Evaluation Manual for the Authorisation of biocides

Active substance approval and product authorisation under BPR

Biocides

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ctgb

Board
for the authorisation
of plant protection products and biocides

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Changes made in the Evaluation Manual

Evaluation Manual Biocides Active substance approval and product authorisation under BPR			
Version	**Date**	**Paragraph**	**Changes**
2.0	October 2016		Initial new version
2.1	June 2017	2.2	TAB for physchem added published in December 2016
		4.1	Adding of article 62 of the BPR, i.e. to avoid animal testing
		4.2	More explanation for the use of SCOEL and Dutch reference values in the SoC approach.
		4.3	Final guidance on DBPs January 2017
		4.1	Document Dermal absorption of PT21 active substances
		4.4	Document ADI and ARfD derivation for biocidal active substances

1. INTRODUCTION EU FRAMEWORK

The present document describes processes, methodology, and legislation applied by the Ctgb regarding authorisation of biocidal active substances and biocidal products according to the Biocidal Product Regulation (BPR). It concerns notification and assessment of biocidal products containing active substances that are approved as a biocide in Europe and notification of new active substances. The EU-part of the evaluation manual is not applicable for biocidal products based on existing substances not yet included on the Union list of Approved Active Substances or Annex I of the BPR (512/2012). Notification of these products will be done according to the Transitional Legislation (TL). General information on the BPR an transitional law is found in the general introduction.

2. PHYSCHEM

2.1. Information requirements for active substances and biocidal products

The information requirements regarding the physchem assessment are explained in Volume I - Part A for which 1.1 (November 2014) is the current version. The information requirements are two-tiered. The core data set (CDS) is mandatory for all product types and has always to be submitted. The additional data set (ADS) must be submitted when required by the intrinsic properties of the active substance or biocidal product, when required by the foreseen use and route of exposure, or when the initial risk assessment must be refined. It is self-evident that the ADS should focus on the information requirements needed for the specific case.

The Ctgb follows the BPR regarding information requirements and has not defined additional requirements. Note that the assessment report for the active substance contains at least the CDS. A letter of access to the relevant active substance dossier(s) is therefore often sufficient, unless additional information requirements are listed in the BPR opinion and/or product specific parameters are necessary.

2.2. BPC working group agreements

In December 2016, ECHA published a new version of the Technical Agreements on Biocides (TAB) on their website, which includes relevant technical agreements made at the BPC Working Groups and, as the Working Groups were previously known, the Technical Meetings. In addition to the TOX and ENV chapters, agreements with regard to the APCP (identity, physical and chemical properties and analytical methods) are now available as well.

3. EFFICACY

3.1. Introduction Efficacy

This chapter describes the assessment of the efficacy of an active substance for placement of this active substance on the Union list and the assessment of a biocide for product authorisation.

In the last decades guidance on the efficacy evaluation has been developed, partly under the BPD, partly as transitional guidance[1] and part is still under development. All this guidance will be combined in one guidance document for the BPR: Volume II Efficacy of the Guidance on biocide legislation. There are some appendices to this guidance which are not included in the guidance itself. The reason for this is the possibility to update them regularly, without going through the whole procedure of updating Volume II Efficacy.

This Volume II Efficacy consists of two parts, Part A and Part B/C. In addition specific guidance that is not (yet) included in Volume II Efficacy Part B/C on the information requirements humaneness and resistance is given.

3.2. Volume II Efficacy Part A: Information Requirements.

This guidance describes the information requirements for active substances and biocidal products in accordance with the Title 1 of Annex II and III of the BPR. Volume II Efficacy Part A was published 28-11-2014 on the ECHA website under *Guidance on biocides legislation*.

This guidance provides an explanation on the different data that is required. This is very general, more detailed guidance on the efficacy data (testing, minimum requirements, criteria, etc.) are described in Volume II Efficacy Part B/C.

3.3. Volume II Efficacy Part B/C: Efficacy Assessment and Evaluation.

This guidance is under development. This guidance contains general chapters on efficacy evaluation for active substance approval and product authorisation and chapters per PT, where the PT specific requirements and norms and criteria for assessment are described.

The first draft of Volume II Efficacy Part B/C is published at the ECHA website under *Ongoing guidance consultations*. In the draft version only the new chapters are shown; the general chapters and new or revised guidance on several PT's. The existing transitional guidance for other PT's will be added before the document is finalised.

