducted in the laboratory on active substances. A dilution series of the active substance identifies the minimum amount of biocide that is required to inhibit microbial growth, under defined laboratory conditions.

In such tests, efficacy is assessed against a range of bacterial, fungal and yeast spoilage organisms. MIC values are usually presented as ppm required to inhibit the growth of a particular test organism; however only the bioavailable amount is effective. The values are useful for determining the spectrum of activity of an active substance.

1.4.1.2 Challenge testing

The usual method for evaluating in-can preservatives in paints or other aqueous products is the challenge test. Typically microbial cells are deliberately added to the test sample. The survival or death rate of these cells is monitored with respect to time. Under certain test protocols, the sample may be re-challenged several times.

1.4.1.3 Heat stability testing

An important property of an in-can preservative is heat stability. In this test the level of active substance is usually measured accurately by a suitable chromatographic method at time zero; the test is not always required. The product is then incubated at an elevated temperature for a defined period of time. The level of active substance is measured again after the incubation period in order to determine whether the biocide has degraded. The length of this test as well as the temperature may vary. The results are useful as an indication of the stability of the active substance in a particular product formulation.

1.5 AVAILABLE STANDARD TEST METHODS

There are a limited number of National standard test methods currently available which claim to assess the effectiveness of biocides for the 'in-can' protection of liquid coatings such as paints, adhesives and thickeners. However, they are either test methods limited to the determination of MIC in artificial matrices, or tests that do not give sufficient detail or guidance to carry out a properly controlled challenge test.

One example of a National standard is ASTM D 2574. This ASTM method utilises only one test bacterium; others use a mixture of fungi, or both bacterial and fungal cells.

An exhaustive list of currently available test standards for use in efficacy testing of In-can preservatives is presented in Appendix 1 of this document.

1.6 CURRENT EPA ASSESSMENT CRITERIA FOR IN-CAN PRESERVATIVES

The EPA requires that active substances proposed for use in preserving water-based products should show effectiveness in controlling spoilage or deterioration caused by bacteria in at least two representative formulations in which the biocide is intended for use.

Tests should be carried out in at least three replicates of each of the two product formulations using pertinent micro-organisms and adequate controls. Actual bacterial isolates (identified at least to Genus) from spoiled product and/or ATCC (American Type Culture Collection) spoilage bacteria should be employed as test inocula. Mixed bacterial and fungal inocula are not acceptable in demonstrating bacterial deterioration.

Efficacy data should be derived from simulated-use type tests with quantitative bacteriological sampling and concurrent observations of product quality. Both test and control samples should be tested for a period of 6 months to 1 year. The test protocol, including such elements as frequency of repeated bacterial challenge, must be appropriate to the intended active substance use pattern.

1.6.1 SUGGESTED EPA PERFORMANCE STANDARD

The data should show control of bacterial growth and control of bacterial-caused deteriorative (physical and chemical) changes in the treated products during the test period. The data from control products should show not only survival of test bacteria but also significant growth and resultant deteriorative (physical and chemical) changes.

APPENDIX 1

CURRENTLY AVAILABLE STANDARD TESTS FOR IN-CAN PRESERVATIVES

STANDARD	DATE	TITLE
AFNOR NF X 41-520	03/68	Test method for the resistance of paints to microorganisms and their protective capabilities.
DIN 58 940 Part 5	08/79	Method for the determination of susceptibility of pathogenic bacteria to chemotherapeutic agents; determination of MIC by broth dilution method.
SABS 1102	1987	Bacterial efficacy of biocides used in water-based emulsion paints.
ASTM D 2571-86 or ASTM D 2574-93	1986	Test method for the resistance of emulsion paints in the container to attack by microorganisms.
ASTM D 4783-89	1989	Test methods for resistance of adhesives preparations in container by bacteria, yeast and fungi.b

PRODUCT TYPE 8 - WOOD PRESERVATIVES

1 LABEL CLAIMS

Attention of experts should be paid to product type 8 on the following facts:

a) The European Union covers territories and climates going from nordic/polar (Finland) to tropical situations (French Caribbean Islands, La Réunion, etc.)

b) The best editorial reference for local peculiarities is art. 3.2 of the Construction Product Directive (89/106/EEC)

c) Insects are different (case of termites), modes of action are different (for insects and insecticides), climates and associated virulence of biological agencies are extremely different, efficacy (doses) rely, not only on target organisms, but also on wood species, occurrence of target organism (maps), virulence, mode of action, processes of application required and classes of exposure (climates)

d) As explained in section 7.2.2, there is no universal dose to be applied for a product type such as type 8, particularly when and where the aim is to preserve the environment and reduce risk (according to current knowledge "adapted doses" may vary in ratios from l to 20 for optimisation in case of product type 8 (e.g. 3 – 40 kg/m^3 or more for CCA).

e) The only case for "product type horizontally" found was a common position by CEN/TC 216 (disinfectants) and CEN/TC 38 (wood preservatives) concerning the mode of action of such products, but the service life of protection is significantly different. Additionally, environmental management aimed at limiting residues does not work because, in the case of wood (pt8), it is the residue in wood which remains active for the purpose of efficacy (therefore called "durability") with regulated guarantees for service life.

1.1 Spectrum of biological activity (including target organisms)

Possible target organisms to be considered are confined to several broad groups as indicated in Figure 1.

Further descriptions and information on the organisms are detailed in Appendix 1 of this annex.

1.2 Mode of action/effect

There are a number of possible 'effects' on target organisms derived from the proposed use of a wood preservative product. The available data which will characterise a wood preservative are designed to be appropriate to determination of the efficacy of products applied as either pre-treatments to prevent biological attack, or as remedial treatments to disinfest or to eradicate existing attack. These data are in a variety of forms, they may yield toxic values, mortality values, subjectively derived ratings or effective retention values.

1.3 Areas of use & sites of application

1.3.1 Areas of use

The use patterns for wood preservative products are seen as falling into two broad categories.

- **Preventive treatment (industrial and non-industrial pre-treatment): fixed facilities**

This includes all processes carried out on timber prior to its installation where some degree of future protection (i.e. preventative treatment) is intended.

- **In situ/remedial treatment: mobile works**

This covers all aspects of eradicant and preventive treatment carried out while the wood remains in its service environment. The termite protection is included: chemical barrier (soil and wall treatment), physical chemical treatment barrier (as grafted polyethylene film with insecticides) and baits.

1.3.2 Sites of application (service environments)

The service environments which treated timber is likely to encounter can be divided into 5 main groupings or classes according to the severity of exposure and wetting and type of biological hazard.

These Use Classes, described in EN 335-1 (see Appendix 2), are defined in terms of service conditions with reference to the generalised moisture content and the prevailing biological agents of deterioration.

1.4 Directions for use (including methods of application)

1.4.1 Application methods

The various methods available can be broadly split into three groups:

- **Penetrating treatments**
  Such processes include the currently practised technologies of double vacuum, vacuum-pressure and diffusion treatments.
- **Surface treatments**
  Such processes include brush and spray techniques and short term immersion (dipping) processes (where wood has only a few minutes contact time with the preservative).
- **Other treatment methods**
  For application methods other than those processes described above then either specifically relevant data will need to be provided or some justification for non-inclusion of data (i.e. details on penetrability/retention, etc.) will need to be available to the competent authority for consideration. Main changes occur currently on the modes of action: delayed activity (at sub-lethal doses); deferred effect (emergence of larvae); hormones; growth inhibitors; shedding inhibitors, etc and may require specific adapted testing and criteria (i.e., today, a rate of mortality is not sufficient if the delay is missing).

2 AVAILABLE DATA

2.1 Standard test methods

Many CEN and national standard protocols are available covering efficacy testing of wood preservatives. (See Appendix 3).

The CEN Standard test protocols cover preservative products applied in liquid form and are mainly intended for pre-treatment (preventive) use of timber.

For products intended for application as solids, pastes or encapsulated forms and those products intended for remedial (in-situ) use, modification of the relevant protocols/testing strategies may be required or some other direct evidence may be given of their potential efficacy against the claimed biological organisms (e.g. for pastes such evidence could be in the form of penetrability and retention characteristics).

Fungi			
(a) Wood rotting fungi			
	wood rotting basidiomycetes	such as	*Coniophora puteana* (brown rot) *Poria placenta* (brown rot) *Gloeophyllum trabeum* (brown rot) *Coriolus versicolor* (white rot)
	soft rot micro-fungi	such as	*Chaetomium globosum* *Glenospora graphii* *Humicola grisea*
(b) Wood disfiguring fungi			
	Blue stain	such as	*Aureobasidium pullulans* *Sclerophoma pithyophila*
	Mould and sapstain	such as	*Ceratocystis* sp. *Philaphora* sp. *Alternaria* sp.
Insects			
(a) Wood boring beetles			
	Common furniture beetle House longhorn beetle Powder post beetle		*Anobium punctatum* *Hylotrupes bajulus* *Lyctus brunneus*
(b) Termites			
	Subterranean termites Dry wood termites		*Reticulitermes* sp. *Kalotermes* sp.
Marine borers			
	Shipworm Gribble	such as	*Teredo* sp. *Limnoria* sp.

Figure 1: *Examples of target organisms for wood preservatives (N.B. These examples are not intended to be exhaustive with respect to target organisms or prescriptive with respect to data generation).*

Data should be available in respect of test formulations relevant to the product for which authorisation is being sought and should use the most relevant application process (penetrative treatments, surface treatments or both, where applicable), against the target organisms specified on the label.

2.2 Specific data to support label claims

In assessing the potential effectiveness of a wood preservative competent authorities should in particular take the following parameters into account:

- the toxicity (and permanence) of the preservative itself towards the target organism(s)
- the method of application (and dose rate, treatment time)
- the environment in which the treated wood is exposed

In considering an assessment for a wood preservative product the claimed target organism(s) will depend on the perceived risks related to the intended conditions of use of the timber it is to protect in service. These perceived risks are the starting point for any assessment of the efficacy of a wood preservative as well as the choice of the tests to be conducted.

The rationale for classifying these risks is based on describing a series of service environments for treated timber (Use Classes).

Particular organisms predominate under the conditions described in the Use Classes. Since the Use Classes are essentially linked to the prevailing moisture conditions, they describe principally the increasing risk from the different types of fungi and/or insects.

When considering the overall evaluation of proposed label claims, competent authorities should ensure that the data and that the method of application and application/dose rates used in the tests are appropriate to the label claims and proposed use of the product.

2.2.1 Preventive efficacy

Most of the available data are laboratory generated and relate to the organisms for which biocidal effectiveness is claimed. Field tests, although desirable in cases where the product is intended for use in the more severe service environments (e.g. in ground contact) are not always considered mandatory to fulfil the minimum performance criteria, as this could lead to a compulsory delay of more than 5 years before a new product could be introduced to the market.

However field data will be compulsory for a product claiming use in the **marine** environment

The assessment of the preventive efficacy of wood preservative formulations has to be made from values derived from a relevant biological test. These values are either the actual quantitative amounts of the product established in the test as causing the appropriate level of mortality of the target organism, or they represent the threshold limits, the so-called 'toxic values'. The toxic values are two concentrations in the series used in the test, the one which just permitted continued attack and the next which just prevented it.

2.2.1.1 Use Class 1

Available data

Suitable laboratory data, performed using test blocks, treated either by impregnation with the test formulation (penetrative treatment) or surface treatment to investigate the protective effectiveness against the various challenge insects. Data should be presented on test blocks subjected to pre-conditioning by an evaporative ageing process (e.g. EN 73 or an equivalent test method).

Test species

The insect test species used will depend on whether a general or species specific efficacy claim is made. Data should be available demonstrating activity against one or more of the following specific insects: Hylotrupes bajulus, Anobium punctatum, Lyctus brunneus, and where appropriate, termites.

Competent authorities should evaluate the available data to determine whether they are sufficient for label claims as follows:

a) for general claims against "wood boring beetles"

- It is acknowledged that the majority of applications for authorisation are likely to be for treatments against *H. bajulus.* Therefore data against this beetle species should be available and will be considered adequate to cover this claim.
- However, suitable data against *A. punctatum*as an indicator species is considered sufficient to cover such a claim.
- If existing data are available (e.g. laboratory screening tests on the active substance) and these data show the active substance to be more or less equally effective against the 3 different wood boring beetles then suitable efficacy data (on test blocks subjected to an evaporative ageing procedure such as EN 73) against any one of the three indicator species are adequate.

- Similarly if existing data are available and these data have shown that the product has different activities against the 3 indicator species, then suitable efficacy data against the most tolerant beetle species tested will be adequate to cover the claim.

b) <u>for claims against a specific named beetle species</u>

- If claims against individual beetle species are detailed on a product label then suitable efficacy data against those named target pests will be required.

These various scenarios for claims against wood boring beetles are summarised in Figure 2.

c) <u>for claims against termites</u>

In cases where the response of a termite test (biological reference value) is higher than the critical value derived from beetles and fungi, this response is taken as critical value or required dose in area infested by termites or susceptible to be infested.

- Data on efficacy against termites will only be required when the product is to be marketed for use as a termiticidal product or where local requirements demand such activity.
- For a product to claim activity against termites suitable efficacy data demonstrating preventive efficacy data against an indicator species such as *Reticulitermes santonensis* will be required. In this situation *R. santonensis* is taken as the most widespread organism and therefore "economically dominant". More tolerant species of termites may be found and could justify local adaptations. Occurrence has to be predicted in classes 1, 2, 3, 4.

2.2.1.2 Use Class 2

<u>Available data</u>

Available data would include suitable laboratory data generated using treated test blocks to determine the toxic values against the fungi and insects as appropriate. Wherever possible these data should be relevant to label claims for penetrative and surface treatments.

<u>Test species</u>

The test species used will depend upon the label claims made and are likely to be one or more of the following target organisms: - brown rot Basidiomycete fungi, wood disfiguring fungi (such as blue stain) and, if appropriate, insects (as in Use Class 1).

Competent authorities should evaluate the available data to determine whether they are sufficient for label claims as follows:

a) <u>For claims against wood rotting fungi the following data should be available:</u>

- Suitable laboratory data demonstrating efficacy against Basidiomycete **brown rot fungi.**
- Data from tests conducted on blocks subjected to evaporative ageing to EN 73 (or an equivalent ageing procedure).
- There is not, at present, a recognised standard test for surface treatments against Basidiomycetes. Data on penetrative treatments as a surrogate should be acceptable.

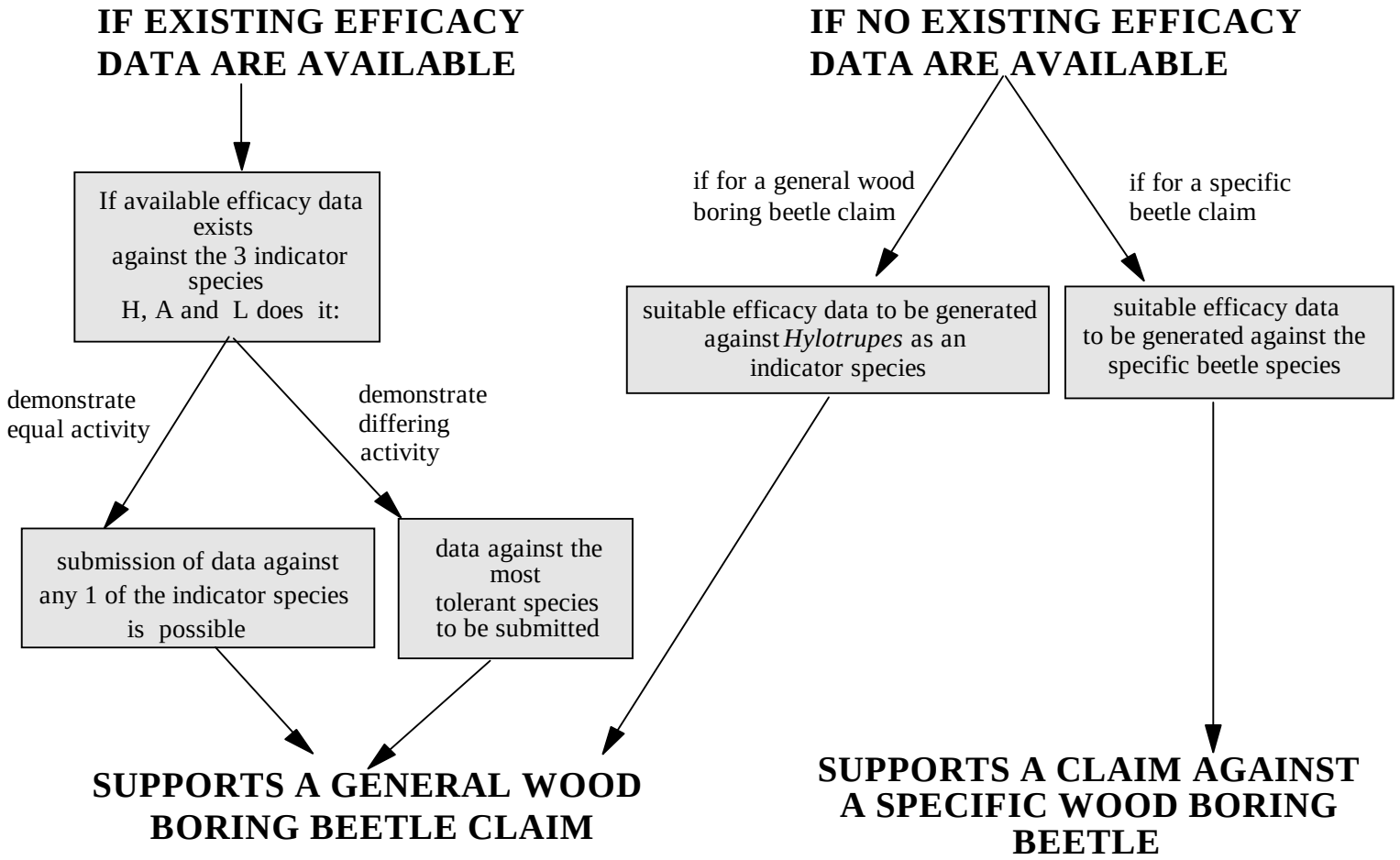
b) <u>For claims against wood disfiguring fungi the following data should be available:</u>

- Suitable laboratory test data on the protective effectiveness of the product against **Blue stain in service** preferably following natural weathering (or alternatively, aged via artificial weathering procedures).
- The application process used in the test (i.e. whether by surface or penetrative treatment) should be in accordance with label claims.

c) <u>For claims against insect pests the following data should be available:</u>

- As outlined in Use Class 1.

Figure 2. *Data required to support claims for activity against wood boring beetles (arising from a number of possible testing strategies).*



key H: *Hylotrupes bajulus*
A: *Anobium punctatum*
L: *Lyctus brunneus*

2.2.1.3 Use Class 3

Available data

Available data would include suitable laboratory data generated using treated test blocks to determine the toxic values against the fungi and insects as appropriate. Wherever possible the data should be relevant to label claims for penetrative and surface treatments.