When the document is finalised it will be published (expected 1st half of 2017) on the ECHA website under Guidance on biocides legislation.

Since the guidance is in different stages of development some explanation is given per chapter of the guidance. In those cases where the guidance is under development and not published yet, applicants can contact the Ctgb Service desk (servicedesk@ctgb.nl) for the latest version of the guidance that they seek. For the other published guidances the links are added.

[1] A "Transitional Guidance" is a document that has been initiated under the "old" Biocidal Products Directive and because it has been finalised before the relevant new Biocidal Products Regulation guidance document (Vol II part B/C) has been fully developed, it is being made available as a Transitional Guidance document until such time as the relevant new document is ready for publication.
Transitional guidance is EU guidance and has nothing to do with transitional legislation in NL.

3.3.1 Part B/C general

Three general chapters contain a general introduction, information on label claims, and general considerations for the development and reporting of efficacy data. Although these are not basically different from the approach taken in former guidance documents, it is a bit more explicit.

The draft version of these chapters can be found in the draft Volume II Efficacy Part B/C.

3.4. Active substance approval

This chapter contains the general principles for efficacy evaluation of active substances, and highlights some specific cases (active substances which are not intended to be used in isolation, dummy products, and treated articles). The approach as was taken and refined over the years for the active substance that have been approved so far is described in this chapter.

In this chapter no PT specific guidance is given. It is assumed that similar tests can be used for the active substance as for the product. Therefore, all the PT specific information is given in the chapters on product evaluation.

The draft version of this chapter can be found in the draft Volume II Efficacy Part B/C.

3.4.1 Product authorisation

This chapter contains a general introduction, a section on product families (efficacy testing for a family, influence of efficacy on deviation in *meta*-SPC's), and a section on treated articles.

The draft version of this chapter can be found in the draft Volume II Efficacy Part B/C. Under this chapter sections per PT or groups of PT's are included.

Disinfectants

This section contains a **general introduction** which was endorsed 31-5-2016 and can be found at the ECHA website under Transitional Guidance.

Some of the appendices belonging to the guidance on disinfectants are only incorporated in Volume II part B/C as a link. These appendices can be found on the ECHA website at the page of the Working Group – Efficacy. These appendices might be up dated more often than Volume II part B/C.

In addition it contains a section on **materials and articles treated to protect humans or animals**. This gives information on testing materials and articles which contain an active substance and have a biocidal claim.

The draft version of this chapter can be found in the draft Volume II Efficacy Part B/C.

PT1-4

This section contains guidance on the efficacy evaluation of products in PT 1, 2, 3, and 4 which was endorsed 31-5-2016. Until *Volume II Efficacy Part B/C: Efficacy Assessment and Evaluation* is finalised this section can be found at the ECHA website under Transitional Guidance.

Appendix 1 (Claims Matrix PT 1-4) and 4 (Overview of standards, test conditions, and pass criteria of the TG on Efficacy Assessment for PT 1-5) of this guidance are not included in the guidance itself, only a link to the location is given.

PT5
This section contains guidance on the efficacy evaluation of products in PT5. This section is under development. The draft version of this section is published together with the final versions for PT1 to 4 and can be found at the ECHA website under Transitional Guidance. This draft version has been commented on and is discussed in a workshop. The major discussion points and their outcome are summarised in the table below.

Division in groups, raw water / water of (near) drinking water quality	A distinction will be made between disinfection of raw water and disinfection of water of (near) drinking water quality. In the draft version the section "Disinfection of raw water and water of undefined quality" is only intended for products used to disinfect water for small scale (<5L/person/day) personal use. Data requirements for large scale disinfection of raw water (in drinking water companies, in mobile homes, etc.) are missing. An extra group will be added.
Soiling in suspension tests	The draft version refers to EN suspension tests for the food area. The soiling in these tests will probably be accepted for disinfection of raw water (ground water, surface water, etc.), however, it is considered too high for water of (near) drinking water quality. For this use soiling conditions according to EN13623 is more appropriate: final concentration of yeast extract in the test is 0.0005%.

When the document is finalised (expected 1st half of 2017) it will be included in *Volume II Efficacy Part B/C: Efficacy Assessment and Evaluation.* A second draft version might be published on the ECHA website under Ongoing guidance consultations end of 2016.