Test species

The test species used will depend upon the label claims made and are likely to one or more of the following target organisms: - brown rot Basidiomycete fungi (and in some situations additional testing against white rot Basidiomycetes may also be required), wood disfiguring fungi (such as blue stain) and, if appropriate, insects (as in Use Class 1).

Competent authorities should evaluate the available data to determine whether they are sufficient for label claims as follows:

a) For claims against wood rotting fungi the following data should be available:

- Suitable laboratory tests as outlined for Use Class 2, but additionally either:
  - (i) for claims against wood rotting basidiomycetes, efficacy should be demonstrated following pre-conditioning of the treated test blocks by a suitable leaching procedure (e.g. to EN 84 or an equivalent procedure); or
  - (ii) If the applicant considers that a leaching procedure is not appropriate (e.g. for overpainted timbers) an above ground field test (painted L-joint type tests or similar) in addition to the test requirements outlined in Use Class 2 should be acceptable.
- Additionally in some situations suitable laboratory data demonstrating efficacy against white rot fungi will be required.

b) For claims against wood disfiguring fungi the following data should be available:

- Suitable laboratory data as outlined for Use Class 2 with the addition that data available should consider the effects on efficacy following natural ageing of the treated test blocks (or alternatively ageing via an artificial weathering procedure).
- The data available should consider an application method similar to that indicated on the label.

c) For claims against insect pests (if relevant) the following data should be available:

- As outlined in Use Class 1, with the addition that efficacy is demonstrated following pre-conditioning of the treated test blocks by a suitable leaching procedure. (e.g. to EN 84 or an equivalent procedure).

2.2.1.4 Use Class 4

Available data

Available data would include suitable laboratory data generated using treated test blocks to determine the toxic values against the fungi and insects as appropriate. In this situation available data should only include application of the preservative by penetrative treatments.

Test species

Test species used will depend upon the label claims made and are likely to include the following target organisms: Brown and white rot basidiomycetes, soft rot micro-fungi and if relevant to label claims, may also include blue stain fungi and insects as appropriate.

Competent authorities should evaluate the available data to determine whether they are sufficient for label claims as follows:

a) For claims against wood rotting fungi the following data should be available

- Suitable laboratory data as outlined for Use Class 3 with the following additions:

  (i) all laboratory data should derive from treated test blocks impregnated (i.e. a penetrative treatment) with the test formulation to determine the toxic values against both brown and white rot Basidiomycetes separately;

  (ii) suitable laboratory test to determine the toxic effectiveness against soft rot microfungi and other soil inhabiting microfungi are required; or, alternatively

- field data: Although not considered mandatory, if available field data are preferred to laboratory tests to demonstrate the relative protective effectiveness of treated wood stakes in ground contact to support use of a product in this situation. The tests should run for a minimum period of 5 years.

b) For claims against wood disfiguring fungi the following data should be available:

- Suitable laboratory tests determining the protective effectiveness of the product against **blue stain in service** preferably following natural weathering (or alternatively, aged via artificial weathering procedures) should be provided.
- The application process must be penetrative treatment .

c) For claims against insect pests the following data should be available:

- As outlined for Use Class 1, with the addition that efficacy is demonstrated following pre-conditioning of the treated test blocks by a suitable procedure (e.g. to EN 73 and EN 84 separately or an equivalent ageing procedure).

2.2.1.5 Use Class 5

Available data

The principal agent of decay in this situation are the marine borers. Therefore in this Use Class available data must include evidence of effectiveness in a relevant marine field trial carried out for a minimum of 5 years (e.g. to EN 275 or an equivalent test).

Decay in this situation by Basidiomycetes fungi does not occur but marine soft rot fungi are very common causing surface softening of timber. Assessment of products against marine fungi is not normally conducted routinely using laboratory tests because of the difficulties in providing conditions which appropriately model the marine environment. There is not, at present, a recognised standard laboratory test for assessment of timber intended for use in salt water.

Test species

Test species used will depend upon the label claims made. The principal agent of decay in the marine environment are the marine borers although claims against fungi can also be made.

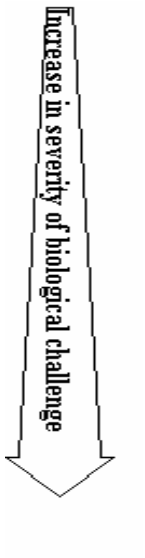
Competent authorities should evaluate the data to determine whether they are sufficient for label claims as follows:

For claims against wood rotting fungi and marine borers the following data should be available:

- for fungi available data as outlined in Use Class 4 as a surrogate should be acceptable.
- for marine borers a relevant marine field trial data carried out for a minimum of 5 years (e.g. EN 275 or an equivalent would be considered a suitable test.)

A SUMMARY OF THE PREVENTIVE EFFICACY DATA AVAILABLE IN EACH OF THE USE CLASSES ARE SUMMARISED IN TABLE 1.

Table 1: *Summary of available data required to support claims for preventive efficacy*



Hazard Class	Service Environment	Minimum Laboratory Tests[1]	
1	**Above ground (Dry)**	**Wood boring insects only (no fungal hazard)**	
2	**Above ground (wetting, protected from the weather)**	**Wood rotting basidiomycetes - brown rot**	**Field Tests[2]**
3	**Above ground (Exposed to weathering, but not in ground contact)**	**Wood rotting basidiomycetes - brown rot and in some cases white rot**	**L-joint test (5 year) optional**
4	**Timbers in contact with the ground or fresh water, or above ground if water trapping or logging exist**	**Wood rotting basidiomycetes - white rot and brown rot Soft rot microfungi**	**Stake test (5 year) optional**
5[3]	**Timbers in the marine environment**	**Wood rotting basidiomycetes - white rot and brown rot Soft rot microfungi Marine borers**	**Marine test (5 year) compulsory**

[1] Appropriate ageing procedures will also be required. Tests against additional risks (including wood boring insects) may apply.

[2] If relevant field data are available for timber used in Use classes 1 to 4 situations then this will be accepted in support of product applications.

[3] Class 5 represent media different from classes 1,2,3,4

2.2.2 Eradicant efficacy

For those remedial wood preservative products claiming eradicant activity, suitable efficacy data are required. The minimum performance requirements are given in prEN 14128:2001.

The assessment of in-situ/remedial treatment systems will be more varied than preventive treatments because of the wide range of likely treatment methods and more complex since both *eradicant (curative)* and *preventive* action may need to be considered.

Data of the type which should be available for preventive efficacy (see Section 2.2.1) will also be relevant for products intended for use as remedial preservatives. However, additional eradicant test methods may be employed for the claims made for remedial preservatives

2.2.2.1 Insects

Data required to support label claims for eradicant efficacy may include tests generated using existing EN standards for the relevant beetle species or other alternative supporting data.

A number of EN standard tests exist for remedial (curative) treatments for insecticides against the 3 wood boring insects *H. bajulus, A. punctatum and L. brunneus*. Required data will depend on the individual beetle species for which activity is to be claimed (see Section 2.2.1.1).

2.2.2.2 Fungi

Any claims for eradicant activity against wood rotting Basidiomycete fungi should be supported by suitable efficacy data or some other direct evidence. No standard test protocols presently exist for remedial (curative) treatments for wood rotting basidiomycetes

In both cases competent authorities should evaluate the data available to determine whether they are sufficient in supporting the label claims.

2.2.3 Temporary (sapstain) treatment efficacy

For this type of treatment, most of the available data are laboratory and field generated, and relate to 2 categories of organisms: 1/ blue stain in service, fungi, and sapstain in freshly sawn timber fungi 2/ moulds growing often on the wood surface.

The assessment of the preventive efficacy of wood preservative formulations has to be made from values derived from relevant biological tests. No EN test exists. Development of one standard is in progress. For France: products should be tested according to the biological tests NF X 41-547 (laboratory test), and NF X 41-549 (field test). A chemical analysis is required.

A dose rate / dipping time is part of the efficacy assessment. The label claim must mention the dose rate, the dipping time and the duration of the efficacy (usually 3 to 6 months).

2.2.4 Antitermite efficacy.

The preservative products relevant to that claim relate to 3 categories:

- chemical barriers: soil and wall treatment,
- physical-chemical barriers,
- baits

2.2.4.1 Chemical barriers

The available data are laboratory and field generated. No EN standard exists, and only French standards exist.

- Soil treatment (preventive and remedial treatment): NF X 41-540 (lab test) after NF X 41-542 (leaching test) + chemical analysis. The efficacy is given by a dose rate that represents 4 times the biological reference value.
- Wall treatment (remedial treatment): NF x 41-541 (lab test) after NF X 41-542 (leaching test) + chemical analysis. The efficacy is given by a dose rate that represents 1.5 times the biological reference value.

The dose rate could be modified after 2 and 5 years according to the results of the field ageing tests (CTBA protocol).

2.2.4.2 Physical-chemical barrier

No EN standard currently exists. All tests available in Europe are CTBA protocols.

Such a barrier is typically a grafted insecticide polyethylene film, and the product is only preventive. The available data are laboratory and field generated.

2.2.4.3 Baits (remedial treatment)

No EN standard currently exists. All tests available in Europe are CTBA protocols.

The available data are laboratory and field generated. Tests are carried out on all species of termites present on a geographic area, due to the type of efficacy of the insecticides.

APPENDIX 1

INFORMATION ON THE PRINCIPLE TARGET ORGANISMS OUTLINED IN THE DOCUMENT

1) **Fungi**

Wood rotting fungi

A wood moisture content of more than 20 % (m/m) is necessary for the development of these fungi.

Wood rotting Basidiomycete fungi

Fungi responsible for brown rot and white rot, but not soft rot.

Soft rot fungi

Fungi responsible for a type of rot characterised by surface softening of the wood although they also cause rot at depth. These fungi need a higher wood moisture content than basidiomycetes. They are of special significance for wood in ground contact or in water.

Wood disfiguring fungi

Fungi causing mould and blue stain in service.

These fungi are only of practical concern in relation to aesthetic appearance, though they can increase wood permeability and degrade decorative coatings.

Blue stain fungi

Fungi causing blue to black permanent discolouration of variable intensity and depth mainly in the sapwood of certain woods. This does not result in appreciable alteration of the mechanical properties but can increase the permeability. They are highly significant where the surface appearance is important.

Mould fungi

Fungi being evident as spots of various colours on the surface of wet wood and they can occur when only the wood surface moisture content is above 20 % (m/m) (for instance, as a result of high relative humidity or of condensation of water vapour). They do not significantly alter the mechanical properties of the wood. They are only of special significance for wood in service if disfigurement is undesirable or unacceptable.

These fungi are not necessarily specific to wood and can occur on any material with a high moisture content.

Sapstain fungi

Sapstain fungi are of economic importance in causing blue-black and brown disfigurement of freshly felled logs or sawn timber. They only infect timber as long as it is green and are controlled by rapid drying. When handling practices cannot ensure rapid surface drying, chemical treatments are sometimes used. The minimum moisture level for growth is approximately 27 % m/m. Sapstaining fungi tend to be resistant to low temperatures and consequently may survive in severely cold and frosty conditions. Attack by sapstaining fungi may reduce the ability of the timber to resist shock and consequently may constitute a risk where the timber in question requires particular toughness. Common sapstaining species include *Ceratostomella pilifera* with other species of staining fungi being *Aureobasidium pullulans* spp., *Alternaria* spp., *Ceratocystis* spp. and *Phialophora* spp.

2) **Insects**

Wood boring beetles (Coleoptera)

Insects which lay their eggs in wood pores or cracks and which have larvae that attack the wood. They are present throughout Europe but the risk of attack varies greatly from high to insignificant. The most important are *Hylotrupes bajulus*, *Anobium punctatum* and *Lyctus brunneus*.

Hylotrupes bajulus (House longhorn beetle)
Attacks the sapwood only of many softwood species and its vitality and longevity depend principally on the ambient temperature and the wood moisture content. Where present, it can be of serious structural significance.

Anobium punctatum (Common furniture beetle)
Insect responsible for attack of the sapwood of certain softwood and hardwood species. The damage can extend to the heartwood in some wood species. Occasionally regarded as of structural significance. Its presence is particularly noted in coastal climates and where damp conditions prevail.

Lyctus brunneus (Powder post beetle)
Insect which attacks sapwood of certain starch-containing hardwoods. Of significance throughout Europe in both European and imported hardwood timbers.

Termites (Isoptera)

The most destructive wood destroying pests in warm climates, about 1800 different species occur in all the warm climates of the world. Termites exist throughout the tropics but extend into Southern Europe. Their life style is quite different from the wood boring beetles. Two distinct groups of termites attack wood: subterranean termites and dry wood termites

The subterranean termites build their nests in contact with the ground and are responsible for the characteristic termite mounds. Only a few of the many species of subterranean termites cause significant damage to buildings (these include the *Reticulitermes* sp. found in Southern Europe). They forage over a distance for their food and build tunnels between their nests and the source of timber. Control of subterranean termites can therefore consist of excluding them from buildings by such means as toxic barriers and soil poisoning or by direct treatment of the timber.

Dry wood termites (Kalotermitidae), in contrast, live independent of the ground excavating clean galleries within the timber structure. The colonies are much smaller but once established in a building they can be difficult to locate and eradicate due to quick and massive swarming, plus erratic landing and distribution. Prevention by exclusion of flying insects and conventional wood preservation are considered to be the most effective measures.

3) **Marine borers**

Term applied to marine invertebrates such as *Limnoria* spp. *and Teredo* spp. which need a certain salinity of water and which hollow out extensive tunnels and cavities in wood. These organisms can cause serious damage to fixed or floating structures.

In European waters the most common marine borers are shipworm (*Teredo navalis*) and gribble (*Limnoria lignorum*). Shipworm is a bivalve mollusc related to the sea snails and mussels. It is a soft, worm like animal with its shell modified into hard grinding jaws. The larvae are part of the microscopic zooplankton and swim freely in the sea until they settle on timber. They develop a shell with which they bore into the wood and lodge there, growing into large worms in holes up to 5 mm in diameter. They destroy the wood by making a massive network of such holes throughout the timber. Gribble is a small shrimp-like crustacean about 4 mm in length. It bores into the surface of the wood and lodges near the surface making numerous side burrows. The combination of this boring and wave action causes rapid erosion of marine timbers.

APPENDIX 2

END USE USE CLASSES (as defined in EN 335-1)

Hazard Class	Descriptor
1	Wood or wood-based product under cover, fully protected from the weather and not exposed to wetting. (e.g. domestic roof timbers). In this Use Class the moisture content is permanently below 18 %.
2	Timbers not in ground contact, protected from the weather but where high environmental humidity can lead to occasional but not persistent wetting. (e.g. general building timbers). In this Use Class the moisture content of the timber will be in excess of 20 % for periods of time.
3	Timbers not in ground contact, either continually exposed to the weather or protected from the weather but subject to frequent wetting (e.g. fencing rails, joinery, cladding). The timber may be above 20 % moisture content for long periods of time.
4	Timbers in contact with the ground or fresh water and permanently exposed to wetting (e.g. fence posts, poles, silage walls, river jetties). In this Use Class the moisture content will be above 20 % for most of the time and often very much higher.
5	Timbers in the marine environment exposed to salt water (e.g. marine piling, harbour jetties).

APPENDIX 3

LIST OF EN STANDARDS FOR EFFICACY ASSESSMENT OF WOOD PRESERVATIVES

Standard	Date	Title
EN 73	1988	Accelerated ageing test of treated wood prior to biological testing. Evaporative ageing procedure
EN 84	1997	Accelerated ageing tests of treated wood prior to biological testing. Leaching procedure
EN 113	1996	Method of test for determining the protective effectiveness against wood destroying Basidiomycetes - Determination of the toxic values
EN 117	1989	Determination of toxic values against *Reticulitermes santonensis* de Feytaud (Laboratory method)
EN 118	1990	Determination of preventive action against *Reticulitermes santonensis* de Feytaud (Laboratory method)
EN 152-1	1988	Laboratory method for determining the preventive effectiveness of a preservative treatment against blue stain in service – Part 1 Brushing procedure
EN 152-2	1988	Laboratory method for determining the preventive effectiveness of a preservative treatment against blue stain in service – Part 2 Application other than by brushing
EN 252	1989	Field test method for determining the relative protective effectiveness of a wood preservative in ground contact
EN 275	1992	Determination of the protective effectiveness against marine borers
EN 330	1993	Field test method for determining the relative protective effectiveness of a wood preservative for use under a coating and exposed out-of-ground contact: L-joint method
ENV 807	2001	Determination of the effectiveness against soft rotting micro-fungi and other soil inhabiting micro-organisms
prENV 839	2001	Determination of the protective effectiveness against wood destroying Basidiomycetes. Application by surface treatment
EN 20-1	1992	Determination of the protective effectiveness against *Lyctus brunneus* (Stephens) – Part 1 Application by surface treatment (Laboratory method)
EN 20-2	1993	Determination of the protective effectiveness against *Lyctus brunneus* (Stephens) – Part 2 Application by impregnation (Laboratory method)
EN 22	1974	Determination of eradicant action against *Hylotrupes bajulus* (Linnaeus) larvae (laboratory method)
EN 46	1988	Determination of the preventive action against recently hatched larvae of *Hylotrupes bajulus* (Linnaeus) (laboratory method)
EN 47	1988	Determination of the toxic values against *Hylotrupes bajulus* (Linnaeus) larvae (Laboratory method)

Standard	Date	Title
EN 48	1988	Determination of eradicant action against larvae of *Anobium punctatum* (De Geer) (laboratory method)
EN 49-1	1992	Determination of the protective effectiveness against *Anobium punctatum* (De Geer) by egg laying and larval survival – Part 1 Application by surface treatment (laboratory method)
EN 49-2	1992	Determination of the protective effectiveness against *Anobium punctatum* (De Geer) by egg laying and larval survival – Part 2 Application by impregnation (laboratory method)
EN 370	1993	Determination of eradicant efficacy in preventing emergence of *Anobium punctatum* (De Geer)
ENV 1390	1994	Determination of the eradicant action against *Hylotrupes bajulus* (Linnaeus) larvae - laboratory method
EN 599-1	1996	Durability of wood and wood-based products - Performance of preventive wood preservatives as determined by biological tests - Part 1: Specification according to Hazard Class.
EN 335-1	1992	Durability of wood and wood-based products - Definition of Use Classes of biological attack - Part 1: General
EN 335-2	1992	Durability of wood and wood-based products - Definition of Use Classes of biological attack - Part 2: Application to solid wood

Example: Efficacy assessment for "Bootle Wood Preservative"

CONSIDERED STEPWISE APPROACH TO ASSESSMENT OF EFFICACY DATA

EFFICACY ASSESSMENT CHECKLIST	YES ☑ or NO ☒
APPLICANT'S LABEL CLAIMS	
1. Has the applicant made any label claims for the candidate product?	☐
2. Have the label claims been matched up and broken down against the parameters outlined in Chapter 7 and the appropriate Annex for this product type?	☐
ASSESSMENT OF DATA	
3. Has each individual study (or other supporting data) been assessed for robustness?	☐
4. Has each individual study (or other supporting data) been assessed for quality assurance?	☐
5. Has each individual study (or other supporting data) been assessed for adequacy (i.e. with respect to reliability and relevance to the label claims)?	☐
DECISION MAKING	
In considering all the available data:	
6. Is the label claim fully supported?	☐
7. Does the label claim require amendment?	☐
8. On the basis of the efficacy data provided can an authorisation be recommended for the use of the candidate product?	☐

APPLICANT'S LABEL CLAIMS

STEP 1

Has the applicant made any label claims for the product?

YES - The claims made for this product are as follows:

"Bootle Wood Preservative, a clear wood treatment designed to give high penetration. For the prevention and eradication of wood rot and insect attack in structural timbers, flooring, panelling, joinery etc."

STEP 2

Have the label claims been matched up and broken down against the parameters outlined in Chapter 7 and the appropriate Annex for this product type?

YES - The claim can be broken down as indicated below:

- Product type **Wood Preservative (Product type 8)**
- Spectrum of biological activity **Wood rotting fungi and wood destroying**
  (including target organisms) **insects**
- Mode of action/Effect **Preventative and eradication**
- Area of use/site of application
  Area of use **In-situ/Remedial treatment**
  Site of application **Structural timbers, flooring, panelling, joinery (Use Classes 1-3, see application methods)**
- Directions for use
  Application methods **Brush and spray (i.e. surface treatments)**
  Application rate(s) **1 litre of product per 3 - 4 m^2 wood surface**

ASSESSMENT OF DATA

Available Data
The following data were provided in support of the product application:

Data available against wood rotting fungi included:-
A modified EN 113 test (i.e. non standard test methodology)
EN 330 (1993) (preventive testing)

Data available against wood destroying insects included:-
EN 46 (1988) (preventive, surface application)
EN 49-1 (1992) (preventive, *Anobium*, surface application)
EN 118 (1990) (termites, preventive, surface application, "barrier effect", not curative)

STEPS 3-5

Has each individual study (or other supporting data) been assessed for robustness, quality assurance and adequacy (with respect to reliability and relevance to the label claims)?

Study	Robustness	Quality Assurance	Adequacy		
			Reliability	Relevance	
				Preventive action	Eradicant action
Modified EN 113	✓(1)	✓	✓	✓(2),(3)	**X** (3)
EN 330	✓	✓	✓	✓ (3)	**X** (3)
EN 46	✓	✓	✓	✓ (4)	**X** (3)
EN 49-1	✓	✓	✓	✓ (4)	**X** (3)
EN 118	✓	✓	✓	**X** (5)	**X** (5)

Key: ✓ acceptable **X** inadequate

Footnotes

(1) In the absence of an EU recognised test for surface treatments against *Basidiomycetes* (prENV 839:2001 for surface treatment is available in parallel with EN 113) the applicant has submitted a study based on a method devised by EMPA designed to mimic application of the product by a craftsman (i.e. brush, spray, etc.). The method is considered acceptable by the competent authority for the determination of the preventive efficacy of ready-for-use products when applied as a surface treatment.

(2) Additionally the test considered the exposure of test blocks to the test organisms after the product had dried and been subjected to ageing via natural weathering.

(3) No data were presented in support of the eradication of either wood destroying insects or wood rotting fungi. (The competent authority notes that although tests do exist for assessment of curative efficacy against insects no standards presently exist for curative treatments for wood rotting fungi, as there is a total collapse of mechanical properties of wood by fungal attack, the only remediation possibility is replacement, while larvae may damage wood locally before eradication).

(4) These tests considered the preventive effectiveness of the product against common wood boring beetles following evaporative ageing of the test blocks

(5) This study considers the preventive efficacy of the product against termites. Such claims for use are not relevant in the UK where termites are not considered to be a significant problem. It must, however, be considered if the product is exported to, e.g., France or Portugal.

DECISION MAKING

In considering the results obtained from the two studies submitted in support of efficacy claims against wood rot the competent authority considers that the label claims for preventive use can be supported for use in out of ground contact situations (i.e. in Use Classes 1-3)

In consideration of the test data submitted in support of the claim for efficacy against insect attack the competent authority consider that a label claim for preventive efficacy against wood boring beetles can be supported.

No data have been provided in support of the claims for eradicant (curative) efficacy and therefore this claim cannot be supported.

Although the non-significance of termites in the UK, further assessment in concerned countries (the Mediterranean countries of the EU) may be necessary in order to achieve a mutual recognition of the authorisation.

STEP 6

Is the label claim fully supported?

NO - Claims for the preventive efficacy for the product against wood rotting fungi and wood destroying insects in out of ground situations are supported. As no data have been provided in support of for eradicant efficacy such claims are not supported

STEP 7

Does the label claim require amendment?

YES - In the absence of supporting data, the applicant will be required to amend the claim to remove reference to claims for eradicant efficacy.

STEP 7A

If the applicant makes an amendment to the label claim as indicated in STEP 7 above then the competent authority can consider recommending an authorisation.

STEP 8

Can an authorisation be recommended for the candidate product?

YES - On the basis of the assessment of the efficacy of the candidate product the competent authority can recommend that an authorisation be granted subject to amendment of the label claims as indicated above.

STEP 8A

The competent authority notes that should the applicant wish to extend the claims made for the product at a later date then data (or other supporting evidence) will need to be submitted for assessment.

Example: Efficacy assessment and review of label claims for wood preservatives

1 – CLAIMS

The following table can be used review the tests supporting the label claim.

Use class and critical value G/m2 – kg/m3	Simulated wood exposure (ageing test)	Targets (biological agents) (*)	Type of test + prior ageing separately	Covered (tick, Yes/no)
1A – interior dry :…….	Evaporation		EN 73	…./….
		Wood boring beetles	EN 46 ….g/m2 EN 47….kg/m3	…./…. …./….
1B = 1A + termites – interior dry : …….	Evaporation		EN 73	…./….
		termites	EN118….g/m2	…./….
			EN117…kg/m3	…./….
2 – interior damp : ……	Evaporation		EN 73	…./….
	Leaching		EN 84	…/….
2A		Wood boring beetles	EN 46……g/m2 EN 47…kg/m3	…./…. …./….
		Disfiguring fungi	EN152/1..g/m2 EN152/2..kg/m3	…./…. …./….
		Decay fungi	EN113 ….g/m2 EN113....kg/m3	…./…. (**)
2B = 2A + termites	evaporation		EN 73	…./….
	Leaching		EN 84	…./….
		termites	EN118…..g/m2	…./….
			EN 117…kg/m3	…./….
331 – protected exterior	Evaporation		EN 73	…./….
	Leaching		EN 84	…./….
		Decay fungi	EN 113 incl. Coriolus versicolor..g/m2 …….kg/m3	…./…. …./….
	Appropriate	Decay fungi	Alternative to EN 84+	…./….

	weathering		EN 113 = EN 330	
332 - Unprotected exterior	Evaporation		EN 73 - Same as for 331	…./….
	leaching		EN 84 – same as for 331	…./….
		Decay fungi	EN 113 including Coriolus versicolor..g/m2 ……kg/m3	…./…. …./….
		Wood boring beetles + disfig. Fungi	Same as for 2A after EN73 & 84	…./….
		Termites	Same as for 2B after EN73 & 84 separately	…./….
441 – In ground 442 – In ground, severe, fresh water	Evaporation		EN 73 – same as for 331	…./….
	Leaching		EN 84 – same as for 331	…./….
		Decay fungi	EN113 + Coriolus after EN 73/84 separately …….kg/m3 only	…./….
		Soft rot fungi	ENV 807..kg/m3	…./….
		Termites	EN 117 - after EN73 & 84 separately ……kg/m3	…./….
	poles	Simulated use	EN 252 ...kg/m3	…./….
5 – Marine (***)				
5 (A – B – C)		Teredinids + Limnoria + pholads	EN 275	…./….

Notes:

(*) targets are limited to dominant species, when recognised by national declarations : *options may be claimed with specific assessment (specialties) ;
(**) efficacy is based on 2 main types of tests (surface application in g/m^2 & mass impregnation in kg/m^3 ; basic equivalence is 100 kg/m^3 = 200 g/m^2 but processes and tests are different, excepted for EN 113 ; an alternative is in progress)
(***) fresh water (class 4-2) and marine waters (class 5) are classified ; brackish waters are subject to expertise for the identification of local, specific biological agencies.

PRINCIPLES OF EFFICACY ASSESSMENT FOR WOOD PRESERVATIVES

For principles of efficacy assessment for wood preservatives see EN 599 - 1 (Performances of Preventive Wood Preservatives based on Biological Tests and tables 1 - 5). For informative labelling, see also EN 599 - 2. Treated wood is specified by EN 351 parts 1 & 2. Performance criteria for products for curative uses against wood attacking organisms, as determined by biological tests are developed in pr EN 14128 (march 2001). Other criteria of performance (i.e. a rate of mortality are developed in the test standards themselves). It is the responsibility of the manufacturers to document the performance criteria to which they refer.

SUMMARY & CONCLUSIONS

The product is shown to be efficiently effective when it is clearly identified (analysis) and meets the criteria of EN 599 (matrix dose-use) and when it is adequately applied to wood, meeting the penetration-retention pattern criteria of EN 351 (process criteria).

PRODUCT TYPE 10 - MASONRY BIOCIDES

1 LABEL CLAIMS

1.1 Spectrum of biological activity (including target organisms)

Possible target organisms to be considered are confined to several broad groups. These are dependent on the intended use of the candidate product (i.e. either as a general surface biocide or for specific use as a dry rot treatment) and are shown in Figure 1.

1.2 Mode of action/effect

There are a number of possible 'effects' on target organisms derived from the proposed use of a masonry biocide and the actual effectiveness of products will depend on a number of variables such as substrate, target organism, persistence and penetration, concentration used and desired effect, Commonly these effects can be described as either kill or prevention of re-growth of organism.

1.3 Areas of use & sites of application

With respect to label claims for masonry biocide product applications, a distinction between two use patterns may be made when evaluating a data package.

- **Masonry biocides intended specifically for the control of dry rot**

In this situation the product is applied to masonry (or other mineral construction materials) in order to prevent the growth of dry rot fungi through or over the treated material.

- **Products intended for general surface biocide use**

In this situation the product (sometimes known as a toxic wash) is applied to a wide variety of hard and/or soft surfaces to control organisms such as algae, yeasts, fungi, lichens, mosses and liverworts.

The possible efficacy label claims for both use patterns are depicted in Figure 2.

2 AVAILABLE DATA

2.1 Standard test methods

Very few international standard test methods currently exist for masonry biocide products. Those recognised standards that are available are presented in Appendix 1 to this document.

Dry rot fungus

Serpula lacrymans

Algae

Pleurococcus spp.
Stichococcus bacillaris (green algae)
Gloeocapsa alpicola (green algae)
Nostoc commune (Blue-green algae)

Fungi/yeasts

Aspergillus versicolor
Aureobasidium pullulans
Cladosporium caldosporioides
Penicillium purpurogenum
Phoma violacea
Rhodotorula rubra
Sporbolomyces roseus
Stachybotrys atra
Ulocladium atrum

Lichens

Lecanora dispersa
Caloplaca spp.
Candelariella spp.
Buellia canescens

Mosses and liverworts

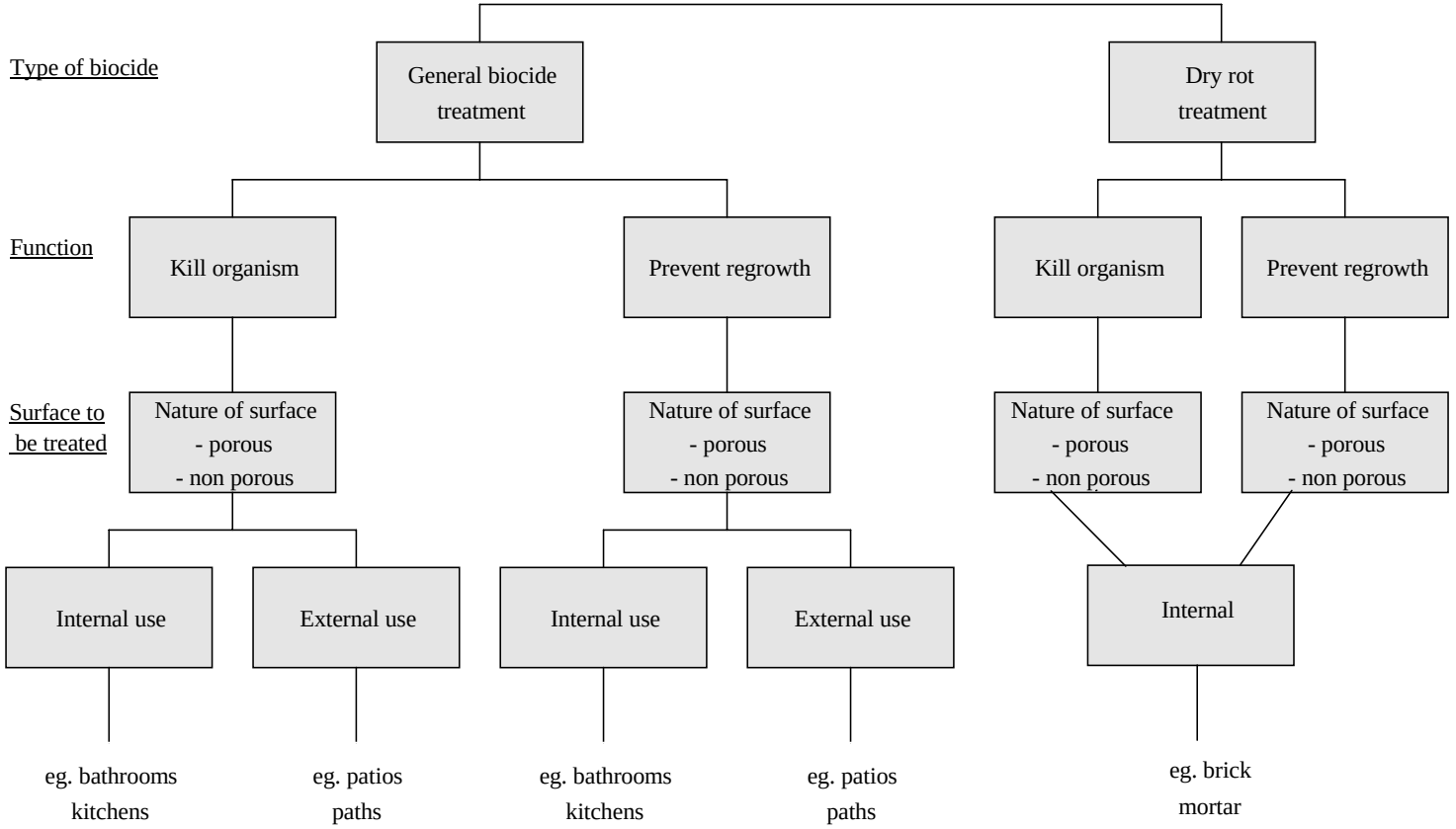
Mosses
Tortula muralis
Barbula cylindrica
Grimmia pulvinata
Camptothecium sericenum
Rhynchostegiella tenella

Liverworts
Lunularia cruciata
Marchantia polymorpha

N.B. The above is not intended to be an exhaustive list of possible target organisms nor is intended to be prescriptive with respect to data generation, it gives some examples only from the major biological groups.

Figure 1: *Target organisms*

Figure 2: *Examples of efficacy claims for masonry biocide products: Breakdown of the information that may be required when considering efficacy testing strategies and the evaluation of data.*



2.2 Specific data to support label claims

In assessing the efficacy for a masonry biocide product competent authorities should in particular take the following parameters into account:

- The toxicity (and permanence) of the product itself towards the target organism(s)
- The intended use pattern for the candidate product
- The method of application (and dose rate)

In considering an assessment for a masonry biocide product the claimed target organism(s) will depend on the intended use pattern; and since particular organisms will predominate in certain situations, the treatment environment.

When considering the overall evaluation of a proposed label claim competent authorities should ensure that the data presented are relevant not only to biological challenge and treatment environment but also that the method of application and application/dose rate used in the test(s) are appropriate to the label claims and proposed use of the product.

Examples of the types of data that would likely to be available for evaluation of biocidal products intended for use as general surface biocides and those products specifically intended for the control of dry rot are presented in Figures 3 and 4.

Competent authorities should evaluate the available data to determine whether they are sufficient to support the label claim.

For claims made for products intended for use as general surface biocides

Available data

For products intended for general surface biocide use the test organisms used will depend upon the label claims made. Examples of the type of data that may be available when considering the efficacy of products intended for general surface biocide use are shown in Figure 3.

Laboratory/screening tests: (see note)

Application of a range of concentrations of the active ingredient, absorbed onto assay discs applied to a suitable nutrient agar medium seeded with either fungal or algae and following a suitable incubation period, determination of the zone of growth inhibition.

Simulated use studies

Laboratory tests employing actual building materials as substrates and permitting full substrate/organism/biocide interaction during testing, e.g. use of moist vermiculite-bed techniques to evaluate the efficacy of a biocide on a range of substrates.

Field studies

Natural exposure trials using samples from actual building material supported on an exposure rack in a region known to be vulnerable to establishment of biological growths, weathered and colonised by the organisms can be used to evaluate the efficacy of a biocide. Application of surface biocides to walls and other structures already colonised with lichens, mosses etc. may be used.

Figure 3: *General surface biocide use*

Note

At present there is no laboratory method for determining the efficacy of surface biocides against lichens, mosses and liverworts. These organisms are likely to colonise building materials placed on exposure racks but only after several years.

Simulated use studies

Laboratory tests employing aged mortar, which is treated with various concentrations or application rates of the test product and then exposed to challenge by *Serpula lacrymans* to determine the ability of the test fungus to grow over or through the treated substrate. One suitable method is described in ENV 12404:1997. See Appendix 1

Field Studies (see note)

Figure 4: *Masonry biocides intended for the control of dry rot*

Note

Field trials for dry rot control are difficult to establish because each outbreak is unique. Thus it is not possible to have "untreated controls". In treatments used to effect dry rot eradication, treatment requires major site works and the implementation of a "package" of measures which together effect control. It is therefore difficult to design a field test which conclusively demonstrates that a product is efficacious, given that the level of actual biological challenge it is required to resist will be altered so much by the associated works and will vary greatly from building to building. The provision of a suitable simulated use test (e.g. one conducted to CEN DD ENV 12404 or an equivalent) will normally be sufficient to give a good indication of field performance.