Preservatives
A general chapter on preservatives was published as transitional guidance 28-5-2014. This chapter is updated and incorporated in the section on preservatives in *Volume II Efficacy Part B/C*. This draft version can be found on the ECHA website under Ongoing guidance consultations.

This section contains a section on **wet-stage preservation** which gives a general view on testing preservatives in PT6, 11, 12, and 13. A section **curative treatments** gives a general view on testing preservatives which claim to have a curative effect. A section **protection of solid material** gives a general view on testing preservatives in PT7, 8, 9, and 10.

PT6
This section contains guidance on the efficacy evaluation of products in PT6. The draft version of this chapter can be found in the draft Volume II Efficacy Part B/C.

PT 7
This section contains guidance on the efficacy evaluation of products in PT7. The draft version of this chapter can be found in the draft Volume II Efficacy Part B/C.

PT 8
This section contains guidance on the efficacy evaluation of products in PT8 which was endorsed and published as transitional guidance on 31-3-2015. Until *Volume II Efficacy Part*

B/C: Efficacy Assessment and Evaluation is finalised this section can be found at the ECHA website under Transitional Guidance.

Recently, a few issues were identified in the published guidance and were discussed in the ECHA Working Group on Efficacy. The major discussion points and their outcome are summarised in the table below. This guidance is currently under revision on these points.

Requirements for general claims against "wood boring beetles"	The requirements for a general claim against "wood boring beetles" are made in line with the EN599-1:2014, section 5.2.3. For this claim all relevant beetle species (*Hylotrupes bajulus*, *Anobium punctatum* and *Lyctus brunneus*) should be tested except if data (relevant and robust literature data, where the materials and methods is detailedor certification data on case by case basis) are provided which demonstrate that one of the targets is the less sensitive , or that the product has an equivalent activity against all beetle species.
Barrier treatment against Serpula lacrymans is preservative treatment and not curative treatment	The dry rot fungus (*Serpula lacrymans* = true dry rot fungus) occurs in buildings, causing brown rot in timber. The fungus can develop at relatively low wood moisture contents and is able to penetrate damp masonry over long distances in order to infect further timber or to develop its fruit-bodies. In general, in case of an infestation of *Serpula lacrymans*, the infected wood is cut away. To prevent the infection of the new placed wood with fungi coming from the surrounding masonry, a curative treatment against dry rot in walls (mortar) will result in creating a 'preventive' barrier in / on walls hindering the fungus to grow through. There is a specific Technical Specification (CEN/TS 12404) for determining the performance of a preservative applied to the upper surface of the mortar in preventing the growth of dry rot through the treated mortar when exposed to the fungus. This method is only applicable to masonry fungicides applied as a true solution of preservative. It is not applicable to rods, pastes and other similar preservative types.
Appendix 2 removed from guidance	Appendix 2 (informative list of standards for efficacy assessment of wood preservatives) will be removed and added to the ECHA Biocides Efficacy Working Group webpage.

When the document is revised it will be included in *Volume II Efficacy Part B/C: Efficacy Assessment and Evaluation.* A draft version might be published on the ECHA website under Ongoing guidance consultations end of 2016.

PT 9
This section contains guidance on the efficacy evaluation of products in PT9. The draft version of this chapter can be found in the draft Volume II Efficacy Part B/C.

PT10
This section contains guidance on the efficacy evaluation of products in PT10. This section

is under development. No draft version is available or foreseen in the near future. As long as no PT10 specific guidance is available the general guidance on preservatives and the section **protection of solid material** (both to be found in the draft version of *Volume II Efficacy Part B/C* which can be found on the ECHA website under Ongoing guidance consultations) should be used as guidance for PT10 products.

PT 11
This section contains guidance on the efficacy evaluation of products in PT11. This section is under development. The first draft version is foreseen in the beginning of 2017 and might be published on the ECHA website under Ongoing guidance consultations. As long as no PT11 specific guidance is available the general guidance on preservatives and the section **wet-stage preservation** (both to be found in the draft version of *Volume II Efficacy Part B/C* which can be found on the ECHA website under Ongoing guidance consultations) should be used as guidance for PT11 products.

PT 12
This section contains guidance on the efficacy evaluation of products in PT12. This section is under development. The first draft version is foreseen in the beginning of 2017 and might be published on the ECHA website under Ongoing guidance consultations.