Available data

For products intended for the control of dry rot the test organism used will be *Serpula lacrymans*. Examples of the types of data that may be available when considering the efficacy of a masonry biocide intended for the control of dry rot fungi are shown in Figure 4.

APPENDIX 1

There are at present only two standardised test methods which are relevant to this area of pesticides efficacy evaluation.

1. British Standards Institution (1989). Methods of test for paints. Part G6. Assessment of resistance to fungal growth. British Standard BS 3900. Part G6, BSI, London, UK. [1]

2. Durability of wood and wood-based products - assessment of the effectiveness of a masonry fungicide to prevent growth into wood of dry rot *Serpula lacrymans* - Laboratory Method. ENV 12404:1997

[1] The BS test has been published but only provides a methodology for production of a test surface for exposure by inoculation with mould growth. Therefore this BS has to be modified to be used as a test method for assessing interior surface biocides.

PRODUCT TYPE 13 - METALWORKING FLUID PRESERVATIVES

1 INTRODUCTION

1.1 Spectrum of biological activity (including target organisms)

1.1.1 Biological activity

Metalworking fluids that contain water may be spoiled by both bacteria and/or fungi, including yeasts. Metalworking fluid preservatives must therefore be capable of adequately protecting metalworking fluids from microbial attack. This may mean total elimination and exclusion of micro-organisms from the metalworking fluid. Alternatively, and more realistically, this may mean preventing the numbers of micro-organisms in the metalworking fluid from reaching levels high enough to cause deleterious effects.

1.1.2 Target organisms

Micro-organisms that spoil metalworking fluids may be free living in the water phase, and metabolise compounds that migrate from the oil phase. In addition, biofilms may develop within a system. The open nature of systems employing metalworking fluids provides many opportunities for microbial contamination.

Oil-in-water emulsion metalworking fluids are normally alkaline (*ca*. pH 8-9), and as they are circulated and thus aerated, the initial microbial contamination is normally by aerobic Gram-negative bacteria such as *Pseudomonas* spp (e.g. *P. aeruginosa*), *Actinobacter* spp. and *Aerobacter* spp. However, Gram positive bacteria such as *Bacillus* spp., and even some fungi may also be present even at relatively high pH values. As the flora within a system increases, oxygen deficiencies occur. Eventually some areas in a system become sufficiently anaerobic to allow sulfate-reducing anaerobic bacteria to proliferate. Anaerobic conditions can be made worse by weekend or other more prolonged plant shutdowns.

Semi-synthetic formulations often contain glycols as a partial replacement for oil. These formulations have a tendency to be more prone to fungal rather than bacterial attack. Fungi that will proliferate under such conditions include common moulds and yeasts.

Changes in pH and temperature will influence the type of microbial flora that proliferates in a particular metalworking fluid. For example, bacterial contamination may lead to a fall in pH, which will allow a secondary fungal attack.

1.2 Areas of use and sites of application

Metalworking fluids are applied to metal being worked (cutting, grinding, rolling, drawing etc). Because of this, metalworking fluids are widely used throughout the engineering industry, and in large quantities.

In a typical machine tool set-up, metalworking fluid is held in a tank. When the machine is operating, the metalworking fluid is pumped via pipes to the tool, where it is applied. The precise way in which the metalworking fluid is applied varies, but common methods are continuous jet, spray or mist. The metalworking fluid then returns to the storage tank. Metalworking fluids may also be applied to tools by hand dispensers.

Wherever metalworking fluids are being used, metalworking fluid preservatives will be required to control microbial attack.

1.3 Methods of application

Preservatives used to protect metalworking fluids from microbial attack may be added to the concentrate by the manufacturer, or to the dilution at the tank side.

Levels of preservatives in the metalworking fluid must be kept sufficiently high in order to maintain efficacy against micro-organisms. Therefore it will be necessary to add additional preservative from time to time, to replace that 'used up' or lost.

1.4 Instructions for use

The instructions for use define the precise way in which the product is used and will typically include:

- Preparation of the formulation for use
- Dilution rate

2 AVAILABLE DATA

2.1 Introduction

Laboratory-based simulated-use tests may be limited in their ability to predict field use-levels of preservatives in metalworking fluids. This is because the many plant variables that will influence overall preservative efficacy cannot be fully reproduced in the laboratory. These plant variables include machine characteristics, the metal being worked, changing fluid characteristics during use, and the particular micro-organisms present. Laboratory tests can be used to rank preservatives, but this ranking will only be relevant to the conditions prevalent during the study. Therefore, the laboratory study of preservatives in metalworking fluids can only give an indication that a particular biocide or combination of biocides will have at least some activity against micro-organisms in the field.

Field or in-use tests may be capable of predicting field use levels, but the recommendations stemming from a particular study will only be relevant for the plant conditions tested, and cannot be reliably extrapolated to other field situations. However, positive results from a number of field studies will provide a good indication that the biocide will be efficacious in other situations.

2.2 Simple laboratory tests

Information regarding the innate toxicity of metalworking fluid preservatives against a wide range of target species can be derived from minimum inhibitory concentration (MIC) studies.

Data from simple laboratory tests alone will not be sufficient to successfully support an application for authorisation.

2.3 Laboratory-based simulated-use tests

Simulated-use tests conducted under laboratory conditions attempt, to a lesser or greater extent, to emulate conditions encountered by metalworking fluid preservatives when in service.

Whilst the precise details of the various available standard laboratory-based simulated-use tests vary, in general they all follow a similar pattern.

Metalworking fluid including preservative is placed in a vessel, and may be shaken on a mechanical shaker, or directly aerated, with humidified air if necessary. Alternatively, a pump can be employed to

maintain a recirculating flow of metalworking fluid that is allowed to fall back into the vessel under the influence of gravity. The shaker, aeration system or pump can be switched off in the evenings and/or at weekends to simulate plant shutdowns. The metalworking fluid may be maintained at ambient temperature, or heated to reflect normal operating conditions.

The metalworking fluid preservative is challenged by inoculation with a microbial culture at the start of test, and at intervals throughout the study period. The microbial culture may be derived from laboratory cultures, or from spoiled metalworking fluid collected in the field. The origins of all test micro-organisms should be stated.

Metal chips/filings/swarf etc may also be placed in the vessel containing the metalworking fluid.

The metalworking fluid may be monitored on a regular basis for changes in any or all of the following parameters:

- Visual appearance
- pH
- Oxygen uptake
- Presence, level and survival of micro-organisms (using standard sampling techniques)

Many multiples of the system described above can be operated at the same time, and for extended periods. Adequate untreated controls should always be included.

Full details of all tests methods should be available.

2.4 Field or in-use tests

In-use testing involves the antimicrobial evaluation of the product under actual conditions of use. Guidance concerning field testing of metalworking fluid preservatives is limited. However, some criteria may be considered:

- Data from field tests where the conditions provide severe challenges from harmful organisms may provide the strongest support for metalworking fluid preservatives.

- The tests should cover all pertinent factors associated with the intended use pattern(s).

- It may be difficult or impossible to run concurrent negative controls.

2.5 Standard test methods

Standard test methods have been produced by ASTM (US EPA and Canada) in North America. These standard test methods are listed in Appendix 1.

Whilst the use of standard test methods may be valuable for the assessment of the efficacy of metalworking fluid preservatives, use of these standards is not mandatory.

Competent authorities will consider testing strategies based on other national or international standard test methods, or, alternatively, non-standard test data, provided that they are both relevant and robust. It is relatively common for metalworking formulators to develop their own in-house efficacy test methods.

Other known test methods that may be used (following modification in some cases) for evaluation of the efficacy of metalworking fluid biocides are listed in Appendix 2.

APPENDIX 1

STANDARD PROTOCOLS FOR EFFICACY ASSESSMENT OF METALWORKING FLUID BIOCIDES (THIS LIST IS NOT EXHAUSTIVE)

Date	Title, organisation
1991	Standard test method for evaluation of antimicrobial agents in aqueous metal working fluids. ASTM, Philadelphia, USA.
1991	Standard test method for evaluation of antimicrobial agents as preservatives for invert emulsion and other water containing hydraulic fluids. ASTM, Philadelphia, USA.
1992	Anonymous, 1992. Standard test method for evaluating the bacteria resistance of water-dilutable metalworking fluids. ASTM, Philadelphia, USA.

APPENDIX 2

OTHER PROTOCOLS THAT MAY BE USED FOR THE EFFICACY ASSESSMENT OF METALWORKING FLUID BIOCIDES (THIS LIST IS NOT EXHAUSTIVE)

Date	Title, organisation
1987	Evaluation of the biostability of aqueous metalworking fluids. Renault test method No. D551721.
1987	A recirculating test rig for the investigation of metal-working fluid spoilage. In; Industrial microbiological testing. Rawlinson, A.P. and Shennan, J.L., 1987. Edited by Hopton, J.W. and Hill, E.C., 1987. Blackwell Scientific Publications, Oxford. ISBN 0 632 01793 7. pp227-231.
1987	South African standard specification for biocides for use in emulsions of aqueous metal working fluid and aqueous hydraulic fluid. The Council of the South African Bureau of Standards. SABS 1435-1987.
1990	Cutting fluid, soluble, biostable joint service designation ZX-9. UK MOD 91-70 issue.
1993	A standardized screening method for determining the bioresistance of and evaluating biocides in aqueous metalworking fluids. IBRG (draft MWF).

PRODUCT TYPE 14 – RODENTICIDES

1 INTRODUCTION

This technical annex provides background information regarding rodenticide use, and amplifies the nature and extent of data that should be available to support efficacy claims relating to these products.

2 USES OF RODENTICIDES

Rodenticides are used to control pest rodent species (commensal rodents). Rats (*Rattus* spp.) and house mice (*Mus* spp.) are major target organisms, but other rodents may also require control in certain regions. It should be noted that under certain situations, such as in forestry, or crop protection in the field, rodenticides would be subject to the Plant Protection Products Directive (91/414/EC) rather than the Biocidal Products Directive (98/8/EC).

3 THE NEED FOR RODENTICIDES

Pest rodent species require control because they cause monitory loss, and may also spread disease.

Monitory loss can occur through consumption and spoilage of foodstuffs and feedstuffs, and as a result of direct and indirect damage caused by gnawing. Burrowing activity can also cause important damage in certain situations.

Rodents can carry and transmit a substantial number of diseases of humans and animals. Many of these diseases are serious, and some are potentially fatal.

4 NATURE OF THE RODENT PROBLEM

There are approximately 2000 rodent species, but only a very small proportion of these are important pest species. The most common are *Rattus norvegicus* Berkenhout (brown, common, Norway, wharf or sewer rat), *Rattus rattus* L. (black, ship, house or roof rat) and *Mus* spp. (house mice), and they are found on a worldwide basis. *R. rattus* is less common that *R. norvegicus* across the EU, and is virtually absent from certain regions.

The systematics of the *Mus* spp. group is both complex and far from agreed. However, it is apparent that in the EU there are 2 subgroups present, which are *Mus musculus domesticus* ('Western' European house mouse found in Western Europe), and *Mus musculus musculus* ('Eastern' European house mouse found in Scandinavia). In addition *Mus spretus* (Lataste's mouse found in Southern France and Spain) and *Mus macedonius* (Eastern Mediterranean short-tailed mouse found in Greece) are also present.

It is worth noting that the rabbit is closely related to rodents, but is a lagomorph, and is not controlled using rodenticides.

5 SPECIES OF PEST TO BE SELECTED FOR TESTING, AND EXAMPLES OF ASSOCIATED RODENTICIDE LABEL CLAIMS

5.1 INTRODUCTION

The pests selected for efficacy testing should be appropriate to the geographic regions in which the product will be used. They should be named on the product label (either common or generic names may be used). For some examples of specific or broad label claims, please see Section 5.2.

A label claim such as 'FOR USE AS A RODENTICIDE' with no further clarification of the target species is not acceptable. This is because it would allow use against rodent species for which the product is not intended (and most likely has not been tested), such as *Sciurus carolinensis* (grey squirrel).

5.2 DATA REQUIREMENTS

FOR USE AGAINST MICE – this will only require testing against *Mus sp.**.

FOR USE AGAINST RATS – this will only require testing against *R. norvegicus*.

FOR USE AGAINST ROOF RATS – this will require testing against *R. rattus*.

FOR USE AGAINST RATS AND MICE – this will require testing against both *R. norvegicus* and *Mus sp.**.

FOR USE AGAINST RATS RESISTANT TO THE FIRST GENERATION ANTICOAGULANTS – this will require testing against warfarin resistant *R. norvegicus*.

* It is likely that data generated using either *M.m. musculus* or *M.m. domesticus* would be acceptable.

6 EFFICACY TESTING OF RODENTICIDES

6.1 INTRODUCTION

It should be noted that any efficacy testing conducted in the European Union on rodents should be in accordance with the Protection of Animals used for Experimental and other Scientific Purposes Directive (86/609/EC).

Although laboratory testing with wild rodents may be preferable, the difficulty and constraints associated with obtaining and maintaining them for testing purposes is recognised. Therefore for tests conducted within the laboratory, animals sourced from recognised commercially available strains are acceptable. Whilst laboratory strains are acceptable for use in the laboratory, the final stage of testing (semi-natural or 'field' trials) should be conducted using wild rodents.

Where wild animals are used in laboratory or semi-natural studies, these may be live trapped from the wild, reared in either outdoor colonies or under laboratory conditions such that it permits the animals to retain much of their natural physiological and behavioural characteristics. Breeding stock used for rearing wild rodents should not be selected for docile qualities or other characteristics that significantly alter their wild tendencies.

No-choice test (single cage), choice test (single cage) and a semi-natural field trial with non-poisonous alternative food (e.g. in special test rooms with a group of the target species) are always considered mandatory to fulfil the minimum efficacy testing requirement. Field tests, although desirable in cases where the product is intended for use in the more severe service environments (e.g. land fields) are not always considered mandatory.

The EPPO Rodent Control Panel (RCP, 1993. Recommendations of the EPPO Panel on Rodent Control (RCP) for the evaluation of rodenticides. Report to European and Mediterranean Plant Protection Organisation (EPPO)) has recommended that the intake of the contaminated food in the choice test should be at least 20% of the total food consumption and in the no-choice test 100% mortality should be required in order to show acceptable/sufficient efficacy.

6.2 LABORATORY TEST METHODS

6.2.1 Acute Oral Toxicity Test (active substance)

This can provide information on the potency of an active substance against target rodents of both sexes. This is derived from the dose-mortality relationship and is normally expressed as an LD_{50} (lethal dose required to kill 50 % of the target population) with 95 % Confidence Limits. Such estimates should be obtained by oral administration to rodents of a solution, or if necessary a suspension, of the active substance to be used in a product.

6.2.2 No Choice Test (product)

In a No Choice Test, the test organisms are offered only contaminated food. This study thus provides information on the potency of a product and demonstrates free feeding. It may also provide information on the bioavailability of the active substance. Finally, where claims are made concerning activity of a product against resistant populations, it can provide supporting evidence.

The duration of the test should be appropriate to the proposed method of use of the rodenticide. Data must be presented to show the daily intake of laboratory diet prior to the test and product during the treatment period, body weight of test animals (pre and post-test), symptoms of poisoning and days to death.

Where claims such as 'controls warfarin resistant populations' or 'controls rats and mice resistant to first generation anticoagulants' are being made, the test should be conducted on known resistant laboratory or wild-caught strains (the location where wild rodents were obtained should be stated). Resistance of rodent strains can be determined by blood clotting response (BCR) (EPPO, 1995) tests or by feeding studies developed by the World Health Organisation (WHO). As an alternative, 'field' trials of the product against known resistant populations may be conducted (see Section 6.3).

6.2.3 Choice Test (product)

In a Choice Test, the test organisms are offered contaminated food as well as uncontaminated food. This study thus provides information on the acceptability or palatability of the product in the presence of a competing alternative food. If conducted on both fresh and aged product it may provide information on the storage stability of the product. If taken to mortality (humane end-points) it may provide information on the potency of the product (and therefore negate the need for No Choice Tests).

In the study, the rodents are given a choice between the product and an untreated diet. The untreated diet should preferably consist of either the standard laboratory diet or EPA meal. Full details of the methods used should be provided and data should be presented to show the daily intake of both untreated diet and product, the palatability ratio (amount of product: amount of untreated diet) or product acceptance (amount of product eaten expressed as a percentage of total [product + untreated diet] consumption) for different sexes of rodent, any signs of poisoning and days to death, with appropriate statistical analysis.

6.2.4 Laboratory studies related to specific product types

6.2.4.1 Contact Rodenticides

In addition to providing an estimation of the oral potency of the product via an acute oral toxicity test, the additional information that should be available in order to demonstrate efficacy will include:-

i) Estimates of time to death from individually caged rodents exposed to the product for stated periods of time. Reference to EPPO Guidelines (EPPO, 1986) should be made.

ii) Evidence from the laboratory that the target rodents will pick up the required dose from the application method recommended.

6.2.4.2 Gassing Agents

The type of information that should be available in order to demonstrate efficacy will include estimates of the potency of the active substance and product by inhalation.

6.2.5 Laboratory studies related to specific efficacy claims regarding suitability for use in damp conditions (product)

Where it is claimed that a product is suitable for use in damp conditions, the following test should be conducted:

i) Prevention of mould growth of the product in damp and warm conditions.

or

ii) Retention of palatability against the target species using 'mouldy' product (if the product is not treated in such a way as to prevent mould growth).

iii) Prevention of germination of the test formulation in damp conditions (only relevant for baits containing grain that has the potential to germinate).

6.3 'FIELD' TRIAL/'FIELD' TRIAL UNDER SEMI-NATURAL CONDITIONS (product)

These studies may provide information on the performance of the product under either natural or semi-natural conditions.

Ideally, sites chosen for 'field' trials should be representative of the range of locations where the rodenticide is to be used, and should be infested with sufficient numbers of the target rodents so that the effectiveness of the product can be clearly demonstrated. It is advantageous if the rodent infestations on the sites chosen are, as far as possible, discrete and not subject to potential rapid re-invasion. Rodent activity on the site should be determined before and after treatments using at least two standard techniques. Sketch maps of the sites approximately to an indicated scale showing all the important features including signs of infestation and location of rodenticide application should be provided. Data should be presented to indicate levels of rodent activity both before and after treatment, amounts of bait consumed and all relevant information regarding treatment details.

Additional evidence of the efficacy of a rodenticide product may be obtained from trials against colonies of wild rodents housed within a semi-natural environment. Such colonies are likely to be family groups, as unrelated animals, particularly males, can be very aggressive towards each other. Studies of this kind may provide useful supporting information, in case incomplete control occurs in 'field' trials due to factors that could not be controlled.

7 AVAILABLE STANDARD TEST METHODS

There are many standard test methods currently available that may be appropriate for the assessment of the effectiveness of rodenticides. A list of such test standards is presented in Appendix 1 of this document.

In addition to the standard test methods presented in Appendix 1, specimen protocols for a No Choice Test and a Choice Test are presented in Appendices 2 and 3 respectively. Appendix 4 provides additional guidance on factors that should be taken into account and controlled when conducting field trials. These Appendicies are intended only to provide further information regarding the types of studies that may be utilised to assess the efficacy of some rodenticides, and some of the factors that should be taken into account.

APPENDIX 1

LIST OF CURRENTLY AVAILABLE STANDARD TEST METHODS FOR RODENTICIDES*

Standard	Title	Target Organism(s)	Mode of Application
EPA/OPP Protocol Number 1.201	Standard Norway Rat and Roof Rat Anticoagulant Liquid Bait Laboratory Test Method	Norway Rat/Roof Rat	Liquid bait
EPA/OPP Protocol Number 1.202	Standard House Mouse Anticoagulant Liquid Bait Laboratory Test Method	House Mouse	Liquid bait
EPA/OPP Protocol Number 1.203	Standard Norway Rat and Roof Rat Anticoagulant Dry Bait Laboratory Test Method	Norway Rat/Roof Rat	Dry Bait
EPA/OPP Protocol Number 1.204	Standard House Mouse Anticoagulant Dry Bait Laboratory Test Method	House Mouse	Dry Bait
EPA/OPP Protocol Number 1.205	Standard Norway Rat/Roof Rat Anticoagulant Tracking Powder Efficacy Laboratory Test Method	Norway Rat/Roof Rat	Tracking Powder
EPA/OPP Protocol Number 1.212	Standard House Mouse Anticoagulant Tracking Powder Efficacy Laboratory Test Method	House Mouse	Tracking Powder
EPA/OPP Protocol Number 1.213	Standard Norway Rat/Roof Rat Anticoagulant Wax Block and Wax Pellet Laboratory Test Method	Norway Rat/Roof Rat	Wax Block and Wax Pellet
EPA/OPP Protocol Number 1.214	Standard House Mouse Anticoagulant Wax Block and Wax Pellet Laboratory Test Method	House Mouse	Wax Block and Wax Pellet
EPA/OPP Protocol Number 1.217	Standard Norway Rat and Rood Rat Anticoagulant Placepack Laboratory Test Method	Norway Rat/Roof Rat	Placepack dry bait
EPA/OPP Protocol Number 1.218	Standard House Mouse Anticoagulant Placepack Penetration Laboratory Test Method	House Mouse	Placepack Penetration
EPA/OPP Protocol Number 1.221	Proposed Norway Rat Anticoagulant Technical and Concentrated Dry Bait Laboratory Test Method	Norway Rat	Technical and Concentrated Dry Bait
EPA/OPP Protocol Number 1.225	Proposed House Mouse Anticoagulant Technical and Concentrated Dry Bait Laboratory Test Method	House Mouse	Technical and Concentrated Dry Bait
EPA/OPP Protocol Number: 1.207	Standard Norway Rat/Roof Rat Acute Liquid Bait Laboratory test method	Norway Rat/Roof Rat	Liquid Bait
EPA/OPP Protocol Number: 1.208	Standard House Mouse Acute Liquid Bait Laboratory Method	House Mouse	Liquid Bait
EPA/OPP Protocol Number: 1.209	Standard Norway Rat/Roof Rat Acute Dry Bait Laboratory Test Method	Norway rat/Roof rat	Dry Bait
EPA/OPP Protocol Number: 1.210	Standard House Mouse Acute Dry Bait Laboratory Test Method	House Mouse	Dry Bait
EPA/OPP Protocol Number: 1.211	Standard Norway Rat/Roof Rat Acute Tracking Powder Efficacy Laboratory Test Method	Norway rat/Roof rat	Tracking Powder
EPA/OPP	Standard Norway rat/Roof rat Acute Placepack Penetration	Norway rat/Roof	Placepack

Protocol Number: 1.219	Laboratory Test Method	rat	penetration
EPA/OPP Protocol Number: 1.220	Standard House Mouse Acute Placepack Dry Bait Laboratory Test Method	House Mouse	Placepack dry Bait
EPA/OPP Protocol Number: 1.222	Proposed Norway Rat Acute Technical and Concentrated Dry Bait Laboratory Test Method	Norway rat	Technical and concentrated dry bait
EPA/OPP Protocol Number: 1.226	Proposed House Mouse Acute Technical and Concentrated Dry Bait Laboratory Method	House Mouse	Technical and concentrated dry bait
EPA/OPP Protocol Number: 1.227	Proposed House Mouse Acute tracking Powder Efficacy Laboratory Method	House Mouse	Tracking Powder
BBA 9 - 3.1	Richtlinie fur die prufung von Nagetierbekampfungsmitteln gegen Hausmause	-	-
BBA 9- 3.2	Richtlinie fur die prufung von Nagetierbekampfungsmitteln gegen Wanderratten	-	-
EPPO 1982	Guidelines for the Biological Evaluation of Rodenticides No1. Laboratory Tests for Evaluation of the Toxicity and Acceptability of Rodenticides and Rodenticide Preparations	-	-
EPPO 1982	Guidelines For the Biological Evaluation of Rodenticides. Field Tests Against Syanthropic Rodents (*Mus musculus, Rattus norvegicus, Rattus rattus*)	-	-
EPPO 1986	Guidelines for the Biological Evaluation of Rodenticides. Laboratory and Field Tests for the Evaluation of Rodenticidal Dusts	-	-
ASTM E 565-95	Standard Test Method for Efficacy of a Single-Dose Acute Rodenticide Under Laboratory Conditions for Commensal Rodents	Norway rat/Roof rat/ House mouse	Dry Bait
ASTM E 593-95	Standard Test Method for Efficacy of a Single-Dose Acute Rodenticide Under Laboratory Conditions	Norway rat/Roof rat/ House mouse	Dry Bait

* This list may not be exhaustive, and makes no comment on the suitability of particular test methods for efficacy testing.

APPENDIX 2

SPECIMEN PROTOCOL FOR A NO CHOICE TEST

To determine the potency of the product against the target species, a no-choice feeding study is conducted against laboratory rodents. The study consists of an acclimatisation period, followed by a pre-test diet take assessment, then a 1- (single dose rodenticide) or 4-day (multiple dose rodenticide) test period and at least 14 days of post-treatment observation.

A group of 10 (5 males and 5 females) healthy, adult rodents of known strain (STATE) are used in the study. Females should not be pregnant. All animals are weighed (for Norway rats and house mice minimum adult body weights should be 150g and 15 g respectively, at the start of the test) and individually caged. Ambient conditions should conform to those prescribed under current legislation controlling animal experiments. Tap water is freely available throughout the study period.

The animals are acclimatised to the test conditions for a minimum of 3 days prior to the no-choice feeding period. A feeding dish is placed centrally at the front in each cage and is filled with ground laboratory diet or EPA meal at the desired rate. All other food is removed. On the third day, a weighed amount of fresh diet is placed in the pot, the quantity to be in excess of the normal daily requirement. After 24 hours, the diet remaining is weighed and the amount eaten by each rat/mouse calculated. Inspection of the figures should confirm that all animals are eating normally from the food pots.

The quantity of product in each pot should be in excess of the rodent's normal daily requirements. Every 24 hours throughout the test period, any product spillage is collected and any extraneous matter such as faeces removed. Unconsumed product is then weighed, and the total amount eaten calculated by subtraction. If the test period is 1 day, the product is then removed and replaced with the normal laboratory diet for the duration of the observation period. If the test period is 4 days, used product is discarded and replaced with a fresh supply each day in a fresh pot. On the last day, uneaten product is replaced with the normal laboratory diet for the following observation period. Throughout the feeding period the rodents are observed at least twice daily. Daily takes are added up and the amount of active ingredient ingested is calculated.

During the observation period the rodents are observed at least twice daily and any toxic symptoms and mortality recorded.

For liquid bait formulations

The test shall be carried out as above with the following exceptions:

i) A suitable compounded laboratory diet shall be freely available

ii) Tap water shall be withdrawn during exposure to the rodenticide.

iii) All procedures relating to the laboratory diet and solid bait shall instead be applied to the tap water and liquid bait, as appropriate.

iv) Liquid baits shall be provided in containers with non-drip nozzles or suitable open pots.

v) A filled container shall be placed out of reach of the animals in order to check for weight loss due to evaporation.

APPENDIX 3

SPECIMEN PROTOCOL FOR A CHOICE TEST

A feeding test is conducted to determine the extent to which rodents will eat the product when they are given a free choice between that and their normal food. This type of palatability test is most suited to slow-acting toxicants. The test consists of an acclimatisation period, followed by a pre-test diet take assessment, then a 4-day test period and at least 14 days of post-treatment observation.

For the test, 20 wild or laboratory strain rodents (10 males and 10 females) are required. Laboratory rodents should be healthy, non-pregnant adults of known strain (STATE). Where wild adult rodents are used they should be healthy and obtained from free-living populations (STATE WHERE). On arrival at the laboratory, the wild strains should be treated with an appropriate insecticide to kill ectoparasites and then caged individually. With wild rats especially, it is advisable to place all items (i.e. food pots) required for the test in the cage before each animal is released into it. Wild rodents should be acclimatised to laboratory conditions for at least 3 weeks to ensure that no females are pregnant when the test begins. During this time they should be offered a laboratory animal diet and water should be freely available. To encourage variation in response, animals with body weights throughout the range normally expected for the species should be used as far as possible.

Before the test period begins, it is necessary to ensure that the animals are feeding normally. Following acclimatisation, 2 food pots placed either side at the front of the cage are filled with ground laboratory diet or EPA meal. All other food is removed, but water remains freely available. The quantity of food placed in each pot (STATE) should be sufficient to meet each animal's daily needs. All used diet should be discarded and the pot refilled with a fresh supply. This procedure should be repeated for a further 3 days and on the last day the animals should be weighed. Also on the last day, the diet remaining in each pot is weighed and the total amount of food eaten by each rodent calculated (STATE). Any rodent not eating normally by the last day should be discarded. The palatability test commences with 2 clean pots, one filled with a quantity of the test product and the other with a suitable challenge diet (e.g. EPA meal or standard laboratory chow). Again, the quantity in each pot should exceed the normal daily requirement for each animal. After 24 hours, the diet remaining in each pot is weighed and the total amount of food eaten by each rodent calculated. All used test and challenge diet is discarded and fresh quantities of each diet are placed in clean pots. In placing the pots back in the cage, the positions of the rodenticide and the challenge diet should be interchanged to avoid place preference. This procedure should be repeated for a further 3 days. After day 4 the animals should be returned to the standard laboratory diet.

During the observation period the rodents are observed at least twice daily and any toxic symptoms and mortality recorded.

Liquid bait formulations

The test shall be carried out as above with the following exceptions:

i) A suitable compounded laboratory diet shall be freely available.

ii) Tap water shall be used as the control bait.

iii) All procedures relating to the solid control and test baits shall be applied instead and as appropriate to the liquid control and test baits.

iv) When the positions of the test and control baits are interchanged the positions of the drinking tubes, if used, should not be interchanged.

v) Liquid baits shall be provided in containers with non-drip nozzles or suitable open pots.

vi) A filled container shall be placed out of reach of the animals in order to monitor weight loss due to evaporation.

APPENDIX 4

GUIDANCE ON FACTORS TO BE TAKEN INTO ACCOUNT AND CONTROLLED WHEN CONDUCTING FIELD TRIALS

Ideally field trials should:-

i) Be conducted with separate rat and mice populations (as appropriate to label claims).

ii) Be carried out at sites that are representative of label claims (industrial, commercial, domestic).

iii) Include sites with 'known' anticoagulant resistant populations (of appropriate to label claims).

iv) Have no rodenticide treatments currently in progress.

v) Incorporate lag phases before and after the treatment phase.

vi) For testing concentrates, cover a range of bait bases.

vii) When a product is sold with a specific bait station then the whole formulation (the bait and its station) must be tested.

The following suggested method for bait formulations details the extent of the data required, but the methods may be replaced or supplemented by new techniques as appropriate.

Suggested procedure for bait formulations:

Trial sites

Each trial site should, as far as possible, comprise a discrete infestation of one target species, with little chance of rapid reinvasion from adjoining areas.

Before the trial begins, draw a sketch map showing all significant features of the site including signs of infestation.

Data on field efficacy is likely to be more reliable if infestations of Norway rats and House mice are selected on the basis that a stable level of activity is obtained during the pre-treatment assessment. The level of activity can be determined by two of the following (as appropriate to the situation, species etc.):-

i) Census baiting

ii) Tracking techniques

iii) Census trapping.

Pre-treatment activity measurement/estimation of numbers

Indices of the target species population should be obtained both before and after the test treatment normally by at least 2 of the following:

<u>Pre-treatment bait census</u>

The position of the census bait points should be indicated on the site sketch plan. Census bait should be laid for at least 4 days to cover the whole infestation in quantities at each bait point which as far as possible exceed the maximum daily take by rodents. The number of census baits should be

approximately the same as the planned number of test bait points. Census points should not be located at the same place chosen to lay poison points but should be at different (intermediate) positions. Census bait should be different to the bait base used in the test product.

The number of points where take has occurred and the take of the census bait should be recorded daily and an indication of the change in weight of the bait due to moisture loss or uptake should be included.

At the end of the bait census all baits and containers should be removed from the trial site. The total amount of census bait consumed will give an index of population size.

Tracking activity measurement

This is recommended for rats only, and should be measured over at least 3 days, simultaneously with the bait census, using tracking patches/boards laid around the site in numbers similar to the census bait points but as far as possible, not in the same locations. The locations of the patches/boards should be indicated on the plan.

The patches/boards should be inspected for signs of activity and resurfaced daily. A simple scoring system can be devised to assess the number of rodent footprints per patch/board: summing the individual scores gives a daily activity index. When the pre-treatment assessment is complete, the tracking patches/boards may be removed from the site or maintained to provide supplementary information on rodent activity.

Census by trapping

This is recommended for mice only, and should be carried out for a period of at least 3 days using rodenticide-free bait in the traps. Traps should be laid around the site in numbers appropriate to the situation and likely population size.

Animals caught should be marked by fur clipping and subsequently released. The numbers caught should be recorded and used to estimate the size of the population.

The traps should then be removed from the test site during the rodenticide treatment.

Lag period

Once the pre-treatment population measurement has been conducted there should be a lag period, normally 3-14 days (or longer for acute poisons where no pre-baiting is recommended) with no experimental interference (other than tracking) on the site.

Test treatment

The test formulation must be applied in accordance with the label or proposed label, for an appropriate period. The locations of test bait points should, as far as possible, be different from those of the census bait points, traps, and tracking patches/boards.

Where applicable the following items should be recorded:

i) The locations of the bait points on the plan.

ii) The amount of bait deposited at each point at each visit and the amount retrieved, including details of the type of container used.

iii) The number and species of rodents and other animals found dead, and the dates on which they were found.

iv) The dates of all observations, treatments and censuses.

v) Any other information deemed relevant. This may include, for example weather conditions, temperature data, site changes instituted by the occupier (including improvements in hygiene and proofing), or supplementary information on rodent tracking activity.

On termination of the treatment all poisoned baits and bait containers should be removed from the trial sites. Similarly rodent bodies should be searched for, removed and disposed of in the appropriate way e.g. burial or burning.

Post-treatment lag period

On completion of the treatment there should be a lag period sufficient to allow poisoned animals to die or survivors to recover from the sub-lethal effects of the rodenticide. This period may be 3-14 days, depending on previous observations of time to death or full recovery. During this period there should be no experimental interference with the site other than tracking.

Post-treatment activity measurement/estimation of numbers

Once the post-treatment lag period is completed, the methods employed to measure pre-treatment activity should be conducted in exactly the same way. Traps, baits and tracking patches should be laid in exactly the same places as in the pre-treatment census.

After each field trial, a comparison of population indices before and after treatment determines how successful the product has been in controlling the target population. The degree of control is expressed as a percentage reduction in the pre-treatment index.

PRODUCT TYPE 15 - AVICIDES

1 LABEL CLAIMS

1.1 Spectrum of biological activity (including target organism)

Bird populations inhabiting urban areas are on the increase, which is perhaps reason to admire the successful adaptation of these wild animals to new and strange environments. However this increased adaptability of birds to the urban environment brings with it many concerns such as the spread of disease e.g. ornithosis; the hazards of collisions with aircraft and ingestion by jet engines; building degradation sue to erosion by acidic faecal deposits; the general unsightliness of droppings; the noise created by birds and the increasingly aggressive behaviour of gulls habituated to people as a food source. Avicides attempt to control bird populations and thus decrease the likelihood of danger to human health, danger to human safety and damage to buildings.

Management of bird species in the E.U. is controlled under the Council Directive of 2 April 1979 on the conservation of wild birds (79/409/EEC). This Directive relates to the conservation and protection of all species of naturally occurring wild birds, their nests and eggs, within the European territory. Examples of some of the bird pests common to the E.U market, together with their common and generic names are shown in Figure 1.

1.2 Mode of action/effect

Avicides are generally either slow acting and reversible or fast acting. The mode of action of avicides will depend on the chemical used. Many avicides may be repellent in nature or may act on the fertility of the pest bird. The available data should give brief details to indicate the route of exposure (e.g. oral, contact or inhalation) and the nature of the effect (e.g. stupeyfying, toxicant, chemosterilant, repellent).

1.3 Areas of use and sites of application

A limited number of biocidal products are currently available in the E.U. for the control of birds. The limited number is mainly due to legislation prohibiting or limiting the use of various control methods, including biocides. This legislation is in place, in part, to protect non-target wildlife from accidental poisoning and to protect public health.

Products may be used both indoors such as in factories, farm buildings or outdoors in a variety of situations such as on rooftops, at airports, in courtyards or other areas where pest birds may be nesting, roosting or feeding.

There would usually be a period of pre-baiting to ensure that the birds are feeding in the area and to reduce any problems of bait aversion. The bait base may also be coloured by a dye so that it can be easily recovered at the end of the treatment.

The label claim should clearly indicate the use pattern for the candidate product so that the competent authority has a clear understanding of the type of chemical control that the product is intended to obtain. This will normally depend upon the mode of action of the chemical and how the product is to be applied or the treatment effected. These factors will affect timing frequency and doses used.

UK COMMON NAME	SPECIES NAME
Great Black-backed Gull	Larus marinus
Lesser Black-backed Gull	Larus fuscus
Herring Gull	Larus argentatus
Common gull	Larus carnus
Black headed gull	Larus ridibundus
Crow	Corvus corone
Rook	Corvus frugilegus

Jackdaw	Corvus monedula
Jay	Garrulus glandarius
Magpie	Pica pica
Starling	Sturnus vulgaris
Collared Dove	Streptopelia decaocto
Feral Pigeon	Columba livia
Wood pigeon	Columba palumbus
House Sparrow	Passer domesticus
Canada goose	Branta canadensis
Brent goose	Branta bernicla
N.B. These examples are not intended to be exhaustive with respect to target organisms or prescriptive with respect to data generation. Care should be taken in the choice of target organism(s) with all due consideration given to local laws and regulations. Genus of species will vary across member states	

Figure 1. *Examples of target organisms for bird control product*

NOTE: The legislation in place in each Member State relating to the control of birds must be consulted carefully before any control methods are carried out or recommended. Biocidal modes of action may be restricted by local law. Claims made must be specific to the species which can be taken, when they can be taken (time of year/day and also in what situations) and in which geographical area.