As long as no PT12 specific guidance is available the general guidance on preservatives and the section **wet-stage preservation** (both to be found in the draft version of *Volume II Efficacy Part B/C* which can be found on the ECHA website under Ongoing guidance consultations) should be used as guidance for PT12 products.

PT13
This section contains guidance on the efficacy evaluation of products in PT13. The draft version of this chapter can be found in the draft Volume II Efficacy Part B/C.

Pest control
This section contains a general introduction on pest control. This section is under development. No draft version is available or foreseen in the near future.

PT 14
This section contains guidance on the efficacy evaluation of products in PT14 which was endorsed February 2009 and is now under major revision. The guidance endorsed in February 2009 is not published as transitional guidance, but can be found in the TNsG on Product Evaluation as Revised appendix to chapter 7 on efficacy of rodenticides. The major discussion points and their outcome as discussed in the ECHA Biocides Efficacy Working Group are summarised in the table below.

More detailed information needed on testing protocols and other rodent species	The following information has been added: - more detailed protocols for testing against voles - a more detailed semi-field protocol - a more detailed sewer test protocol - more detailed protocols for gassing agents - more examples of intended uses/claims
Requirements for ‘use against rats’ claim	When ‘use against rats’ is claimed testing against both *Rattus norvegicus* and *Rattus rattus* is required.
Necessity of mortality tests	Since mortality tests give very little information in addition to data from the bait choice feeding tests and in order to reduce the number of animal experiments, mortality tests

	(i.e. no-choice feeding tests) are not recommended and are not required. However, many applicants may have no-choice studies on their products as they have been conducted in the past. These can still be submitted as part of the data package but no new studies should be conducted.
How to test palatability at the end of shelf life of bait products	Based on expert opinion, most bait products have been found to be effective and palatable for 24 months (with preservatives) and 12 months (without preservatives). Efficacy testing should therefore only be provided for: • bait products with preservatives that claim a shelf life of longer than 24 months; • bait products without preservatives that claim a shelf life of longer than 12 months; • bait products for which the degradation of the active content is >10% and assessment of the degradation on the efficacy is needed to substantiate the shelf life claim. For bait products with a shorter shelf life claim than stated above, no efficacy tests on aged bait (i.e. product at the end of maximum storage) have to be provided. For these products it is sufficient to provide tests on fresh bait (i.e. newly produced product). For bait products with a longer shelf life claim, the applicant must deliver data on the palatability of the product at the end of maximum storage for all target organisms claimed. The palatability of the aged product preferably is tested in bait choice feeding trials, but can be tested in field trials, provided these tests are scientifically valid (see section 2.6 below). Accelerated ageing studies, i.e. palatability studies in which the product tested is stored under challenging conditions, are not acceptable as these cannot simulate longer storage periods.
How to deal with a biocidal product family of bait products with different formulations	A BPF of rodenticide baits may contain several bait products with different formulations, for example, various grain, block, paste and gel products. Each bait formulation should be allocated to a different meta-SPC. Each bait formulation within the BPF has to be tested, because it cannot be predicted which form is the least palatable. It would also be difficult to select one product that could be regarded as a 'worst case scenario' for testing all the formulations. Within a given meta-SPC, an individual product should only be tested to consider the minimum level of efficacy within the concentration ranges of the active substance in that meta-SPC.
Field trials are not animal experiments	Field trials should be conducted on wild rodent infestations and are not considered animal experiments provided the respective tests on efficacy, palatability and humaneness have been confirmed under controlled laboratory studies.
Explanations added on the possibilities of waiving	For bait products, because the composition of the bait determines the palatability and hence efficacy of the

	product, even small changes in ingredients may affect the attractiveness. This may differ between target organisms and is difficult to predict in advance. Laboratory testing of bait products (bait choice test or semi-field trial) should always be requested for new active substances, or if a product was altered regarding the active substance concentration and/or bait formulation. One exception would be if there were already tests with a fully comparable bait containing an active substance with the same mode of action and similar or lower toxicity (a table with ranking of toxicity is provided in the guidance). Field trials are always required when the composition of a product is changed. Exceptions could possibly include changes of minor importance in ingredients that are likely not to have an effect on palatability or efficacy, such as change in colour of a product. In case of waiving, the applicant needs to provide a robust justification why no testing was performed. Read-across between species could be acceptable if the applicant could argue that the species were very similar (e.g. common vole and bank vole). Testing of *R. norvegicus, R.rattus* and *M. musculus* would however always be requested and no read-across is possible between these species.
Resistance claims	Still under discussion, not decided yet

After revision the PT14 guidance may either be published as Transitional Guidance at the end of 2016 or included in Volume II Efficacy Part B/C (expected 1st half of 2017 on the ECHA website under Guidance on biocides legislation), (procedure is not defined yet). As there are still many discussions on the paragraph on resistance and there is no clear way forward, this part of the PT14 guidance will be marked as 'under review'. These parts will be under full ECHA consultation and PEG meeting and are expected to be finalized end of 2017.