Under the Directive birds may be controlled:

1) *In the interests of public health and safety*; in the interests of air safety, to prevent serious damage to crops, livestock, forests, fisheries and water, for the protection of flora and fauna

2) *For the purposes of research and teaching, of re-population, of re-introduction and for the breeding necessary for these purposes*

3) *To permit, under strictly supervised conditions and on a selective basis, the capture, keeping or other judicious use of certain birds in small numbers.*

The Directive prohibits the killing of birds by large scale or non-selective measures, including poisoned or anaesthetic bait, although licences can be obtained in special circumstances.

Biocide formulations and common areas of use for these products may include, but are not limited to; admixture with a known food source, ready prepared grain/seed baits, liquids, gels, perch treatments, repellents or other contact formulations. For the purpose of these guidelines some illustrative descriptors of the common use patterns are provided below.

1) Stupeyfying baits

A suitable bait base, generally based on typical feed of the resident pest bird population, is treated with the stupeyfying agent. Often it will be necessary to lay untreated bait for several days before the operation to ensure the success of the treatment. This period of pre-baiting may be necessary to ensure that local birds will feed from a particular area and subsequently increase the likelihood of sufficient bait take during the treatment period. On taking the treated bait the birds become stupefied and then may be taken and dispatched humanely. The use of this type of treatment may prevent the unintentional poisoning of non-target species.

2) *Toxic baits*

Use of these chemicals is often restricted by legislation but may be used in some Member States for particular situations. As with the stupeyfying baits these are generally based on a suitable feedstuff for the target population. Toxic baits may be slow acting, so that the birds do not associate feeding with symptomatic responses, therefore alarming other birds and preventing them from feeding. Slow acting

toxicants also mean that large bird kills in surrounding areas soon after a treatment are unlikely to occur. Toxicants may also be fast acting resulting in a treated area becoming strewn with dead birds shortly following pesticide application. These would be removed by the operator who would be present on site. The fast acting toxicants would almost certainly require a period of pre-baiting.

3) *Perch treatments*
This method comprises an "out of reach" perch with a toxicant incorporated onto the perch station, generally used for the treatment of starlings, pigeons and sparrows. These act by contact with the toxicant being absorbed through the feet of the perching birds. This type of treatment may reduce the risk of exposure to non-target non-bird species.

4) *Repellents*
Please refer to the Technical Guidance Document for Product Type 19: Repellents and Attractants

This type of control method is mostly applied in agricultural situations for the protection of plants and plant products, but may also be used in certain public hygiene situations. Chemical repellents may be successful in some situations but are unlikely to impart great success where there is high bird pressure. Use of repellents may also exacerbate problems by shifting a pest population from one area to another equally unsuitable situation. To be successful repellents must exert their effect even when no alternative food is available, they should persist for a reasonable length of time and should not be harmful to birds, mammals or plants. Frightening agents may also be used as repellents. These may be lethal if sufficient is eaten, but aim to work by causing distress in certain individuals who have eaten the bait, who in turn frighten other birds through their distress calls.

5) *Chemosterilants*
These chemicals are designed to control a pest bird population rather than eradicate it. These agents cause sterility amongst birds, often by inhibiting egg production. These are mainly used in the control of pigeons. Again it is normally presented on a grain base, which can be used to target the application by making the grains too large, in the case of pigeons, resulting in no other species being able to feed on it.

1.4 Other information relevant to the label claim

Other parameters that should be taken into consideration when evaluating a label claim for an avicide product are the instructions for use. These define the way in which the product is used and will typically include:

- Preparation of the formulation for use
- Application method/technique
- Application rate/dose rate/treatment frequency
- Guidance on pre-baiting
- Any restrictions on use

2 AVAILABLE DATA

2.1 STANDARD TEST METHODS

Few international standard test methods currently exist for bird control products. A list of these is presented in Appendix 1 to this document.

Competent authorities should take this into consideration when evaluating a data package they should recognise that performance of studies to such standards is not mandatory and will not often be possible. Alternative testing strategies and non-standard test data should be considered on their own merits.

Data should be available in respect of the test formulation relevant to the product for which authorisation is being sought and should use the most relevant application process against the target organism specified on the label. Where a product is to be presented with a food source (such as grain) then a typical bait base for each bird species should be chosen for data generation.

All study conditions must conform to those prescribed under any current applicable legislation controlling animal experiments for both laboratory and field studies in the country in which the work has been carried out.

2.2 Specific data to support label claims

In assessing the effectiveness of an avicidal product competent authorities should in particular take the following parameters into account:

- Target organism(s)
- Mode of action/effect
- How the product will be presented
- Use patterns
- Application rates

The data provided in support of the efficacy claims must be sufficient to cover these key parameters.

2.2.1 Examples of specific label claims with respect to target organisms

For specific target pests where efficacy against only one genus is claimed, data against only a limited number of pest species will normally be required. To illustrate this point, a number of examples are given below:

FOR USE AGAINST HOUSE (ENGLISH) SPARROWS - Data against *Passer domesticus* should normally be available.

FOR USE AGAINST FERAL PIGEONS - Data against *Columba livia* should normally be available.

2.2.2 Example of a more general label claim with respect to target organisms

General label claims, such as “avicide”, should be accompanied by qualification of the range of pests against which the product may be used. When general claims are made, data on representative pest species will need to be provided for the range of pest genera against which efficacy is claimed. As stipulated throughout this guidance due consideration should be given to Directive 79/409/EEC and any local legislation in place to protect particular bird species and control of birds in general.

2.3 General considerations

Available data submitted in support of applications for authorisation of an avicidal product may be generated through laboratory and/or field trials.

The attributes of a formulation that contribute to its efficacy are, primarily, its toxicity, its ability to stupefy the target or repel it and any taint/alarming effects of a concentrate when applied to a bait base.

Laboratory studies are generally LD_{50} or acceptance studies. Laboratory strains of the target species are generally acceptable. The origins of all test animals should be stated. Acceptance data should be conducted on caged juveniles as well as both sexes of each species.

In all laboratory studies adequate untreated controls should be included. Full details of all test methods should be available.

Results from laboratory studies on the efficacy of the product must be available when applying for inclusion a new active substance or a change in concentration, formulation or method of application of an active substance already listed.

The ultimate test of efficacy is however an assessment of how the product will perform in actual field conditions. Under these conditions additional factors come into play, notably the occurrence of alternative food sources and the various pressures associated with this. Field trials of representative formulations and appropriate methods of application are therefore necessary to validate label claims as to efficacy, particularly where the composition of the formulation or the method of application departs from the norm.

Results of field trials to demonstrate efficacy of all new active substances against representative pest populations of each target species must be available. Field tests may also be required for major new formulations or different application methods and/or presentation of the avicide.

3 CONCLUDING COMMENTS

These guidelines are designed to be flexible and are intended to provide advice as to the nature and type of efficacy data required to support the approval of active ingredients for use in avicides. They do not set out a protocol verbatim nor do they specify rigid protocols to which tests must be conducted in the process of producing efficacy data. It is recognised that their is a limited range of products and intended uses, however each study presented will be evaluated on its own merits. However, Applicants are encouraged to submit data performed to a sound scientific standard using their own testing strategies or studies conducted to nationally or internationally recognised efficacy methods.

4 APPENDIX 1

Standard Reference	Title
ASTM E 551-95	Standard Test Methods for Developing Effective Bird Control Chemicals
ASTM E 554-95	Standard Guide for and Development of Strychnine as an Avicide
ASTM E 589-95	Standard Guide for the use and Development of PA-14 Avian Stressing Agent
ASTM E 657-95	Standard Test Method for Comparative Acute and Long-term Oral or Gustatory Avian Repellency
EPA 96-5	Avian Toxicants
EPA 96-7	Avian Frightening Agents

PRODUCT TYPE 18 - INSECTICIDES, ACARICIDES AND PRODUCTS TO CONTROL OTHER ARTHROPODS

1 LABEL CLAIMS

1.1 Spectrum of biological activity (including target organisms)

It will not always be necessary to include on the product label the entire range of pests against which an insecticide/acaricide product is intended to be used. It is recognised that efficacy claims for such products may often be very specific in nature with respect to target organisms or alternatively they can also be very broad.

In the case of very broad label claims it will not be appropriate or realistic to include the entire range of target organisms to which the product will be exposed to in practice, instead principal pest organisms representative of the biological challenge should be identified.

The pests selected for efficacy testing should be appropriate to the proposed product label claims for use in the territory in which the product is to be placed on the market. When broad claims are made, tests on representative pest species need to be provided for the range of **pest orders** on the label.

Examples of some of the pest orders common to the EU market, together with the common or generic names by which these orders are known are shown in Figure 1. **This list is not intended to be exhaustive with respect to target organisms and claims, nor prescriptive with respect to data generation.**

1.2 Mode of action/effect

There are a variety of modes of action and possible effects on target organisms derived from the proposed use of an insecticide/acaricide product. The available data should give brief details to indicate the route and nature of the action (e.g. whether action is by contact or stomach poison), and the nature of the effect (e.g. cholinesterase inhibitor, chitin synthesis inhibition, juvenile hormone analogue giving rise to sexually immature adults or supernumerary nymphs).

Additionally the available data should indicate what effect application of the product is expected to achieve. Examples could include:

- knockdown;
- kill;
- residual activity;
- flushing activity;
- ovicidal, larvicidal or other developmental effects; and
- ability to control strains of pests exhibiting resistance to other insecticide/acaricide products.

Insect orders	
Thysanura	Silverfish and other bristletails
Dermaptera	Earwigs
Dictyoptera	Cockroaches
Pscoptera	Booklice
Hemiptera	True bug
Lepidoptera	Moths
Siphonaptera	Fleas
Coleoptera	Beetles
Hymenoptera	Wasps and ants
(Formicoid hymenoptera)	(Ants)
Diptera	True flies
Arachnid orders	
Araneae	Spiders
Ixodida	Ticks
Astigmata	}
Prostigmata	}Mites
Gamasida	}
Other Orders	
Isopoda	Woodlice
Myriapoda	Centipedes and millipedes
N.B. These examples are not intended to be exhaustive with respect to target organisms or prescriptive with respect to data generation	

Figure 1: *Examples of target organisms for insecticide/acaricide products.*

1.3 Areas of use and sites of application

A wide variety of biocidal products are used for the control of a large range of invertebrate pests such as insects, mites and arthropods. They are applied by many different methods in numerous kinds of formulations. Products are used in public health programmes, households and industry in a variety of different environments both indoors and out of doors. Indoor use for example includes domestic or residential premises, industrial and commercial buildings such as hotels, restaurants and other food preparing and handling establishments, hospitals and schools. Outdoor use includes in/around dustbins, refuse tips, sewage treatment works and animal houses/rearing units.

The label claim should clearly indicate the use pattern for the candidate product so that the competent authority has a clear understanding of the type of chemical control that the product is intended to obtain. This will normally depend upon the mode of action of the chemical and how the product is to be applied or the treatment effected. These factors will affect timing, frequency and dosages used.

Biocide formulations used for the treatment of premises include, but are not limited to, liquid or pressurised products for spray treatments and pastes, powders and granules for bait formulations. Additionally use may often be made of impregnated materials (e.g. insecticidal strips for fly control). The most common areas of use for these products fall into the following list of categories (N.B. biocidal products for control of invertebrate pests may often incorporate treatments using one or more of these use patterns. **The list is not exhaustive**):

- General surface treatments
- Contact (direct) spray treatments
- Crack and crevice treatments
- Space treatments
- Spot treatments
- Baits

For the purpose of these guidelines some illustrative descriptors of these common use patterns are provided below.

1) General surface treatments
These products are applied to broad expanses of surfaces such as walls, floors and ceilings or as an outside treatment to surfaces. This will normally include those products used for the control of pests on surfaces by biocidal treatments applied directly to the surfaces.

Evaluation of products designed to be applied as surface treatments must be considered against the proposed label claims and the claimed effects (e.g. non-residual or residual).

Examples include coarse sprays (including pressurised packs), dusts, lacquers, liquid water sprays or granular formulations applied as larvicides to permanent or temporary water bodies (e.g. for the control of mosquito or blackfly larvae) or to solid and semi-solid manure (e.g for the control of flies or beetles in animal houses/rearing units).

2) Crack and crevice treatments
This refers to the application of small amounts of biocidal product into cracks and crevices where insects hide or through which they may enter the building. Such openings commonly occur at expansion joints, between different elements of construction and between equipment and floors. These openings may lead to voids such as hollow walls, equipment legs and bases, conduits and junction or switch boxes.

3) Contact (direct) spray treatments
Application directly onto insects is only likely to be possible when the insects are **visible** and **available** to a spray, and in practice this generally restricts direct application methods to controlling flying insects such as adult moths and houseflies. However, limited control of minor infestations of crawling insects such as ants or beetles may be possible in some situations.

4) Space treatments
The control of flying insects can be achieved using non-residual space treatments with products dispersed in the atmosphere, e.g. fogs, mists, aerosols (including pressurised packs), vapourisers, smokes, etc., where small insecticide particles are applied into the air when insects are present. The very small particles (generally less than 80 µm volume medium diameter) will stay in the air for several hours in still conditions - but exposed insects should be contacted very quickly. Insecticide active substances which have some residuality in structural sprays are unlikely to demonstrate a residual effect when applied as a space treatment, due to the relatively low dosages applied with the latter.

5) Spot treatments
These are products applied to limited areas on which insect pests are likely to occur, but which will not be in contact with food or utensils and will not ordinarily be contacted by workers. These areas may occur on floors, walls and bases or undersides of equipment. For this purpose a "spot" will not normally exceed an area of 0.19 m^2.

6) Baits
Bait products are intended for the control of pests by attracting them to a point where they will pick up the biocidal product by feeding or contact. These products usually utilise a palatable food base and sometimes incorporate an attractant (e.g. a pheromone) which may draw the pest to the bait over some distance.

1.4 Other information relevant to the label claim

Other parameters that should be taken into consideration when considering the evaluation of a label claim for an insecticide/acaricide product are the instructions for use. These define the way in which the product is used and will typically include:

- Preparation of the formulation for use
- Application method/technique
- Application rate/dose rate/treatment frequency
- Other information pertinent to efficacy e.g. the contribution made by other components of Integrated Pest Management procedures where these are essential to achieve control.

An example of *some* of the typical label claims (**not exhaustive**) which can be made for biocidal products intended for use as public hygiene insecticides/acaricides and control of other arthropods is shown in Figure 2.

2 AVAILABLE DATA

2.1 Standard test methods

Item 52 of Annex VI of Directive 98/8/EC states that testing should be carried out according to Community guidelines if these are available and applicable. Where appropriate, other methods can be used as shown in the list below. If relevant acceptable field data exist, these can be used.

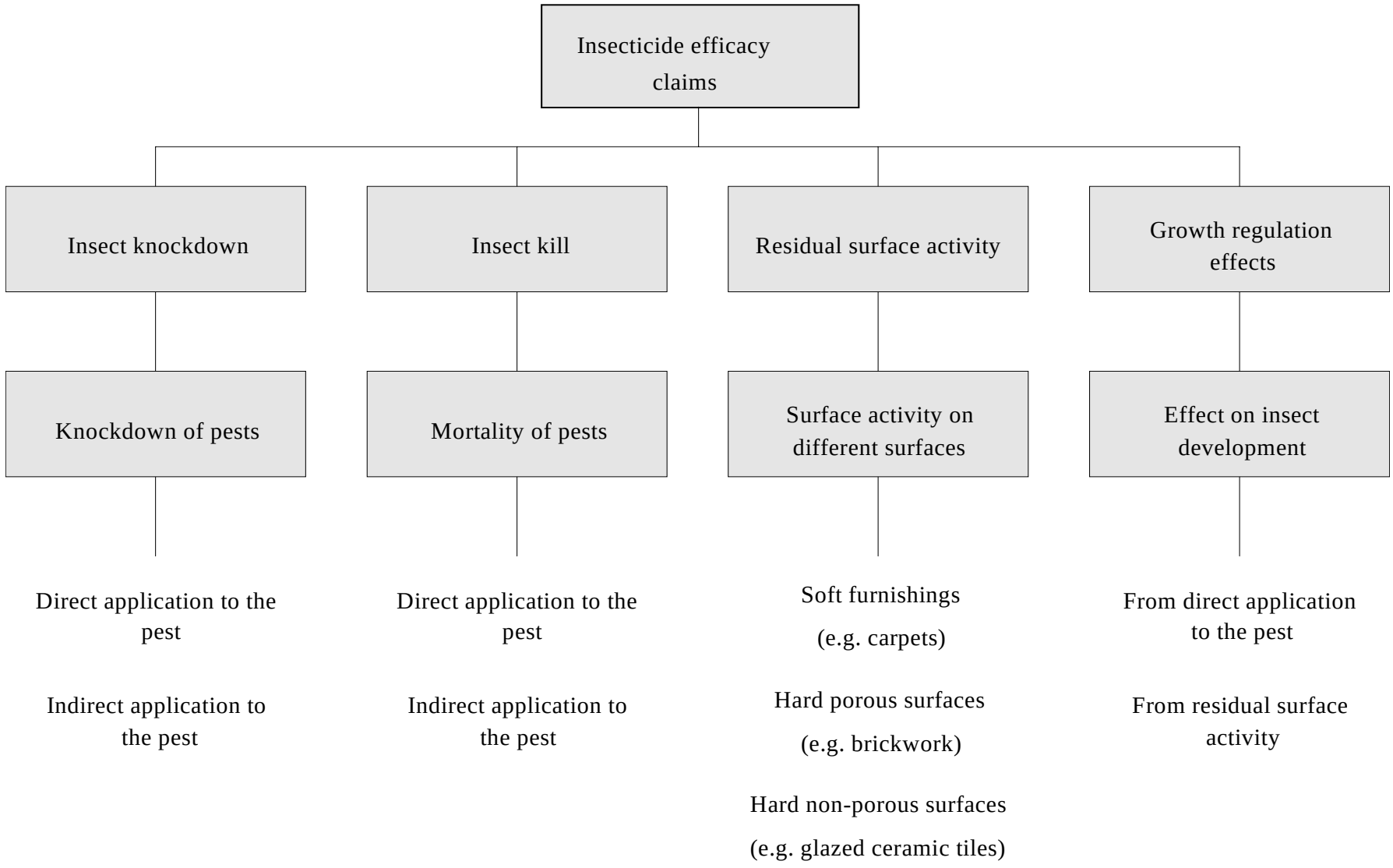
- ISO, CEN or other international standard method
- national standard method
- industry standard method (accepted by Member State)
- individual producer standard method (accepted by Member State)
- data from the actual development of the biocidal product (accepted by Member State).

Few international standard test methods currently exist for insecticide/acaricide products. A list of these is presented in Appendix 1 to this document.

Competent authorities should take this into consideration when evaluating a data package they should recognise that performance of studies to such standards is not mandatory and will not often be possible. Alternative testing strategies and non-standard test data should be considered on their merits.

Data should be available in respect of test formulations relevant to the product for which authorisation is being sought and should use the most relevant application process against the target organisms specified on the label.

Figure 2: *Examples of possible efficacy claims for insecticide/acaricide products: a breakdown of the information which may be required by the generation and assessment of data*



2.2 Specific data to support label claims

In assessing the effectiveness of an insecticide/acaricide product competent authorities should in particular take the following parameters into account

- Target organisms/spectrum of activity
- Mode of action/effect
- Use patterns/methods of application
- Dose rate

The data provided in support of the efficacy claims must be sufficient to cover these key parameters.

2.2.1 Examples of specific label claims with respect to target organisms

For specific target pests where only efficacy against one insect/arachnid order or a certain family within that order is claimed, data against only a limited number of pest species will normally be required. To illustrate this point, a number of examples are given below:

FOR USE AGAINST DUST MITES - Data against *Dermatophagoides sp*. should normally be available.

FOR USE AGAINST FLEAS - Data against the cat flea (*Ctenocephalides felis*) or the dog flea (*C. canis*) should normally be available.

FOR USE AGAINST COCKROACHES - Data against two key species such as German cockroach (*Blattella germanica*) and the oriental cockroach (*Blatta orientalis*) should normally be available.

2.2.2 Examples of broad label claims with respect to target organisms

Broad label claims, such as "*crawling insect killer*" or "*flying insect killer*", should be accompanied by qualification of the range of pests against which the product may be used. When broad claims are made, data on representative pest species will need to be provided for the range of pest orders against which efficacy is claimed.

Representative pests from these orders will have to be appropriate to the use pattern of the biocidal product i.e. the environment of the areas to which the biocide is to be applied and the nature of the application (e.g. whether it is a space application or surface application) will define the most appropriate pests to be tested.

For each order stated, at least the principal target species will need to be tested for public hygiene use, before a general claim is likely to be supported. In more specific areas, such as use against stored product pests, data on at least two major representatives of the orders in question will normally be needed before a general claim is likely to be supported. Where such a claim covers a diverse range of pest habitats and pest morphology and biology, data from a greater number of representative species will need to be provided.

2.2.3 The distinction between principal target and secondary/incidental target pests

When a broad claim is made for a product, it may be possible to define the pests within the target range as principal target pests and secondary/incidental target pests.

For example:

A general insecticide/acaricide spray claim for use against ants, fleas, cockroaches, silverfish, earwigs and spiders.

The applicant may consider that the principal target pests are ants, fleas and cockroaches but that the end user of the product may occasionally wish to use it against other pests under the same treatment parameters and use patterns. Therefore, silverfish, earwigs and spiders may be considered by the

applicant as secondary/incidental target pests which they wish to claim the product may be used on the product label.

In such situations where there is a clear distinction between two target groups on a label the secondary/incidental pests may only require relatively simple but appropriate laboratory-based efficacy testing, to supplement the more extensive studies conducted on the principal target pests.

The competent authority will not impose such distinctions. The responsibility for deciding whether principal and secondary/incidental targets exist within the claims made for the product rests with the applicant. The opportunity to use such discretion does not mean that applicants may use such arguments to avoid thorough efficacy testing against those public hygiene pests considered to be of significant importance e.g. cockroaches.

Occasionally there may be an application for the broadening of an **existing** label claim for an product already authorised for use in a territory. In these cases the competent authority will make a decision considering largely the extent of data submitted and the relevance of the representative target organisms selected (with respect to morphology, biology and behaviour, as appropriate) to the proposed further use of the candidate product.

The degree to which a product application is supported is likely to depend on the nature and extent of data presented in the efficacy data package provided in support of the label claims for the product.

2.3 Mode of action/effect

A variety of molecules exist which control invertebrate pests by preventing successful completion of the insect's life cycle rather than being acutely toxic to the insect. Examples of such biorational molecules include chitin synthesis inhibitors and juvenile hormones. The chitin synthesis inhibitors act by disrupting the deposition of chitin during the formation of the insects larval cuticle after moult, whereas juvenile hormones (and their analogues) aim to interfere with the hormone based control of metamorphosis and reproduction. These two types of biorational molecules are often referred to as insect growth regulators to distinguish them from conventional insecticides with neurotoxic action.

Consequently molecules that affect the developmental cycle of insects may be effective without resulting in the immediate death of the insect and therefore efficacy trials should be designed to address the most appropriate life cycle stage of the insect sensitive to the molecule of interest and also to measure any long term effects (e.g on the fertility and fecundity of females or any effects on the embryonal development in the egg stage).

For example, in measuring the effectiveness of juvenile hormone analogues, trials should be designed to record the number of adults produced from treated nymphs, the number of adults with deformed wings or terminalia and the mortality of insects prior to and at metamorphosis. Additionally a number of newly moulted females should be selected randomly from each treatment dose/formulation and their ability to produce viable oothecae after pairing with untreated males should be recorded.

2.3.1 Claims for residual efficacy

Most insect pests are cryptic and/or nocturnal in behaviour and are unlikely to be contacted directly by a space spray. For this reason the majority of control programmes involve the use of relatively stable active substances applied to buildings and other surfaces at higher dosages. These compounds are intended to remain chemically active and therefore effective for periods of weeks up to several months following treatment, i.e. they have a high residuality. Such treatments are best applied to areas most frequently used by walking insects (e.g. wall/floor margins). Residual life is a term to describe the period during which the insecticide will be present in sufficient quantity to kill insects which walk upon it for a sufficient period of time to pick up a lethal dose.

Residual treatments may also involve the use of palatable baits which remain "attractive" and chemically active over a period of weeks or months.

It follows that the amount of biocide residue deposited on treated surfaces is critical to the effectiveness of many treatments against crawling (and flying) insect pests. The amount of residue deposited should be determined under actual or simulated use conditions and the method(s) of determination must be available with the test data. The types of surfaces to which residual products are applied must be reported since surface type has a pronounced effect on the amount of active residue available to pests. In general a selection of both absorptive and non-absorptive surfaces should be tested when supporting a residuality claim for crawling (and flying) insect pests. These could include vinyl tile or linoleum, stainless steel, painted and unpainted wood and ceramic tile.

Efficacy data submitted to the competent authority in support for residual treatments should indicate the appropriate dosage and the utility of the formulation when used as directed. Usually, laboratory testing is performed to establish the effective dose range, to determine if the formulation is repellent to the point of adversely affecting the efficacy of the product and to evaluate the effects of the various substrates upon which deposition is to occur. Field or alternatively simulated use test data can be submitted to provide an indication of the efficacy of the formulation under actual use conditions.

2.4 Methods of application and dose rates

When considering the overall evaluation of a proposed label claim competent authorities should ensure that the data presented are relevant not only to biological challenge and treatment environment but also that the method of application and application/dose rate used in the test(s) are appropriate to the label claims and proposed use of the product. The application technique should therefore reflect the claims proposed on the label, whether crack and crevice, spot, space spray, contact spray or total release.

2.5 General considerations

The efficacy data submitted should demonstrate that the biocidal product, when used as directed by the product label, will result in a measurable beneficial effect. The data supplied should demonstrate that an acceptable level, consistent and duration of control or other intended effect will result from the use of the product at the recommended dose rate. This may, depending on the individual product, be measured as a reduction of the pest population to an acceptable level or a reduction in damage. The acceptable level may vary depending on the purpose of the proposed use.

Competent authorities should evaluate available data to determine whether they are sufficient to support a label claim.

The competent authority will examine the submitted data package and a judgment will be made as to whether any data omissions are considered significant as to delay assessment. Those so identified will be communicated back to the applicant for supplemental data submission before the evaluation can be undertaken.

Examples of the types of data (expressed as either laboratory or simulated use tests) that may be available for evaluation for insecticide/acaricide products applied by surface, space or bait treatment methodologies are presented in Figures 3 - 5.

These examples are illustrative and only consider a few common scenarios and a few typical target species. They do not include examples of relevant field data that may also be available to support the efficacy claims for insecticide/acaricide products

In many situations data based on simple laboratory/screening studies alone are unlikely to be enough to support the commercial authorisation of a product. The provision of other types of data (e.g. either simulated use tests or actual field studies) are more likely to lead to a successful application. Often therefore conclusions are drawn on the efficacy of a biocidal product based on the results of a series of studies submitted in support of the application.

For claims made for products intended for use as general surface treatments

Available data

Examples of the types of data that may be available when considering the efficacy of insecticide/acaricide products intended for use as surface treatments are given in Figure 3. The details of the product claim against which these data may lend support is given in brackets.

Laboratory/screening studies:

Direct cuticle application of active substance in solvent to oriental cockroaches (*Blatta orientalis*) to assess contact toxicity (**product claim = public hygiene contact residual surface spray against cockroaches)**.

Direct cuticle application of active substance to last instar nymphs of *Blattella germanica* to assess the degree of inhibition of emergence, assessment by scoring system (e.g. scored as:. normal adult, adult with melanic colouration, wing twist or supernumerary nymph [adultoid and permanent nymph]) **(product claim = public hygiene contact residual surface spray, insect growth regulator against cockroaches)**.

Active substance present in a range of concentrations in flea rearing medium containing cat flea (*Ctenocephalides felis*) eggs **(product claim = residual surface spray against fleas)**.

Sawtoothed Grain beetle (*Oryzaephilus surinamensis*) introduced into petri dishes containing a surface coating of a dust formulation for a defined period of time **(product claim = contact dust against stored product beetles).**

Simulated use:

Oriental cockroaches (*B. orientalis*) introduced into choice boxes with one half of the base surface being sprayed with a test formulation. Variations on this test would be to bioassay test insects exposed (voluntary contact) to a variety of different treated surfaces, e.g. plywood, cement, vinyl, ceramic tiles, glass etc. (**product claim = public hygiene residual surface spray use against cockroaches**).

Cat flea (*C. felis*) eggs are introduced onto treated carpet mat disc samples removed from a carpet mat which has been placed in a representative field site for a number of months **(product claim = residual surface spray against cockroaches)**.

Sawtoothed Grain beetle (*O. surinamensis*) are introduced into 0.06 m^2 container containing harbourages treated with a dust formulation **(product claim = contact dust against stored product beetles)**.

Figure 3: *Surface treatments*

For claims made for products intended to be used as space spray treatments

Available data

Examples of the types of data that may be available when considering the efficacy of products intended for use for application via space treatments are given in Figure 4.

The details of the product claim against which these data may lend support is given in brackets.

Laboratory/screening tests:

Direct cuticle application of active substance in solvent to common housefly *Musca domestica* to assess contact toxicity **(product claim = public hygiene spray against houseflies**).

Simulated use tests:

An aerosol dispenser containing the candidate product is discharged into a test chamber under controlled conditions, with an internationally recognised susceptible strain of the housefly *Musca domestica.* Knockdown is assessed at periods up to 15 minutes and at 24 h after discharge of the spray. The results of suitable number of replicate determinations for both candidate product and calibrated reference dispenser are determined (expressed as % knockdown). One suitable method is described in BS 4172 (1993) **(product claim = indoor aerosol use; knockdown and kill against houseflies)**.

A study conducted in a 30 m^3 chamber using an impregnated vaporising mat impregnated containing the candidate active substance placed at the centre of the chamber. Tests conducted against caged test insects (e.g. mosquito species *Culex pipiens palens* and *Aedes aegypti*), placed at central and peripheral locations in the chamber, to determine knockdown effect (KT_{50} and KT_{90}) and subsequent mortality after 24 h **(product claim = indoor use of vaporising mat; knockdown and kill against mosquitoes).**

Figure 4: *Space spray treatments*

For claims made for products intended for use as baits.

Available data

The important factors relating to testing bait products are to:

(a) establish the appropriate dosage and intrinsic attractancy of the formulation in laboratory tests. The most important factor involved in laboratory testing is to provide a free choice alternative food source to the test insects. This may be laboratory dog chow for insects such as cockroaches, or sugar based materials for house flies. The formulation should demonstrate acceptable toxicity in competition with the alternative food source; and

(b) evaluate the utility of the product under actual use conditions.

Examples of the types of data that may be available when considering the efficacy of products intended for use for application via bait treatments are given in Figure 5.

The details of the product claim against which these data may lend support is given in brackets.

Laboratory/screening tests

Dietary bioassay studies conducted using varying ranges of concentrations of active substance (e.g. 100 - 1000 ppm) ground into a pellet base using dog food and water. Replicate groups of test insects (e.g. *Blatta orientalis* and *Periplaneta americana)* exposed to either a continuous toxic diet, a toxic diet for 24 hours and then a non-toxic diet for rest of test period. Results for moribundity described by bioassay and concentration **(product claim = indoor use for bait product against cockroaches**).

Bait palatability studies to compare the mortality rate of the candidate preparation on nymphs and adults of German cockroaches (*Blattella germanica*) against either that of a non-toxic food source (known to be a strong feeding source for the test species e.g. commercially available dog food) and/or against a positive reference bait (i.e. one currently authorised and on the market) **(product claim = indoor use for bait product against cockroaches**).

Simulated use studies

Studies conducted with the candidate bait or gel contained within a bait station to compare the efficacy of the insecticidal bait/gel on a population of ants in a closed arena under carefully controlled conditions (e.g. with respect to temperature, relative humidity, photoperiod, etc.). Arenas containing suitable harbourage, water and an alternative food source and test insects allowed acclimatise for 24 h before introduction of bait. Efficacy assessed as mortality as a function of time which represents the attractivity, palatability and toxicity of the bait **(product claim = indoor use for bait product against ants)**.

Figure 5*: Bait treatments*

APPENDIX 1

Recognised standard methods for the efficacy testing of biocidal products intended for the control of Insects, acaricides and other arthropods.

1. Flying Insects

Title of Standard	Date	Title
British Standard BS 4172: Part 1 BS 4172 Part 2	1993 1993	Aerosol space sprays - Houseflies (adaptable for other flying insects) - Method and specification
US CSMA Aerosol Guide 7 th Edition, pages 129-134	April 1981	Test method for aerosol space sprays against flying insects
AFNOR Norme Française - NF T 72-320	March 1977	Method for aerosol space sprays against houseflies
World Health Organisation WHO/VBC/81.805	1981	Instructions for determining the susceptibility or resistance of adult mosquitoes to organochlorine, organophosfate and carbamate insecticides, - establishment of the baseline.
World Health Organisation WHO/VBC/81.806	1981	Instructions for determining the susceptibility or resistance of adult mosquitoes to organochlorine, organophosfate and carbamate insecticides - diagnostic test
World Health Organisation WHO/VBC/810	1981	Instructions for determining the susceptibility or resistance of adult blackflies, sandflies and biting midges to insecticides
World Health Organisation WHO/VBC/813	1981	Instructions for determining the susceptibility or resistance of houseflies, tsetse flies, stableflies, blowflies etc. to insecticides
South African Bureau of Standards Method 807		Methods for testing insecticides against flying and crawling insects.

3. Fumigants

Title of Standard	Date	Title
EPPO, Paris	1982	EPPO Recommendations on fumigation standards (2nd Edition)
EPPO Bulletin, 15 Pages 1-119, Paris	1983	The EPPO Conference on Fumigation, Paris, 1983

2. Crawling Insects

Title of Standard	Date	Title
US CSMA Aerosol Guide 7 th Edition, pages 135-139	April 1991	Test method for pressurised spray products against cockroaches
US ASTM Designation E654-90		Direct spray test method for spray insecticides against cockroaches
World Health Organisation WHO/VBC/75.593	1981	Instructions for determining the susceptibility or resistance of cockroaches to insecticides
World Health Organisation WHO/VBC/81.808	1981	Instructions for determining the susceptibility or resistance of body or headlice to insecticides
World Health Organisation WHO/VBC/81.809	1981	Instructions for determining the susceptibility or resistance of adult bed-bugs to insecticides
World Health Organisation WHO/VBC/81.814	1981	Instructions for determining the susceptibility or resistance of adult ticks to insecticides
World Health Organisation WHO/VBC/81.815	1981	Instructions for determining the susceptibility or resistance of fleas to insecticides
South African Bureau of Standards Method 807		Methods for testing insecticides against flying and crawling insects

4. Larvae

Title of Standard	Date	Title
British Standard BS 4797 ISO 3998	(1978) 1977	Test method for textiles to determine resistance to insect pests (e.g. moths, carpet beetles)
US AATCC Technical Manual Method 24	(1992) 1989	Test method for textiles to determine resistance to insects (e.g. moths, carpet beetles)
World Health Organisation WHO/VBC/81.807	1981	Instructions for determining the susceptibility or resistance of mosquito larvae to insecticides
World health Organisation WHO/VBC/81.212	1981	Instructions for determining the susceptibility or resistance of mosquito larvae to insect development inhibitors
World Health Organisation WHO/VBC/81.811	1981	Instructions for determining the susceptibility or resistance of blackfly larvae to insecticides

PRODUCT TYPE 21 - ANTIFOULING PRODUCTS

1 INTRODUCTION

This technical annex amplifies the nature and extent of data that should be available to support the efficacy of antifouling products.

Antifouling productsfall into two main usage categories; marine and freshwater. Many freshwater antifoulants will not perform satisfactorily in marine water, and to some degree the reverse is also true.

Antifouling products are used to control aquatic fouling pest organisms (such as slime, algae, weed, barnacles, mussels and other molluscs) on ships, small boats and other surfaces such as submersed equipment (such as aquaculture nets and cages, irrigation weirs, power plant intakes and outflows and pipelines) found in freshwater and marine environments, but the main usage is on the hulls of ships and boats.

1.1 Categorisation of Antifouling Products

Antifouling products can be broadly divided into two types: Those that contain tributyltin (TBT) and those that are TBT-free.

All organo-tin-containing antifouling products are subject to an international ban under the International Convention on the Control of Harmful Anti-fouling Systems on Ships. This ban means that by January 1st 2003, TBT-containing antifouling productscan no longer be applied. By 2008 these antifoulants must either be removed from ships' hulls, or sealed-in to prevent leaching. Because of this ban, there will be no further discussion of TBT-containing antifouling products in this document.

TBT-free products typically contain copper or a copper compound (e.g. copper (I) oxide, copper (I) thiocyanate) as the principal biocide, and as some of the common algae e.g. *Enteromorpha spp*. and *Amphora spp*. are tolerant of copper, they are often 'boosted' by the presence of one or more organic biocides (such as chlorothalonil, irgarol, zinc pyrithione etc.). These compounds are usually algicides but may in addition possess a wider spectrum of antifouling activity.

Copper is also used to enhance the performance of TBT products against organisms such as *Ectocarpus* and *Achanthes* that are tolerant of tributyltin oxide (TBTO).

1.2 Types of Coatings

The antifouling products currently available can be further categorised into the following ***broad*** coating types:

- Soluble matrix
- Insoluble matrix
- TBT-free self polishing

The categorisation of coating types outlined above is a very generalised picture. It should be noted by Competent Authorities that the majority of antifouling products do not necessarily rely on one single coating technology and a composite of different technologies have been developed by antifouling formulators to suit customer specifications and environmental requirements. Further detail and descriptors for the individual coating types can be found in Appendix 1.

Table 1 presents the European Council of Paint, Printing Inks and Artists' Colours Industry (CEPE) agreed maximum protection periods that can be expected for each type of antifouling coating.

Table 1: Maximum periods of service expected for the different types of antifouling coating type (CEPE)

Type of coating	Soluble matrix	Insoluble matrix	TBT-free controlled depletion polymer	TBT-free self polishing
Maximum Period of Service	18 Months	24 Months	3 years	5 Years

It should be noted that the maximum protection periods presented in Table 1 are a generalisation of maximum protection periods that may be achieved within these very broad groupings and these agreed intervals reflect a compromise position reached between CEPE Members. In addition the Table does not provide an indication as to the level of performance that can be obtained by a product specified within those time periods or the level of performance required by a particular specification. Performance ratings are heavily dependent upon the particular coating being applied to specification (surface preparation, primers, undercoatings, dry film thickness etc.) trading and sailing pattern of the vessel and a wide variety of environmental factors.

Aquaculture equipment is generally retreated on a yearly basis.

2 LABEL CLAIMS

2.1 Spectrum of activity

The situation with respect to target organisms is complicated by the main problem that they belong to ecologically very different groups. There are many organisms that can live within the 'fouling' community, but only a few cause severe fouling problems. This in turn depends on the local conditions for their growth, which are usually totally different in tropical and temperate regions but which may also vary locally from one area to another on the same coast.

Therefore, whilst it is not feasible to claim efficacy against specific target organisms applicants should indicate on the product label that their candidate product is an 'antifouling product' and supplement the claim with an indication as to whether the product is effective against one or more of the following fouling groups:

- slime
- aquatic plants (incl. weeds, grasses etc)
- animal (barnacles, mussels, other shell fouling etc.)

2.2 Mode of action

Antifouling products form films that act as control release vehicles for biocides contained in the paints. Biocides are released over the paint specification lifetime, creating a microlayer of biocide of a certain concentration at the paint surface, deterring settlement of fouling organisms. More detailed descriptions of the respective mode of action and physical characteristics of the various coating types are outlined in Appendix 1 of this document.

2.3 Areas of Use/Site of Application

A statement on the label or associated literature regarding the anticipated or recommended use(s) for a product will also be required. The uses may include: aquaculture - marine/or freshwater, deep sea, or use on yachts.

2.4 Application method/dose rate

Antifouling coatings may be applied using a range of methods including dipping and immersion (aquaculture), airless and conventional spray, brush and roller. The total dry film thickness will vary depending on the type of coating and required specification (see Appendix 1).

3. EVALUATION OF EFFICACY

The parameters that will define the effectiveness and therefore influence the service life of an antifouling product include:

- trading patterns
- fouling conditions (tropical or temperate waters, marine or freshwater)
- physico-chemical conditions of the water, e.g. pH, salinity and temperature
- coating type and film thickness

The efficacy data submitted in support of an application will be assessed to establish if the product containing the biocidal active substances has a reasonable level of performance with respect to its coating type and any product literature claims.

For an evaluation to be undertaken, statements will be required concerning product claims, including recommended retreatment intervals (i.e. the period between being taken out of service for the purpose of removal of old coating and application of a new one).

It is recognised that the maximum period of service life of an antifouling product is dependent on a range of factors, which may include trading pattern, film thickness and type of antifouling coating.

It is also recognised that the individual specifications of an antifouling product for a vessel's particular operating conditions will vary considerably, but the general effectiveness of a product under typical fouling conditions will need to be demonstrated.

4. AVAILABLE DATA

Laboratory tests (including *in-vitro* screening tests)

Such data are typically conducted with a limited number of test organisms and may provide information about a specific action against a known fouling species e.g barnacles. For the further development of 'bio-active' antifoulants it is often appropriate to seek specific active substances, which deter or kill only a limited number of species. This may be done in screening type laboratory tests to assess the toxicity of the biocide.

It is acknowledged that model target organisms may be used in these tests. In cases where they are used a reasoned case/argument for their use should be given. Consideration should be given to the use of the species known to be tolerant/resistant to existing antifouling biocides, in addition to those regarded as sensitive.

An illustrative example of the types of tests available is presented in Figure 1 of this annex.

Simulated field tests

These may be studies that are conducted with the active ingredient/biocide incorporated into a model coating type or the candidate product. Such tests would include static raft testing with panels coated with a test coating and immersed for a period of months at an appropriate locality in a river, estuary or sea, or sections or whole nets or cages treated with the candidate product and immersed at an appropriate site for up to 1 year.

Efficacy data on the candidate antifouling coating should be available following testing over periods of one or more 'seasons' of peak fouling activity in locations typical of intended usage, depending on the label claims. The length of a 'season' may vary from six months to one year, depending on the location of the test site. Testing should be conducted in locations when the fouling organisms are present throughout the year. Since some variation in performance will occur depending on conditions at individual locations, it is recommended that if available a reference coating of proven or known performance be included in the tests together with a blank (negative) control. The use of the nontoxic untreated control is required to properly evaluate the fouling potential and provides a survey of the fouling community that would be noted if no toxicant were present in the coating under test, or if the test coating were ineffective.

Available data should include monthly scorings/ratings of fouling during the exposure period. Identity of slime, algae, barnacles, weeds or other fouling organisms as to genus and species is unnecessary.

Available data should also include the assessment method and rating/scoring for test panels together with full results data (including photographs and/or diagrams where appropriate) and interpretation. Within a particular study it is preferable for the same operator to carry out all of the visual rating/scoring. This will reduce errors introduced by inconsistencies between operators.

An illustrative example of the types of tests available is presented in Figure 1 of this annex.

Field tests/In service monitoring

Since field tests involve long-term exposure to practical conditions, they can be regarded as service tests. As such, any field data generated in support of an application should be conducted on products or representative products that closely resemble the fully formulated commercial product.

These may be studies that are conducted with the coating that is intended to be marketed, i.e. the one for which authorisation is sought. Field tests permit antifouling products to be tested under similar operating conditions and stresses as those encountered when the antifouling product is in service. Possible examples of these tests include:

- panel tests where coated panels are attached to a vessel for a short period of time;
- patch tests where vessels are painted with the test coating as a strip or patch on the side of the hull;
- in service monitoring of aquaculture nets, cages etc.

It is recognised that it may not be possible to run concurrent untreated panels or patches during such field trials. Information concerning the main antifouling coating and its performance over the test period should therefore be included.

Monitoring reports of the performance of an antifouling product on a fully treated vessel, where available, may also be submitted.

It is recognised that data generation from field trials may require many years to carry out and are more likely to be available for products incorporating established biocides in coatings of well known technology, rather than for products containing newer biocidal active ingredients and for coating types based on new technology.

Where field data are not available the applicant has the option to provide existing data concerning other appropriate formulation(s) and link them to the current application through scientific reasoned cases and arguments. Such studies could be compiled on the basis of:

- Composition of 'old' (and well documented) and 'new' antifouling product
- Simulated field tests of 'old' and 'new' antifouling products

- Field data on 'old' antifouling formulations
- Further justification, such as why bridging is appropriate (e.g. in-service monitoring)

Additionally it is understood that where established biocides have been introduced into products based on new technology neither extensive field data nor bridging data will always be available.

An illustrative example of the types of tests available is presented in Figure 1 of this annex.

4.1 Standard Test Methods

Laboratory and Simulated use test methods

There are currently two standard test methods available for the generation of simulated field data through raft testing of antifouling coatings. These are:

1. Antifouling coatings - Method of the generation of efficacy data. CEPE Antifouling Working Group, 1993.

2. American Society of Testing Methods (ASTM) - Standard Test Method for Testing Antifouling Panels in Shallow Submergence. D3263 - 78a, 1987.

Field/In service tests

There are currently no national or international standards that cover field evaluation of antifouling products.

4.2 Formulation/coating type to be used in the generation of efficacy data.

The formulations used in screening studies in the laboratory may be simple solutions of the active substance/biocide, whereas those used in simulated use studies should mirror the type of coating/formulation for which authorisation is sought or may be the actual product that is intended to be marketed. It is recognised that field studies are more likely to be conducted on a product that resembles the commercial product for which authorisation is sought.

Table 2 shows a summary of the kinds of test that can be conducted on the different stages of the development of a new antifouling product.

Table 2. Examples of types of efficacy study conducted with the different development stages of a new antifouling product.

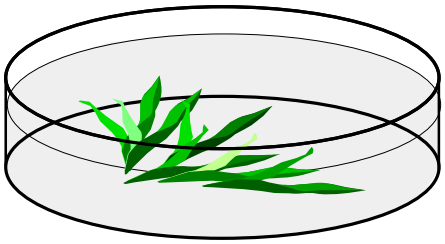
Type of study	Biocide (active substance) in simple solution	Model or 'frame' coating(s)	Coating/product for which approval is sought
Laboratory test	✓	×	✓/×
Simulated field test	×	✓	✓
Field tests	×	×	✓
In-service reports	×	×	✓

✓ same as in the proposed product application

× not always necessary to resemble or mirror that proposed in the product application

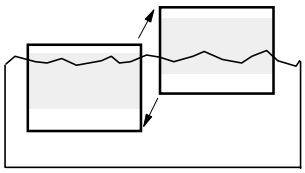
The table illustrates the principle that efficacy studies generated before the final product coating has been developed have a part to play in the evaluation of an active substance/biocide in an antifouling product.

Laboratory studies e.g. In-vitro toxicity screening tests



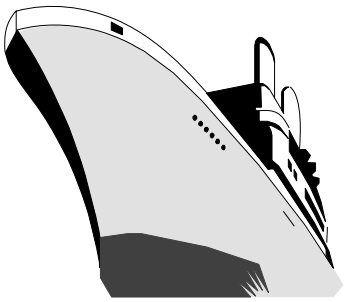
To demonstrate the inherent biological properties of an ingredient as an anti-weed, anti-animal agent .

Simulated field tests e.g. Raft tests



Panels coated with the test formulation
immersed in water for a period of
Demonstrates antifouling capability under static conditions

Field Tests e.g. Patch tests



Strips or patches of a test product applied
the hull of a vessel. Demonstrates
antifouling capability under in use service conditions

Figure 1: Examples of possible studies that may be used to assess antifouling efficacy

APPENDIX 1

CURRENT ANTIFOULING COATINGS

The major types of antifouling coatings together with a brief description of their properties are outlined below. These coating types will be used when considering efficacy evaluations for antifouling products. This list is not an exhaustive one into which all product applications must be categorised. Applicants may submit novel coating types not covered in this list or they may, in some cases, wish to submit a reasoned case in support of their product application if a product cannot be readily categorised into one of these groups.

Coating Type	Description, mode of action and properties
Soluble matrix	In coatings of this type the biocide(s) have been physically mixed ('freely associated') into a rosin matrix. Upon exposure to seawater the slightly acidic matrix slowly dissolves releasing the biocide(s) into the water. (Sea water is slightly alkaline (pH8) and the acidic matrix readily dissolves). Continuous dissolution of the coating surface occurs resulting in fresh biocide(s) being released until eventually the film is exhausted. Soluble matrix antifouling products typically show a biocide release rate curve which decays exponentially. The soluble matrix coatings have poor mechanical properties that limit film thickness, the paint film thickness of these coatings depletes over time in an imprecise manner and the film does not show smoothing characteristics on ships in service. As the matrix rosin is a natural product, batches differ and therefore coating lifetime is unpredictable. Such coatings are normally specified for lifetimes approximating 12-18 months. Typically coatings are applied in two coats by airless spray giving a total dry film thickness of 100 - 150 microns (mm).
Insoluble matrix	Within this type of coating the binder or matrix is insoluble, the biocide(s) is physically mixed into the matrix (often at higher concentrations than is the case with the conventional coatings). As sea water enters the paint film the biocides are released by dissolution and diffusion from within the insoluble matrix. After biocide is released from the film the binder remains intact and an empty 'honeycomb' structure (the leached layer) remains at the paint surface. This type of coating has a high initial release rate, which decreases exponentially with time as the biocide(s) has further to travel through the paint film. Rate of diffusion of biocide from within the film then becomes a limiting factor in maintaining an effective biocide release rate and hence preventing fouling. Insoluble matrix antifouling coatings do not show film-depletion or polishing as the resin is insoluble. This release process continues until exhaustion of the coating. The higher mechanical strength obtained with these coatings allow applications of thicker systems and coating lifetimes of approximately 24 months are attainable. Application of these coatings is typically by airless spray, two coats resulting in a dry film thickness of 150 microns.
TBT-free self polishing	Coatings of this type rely on soluble medium, such as rosin, in combination with insoluble polymers to form a matrix which wears away *physically* at a controlled rate. The biocide(s) is mixed into the matrix and released by dissolution at a rate determined by the rate of physical ablation of the polymer. The physical ablation process is less controlled and predictable than the chemical ablation process. Therefore the steady release rate, predictable life, smoothing and recoating properties of the

	TBT self polishing co-polymer coatings are difficult to achieve with this group of coatings. These TBT-free copolymer coatings have to date demonstrated that dry docking intervals of 3 years or better can be achieved. Extended in service periods of up to 4 - 5 years can potentially be claimed the better performers within this group of coatings.

Appendices to chapter 9

Examples of the use of frame formulations when granting authorisation/registration of products

Example 1 - A wood preservative application for a product to be marketed in a range of colours which can be considered as a single frame formulation.

Ingredients	**Formulation details of the colours in the range (presented as % w/w)**			
Name	Light brown	Dark brown	Sunset	Gold
Active substance	10	10	10	10
Low odour kerosene	86.5	85.5	87.5	85.6
Iron oxide (red)	1.1	1.9	2.5	0.4
Iron oxide (yellow)	2.0	2.5	-	4.0
Carbon	0.4	0.1	-	-
Classification and labelling	All 4 formulations would carry identical classification and labelling phrases			

Notes: The active substance level is the same in all four formulations and the solvent levels vary to compensate for the pigment combinations to obtain each colour. Not all of the colours contain all of the pigments; "Sunset" contains only one of the three pigments and "Gold" contains two of the three pigments.

Therefore the frame could be summarised as presented below. It should be noted that this frame also includes the provision of a colourless formulation because the active substance and low odour kerosene formulation would carry the same classification and labelling phrases as any coloured product included in this frame formulation.

Ingredients	**Formulation details of the range (presented as % w/w)**
Active substance	10
Low odour kerosene	85.5 - 87.5
Iron oxide (red)	0.4 - 2.5
Iron oxide (yellow)	0 - 4.0
Carbon	0 - 0.1
Classification and labelling	Classification and labelling the same in this range

Example 2 - A wood preservative application for a product to be marketed in a range of colours which can not be considered as the same frame formulation.

Ingredients	**Formulation details of the colours in the range (presented as % w/w)**			
Name	Meadow yellow	Autumn green	Bottle green	Spring green
Active substance	10	10	10	10
Water	87.5	86.7	87.5	84.6
Pigment green XEZ	0.1	0.7	2.5	1.4
Iron oxide (yellow)	2.0	2.5	-	4.0
Carbon	0.4	0.1	-	-
Classification and labelling	These two products are not classified		These two products are classified as Harmful with the same labelling phrases	

Notes: The active substance level is the same in all four formulations and the solvent levels vary to compensate for the pigment combinations to obtain each colour. The formulations do not carry the same classification because the levels of "Pigment green XEZ" cross the "Harmful" classification trigger value of 1.0 % w/w. Therefore these four formulations have to be divided into two frame formulations. These two frames could be summarised as presented below.

Ingredients	**Formulation details of the range (presented as % w/w)**	
	Frame 1	Frame 2
Active substance	10	10
Water	86.1 - 90.0	84.6 - 87.5
Pigment green XEZ	<1.0	1.0 - 2.5
Iron oxide (yellow)	0 - 4.0	0 - 4.0
Carbon	0 - 0.4	0 - 0.4
Classification and labelling	Not classified	Harmful with the same labelling phrases

It should be noted that frame 1 also includes the provision of a colourless formulation because the active substance and water formulation would carry the same classification and labelling phrases as any coloured product included in this frame formulation.

In addition, the concentration range for "iron oxide (yellow)" in frame 1 can be up to the maximum presented in the "Spring green" product because a level of 4.0 % w/w does not result in this combination attracting a different classification from other products in frame 1.

Such considerations are also valid when examining the ranges possible in frame 2. Therefore the range within the frame 2 definition can be broader than just including the formulations for the "Bottle green" and "Spring green" products.

Example 3 - A disinfectant toilet rim block application for a product to be marketed in a range of fragrances which can be considered as a single frame formulation.

Ingredients	**Formulation details of the fragrances in the range (presented as % w/w)**		
Name	Pine fresh	Lavender fresh	Lemon fresh
Active substance	20	22	25
Alkyl benzene sulfonate	55	48	50
Calcium carbonate	12.85	19.9	16.88
Sodium sulfate	12	10	8
Cedarwood perfume	0.15	-	-
Lavender perfume	-	0.1	-
Citronella perfume	-	-	0.12
Classification and labelling	All 3 formulations would carry identical classification and labelling phrases.		

Notes: The active substance level and the solvent levels vary to compensate for the perfume combinations to obtain each fragrance, in addition all three formulations contain different perfumes. However following the evaluation of the competent authority they were considered to be within the same frame because the variations in active and non-active substance levels does not affect the classification of the products within this frame, and the efficacy of these products is not compromised by the variations in active substance levels.

Therefore the frame could be summarised as presented below. Any formulation containing one of these three fragrances at up to 0.15 % w/w would carry the same classification. However, if a combination of these fragrances was used and this resulted in a perfume content of greater than 0.15 % w/w, the competent authority would have to ensure that this did not result in a change in classification if such formulations were still to be defined by this frame.

Ingredients	**Formulation details of the range (presented as % w/w)**
Active substance	20 - 25
Alkyl benzene sulfonate	48 - 55
Calcium carbonate	12.85 - 19.9
Sodium sulfate	8 - 12
Lavender oil or Citronella oil or Cedarwood oil	0 - 0.15
Classification and labelling	All formulations would carry identical classification and labelling phrases.