PT15, 16, & 17
This section contains guidance on the efficacy evaluation of products in PT15, 16 &17. This section is under development. No draft version is available or foreseen in the near future. As long as no PT15, 16 &17 specific guidance is available, the general principles as described in the first chapters of the draft *Volume II Efficacy Part B/C: Efficacy Assessment and Evaluation* should be used as guidance for PT15, 16, &17 products.

PT18 and 19 on arthropods
This section contains guidance on the efficacy evaluation of products in PT18 and 19 on arthropods which was endorsed December 2012 and published as transitional guidance on 16-9-2016. Until *Volume II Efficacy Part B/C: Efficacy Assessment and Evaluation* is finalised this section can be found at the ECHA website under Transitional Guidance.

Recently, several data gaps and a few issues were identified with respect to the PT19 guidance included in the published guidance and were discussed in a dedicated Efficacy workshop on repellents. It was decided that in the future revision of this guidance, PT18 and PT19 guidance should be separated. PT19 guidance should be developed for sand flies, wasps, bedbugs, head lice, spiders and midges and should be improved for mosquitoes,

ticks and ants. This revision on the PT19 guidance on arthropods is not foreseen in the near future.

Please note that for repellents against mosquitoes that it is agreed among MSs that **arm-in-cage tests are worst case for mosquitoes and are always needed and that field tests are not mandatory**, but can be provided as additional information.

PT19 non-arthropods
This section contains guidance on the efficacy evaluation of products in PT19 on non-arthropods. This section is under development. No draft version is available or foreseen in the near future. As long as no PT19 non-arthropods specific guidance is available, the general principles as described in the first chapters of the draft *Volume II Efficacy Part B/C: Efficacy Assessment and Evaluation* and the general introduction of the PT18/19 guidance on arthropods should be used as guidance for PT19 non-arthropods.

PT20
This section contains guidance on the efficacy evaluation of products in PT20. This section is under development. No draft version is available or foreseen in the near future. As long as no PT20 specific guidance is available, the general principles as described in the first chapters of the draft *Volume II Efficacy Part B/C: Efficacy Assessment and Evaluation* should be used as guidance for PT20 products.

Humaneness
According to the BPR (Article 19(1)(b) criterion ii and common principles point 49 and 76 in Annex VI) biocidal products should cause no unacceptable effects on the target organisms, including unnecessary suffering and pain for vertebrates (humaneness). This criterion is relevant for biocides in the Pest Control PT14, 15, 17, 19 (repelling or attracting vertebrates) and 20.

For these biocides an assessment shall be made to demonstrate that the biocidal product does not cause unnecessary suffering in its effect on target vertebrates. This shall include an evaluation of the mechanism by which the effect is obtained and the observed effects on the behaviour and health of the target vertebrates; where the intended effect is to kill the target vertebrate, the time necessary to obtain the death of the target vertebrate and the conditions under which death occurs shall be evaluated.

A biocidal product intended to control vertebrates shall not normally be regarded as satisfying criterion (ii) under point (b) of Article 19(1) unless:
— death is synchronous with the extinction of consciousness, or
— death occurs immediately, or
— vital functions are reduced gradually without signs of obvious suffering.

For repellent products, the intended effect shall be obtained without unnecessary suffering and pain for the target vertebrate.

Guidance on the assessment of humaneness is currently not included in *Volume II Efficacy Part B/C: Efficacy Assessment and Evaluation*, but some general guidance can be found in the TNsG on Product Evaluation Chapter 6.

Other biocidal products
PT21
This section contains guidance on the efficacy evaluation of products in PT21 which was endorsed and published as transitional guidance on 28-5-2014. Until *Volume II Efficacy Part*

B/C: Efficacy Assessment and Evaluation is finalised this section can be found at the ECHA website under Transitional Guidance.

PT22
This section contains guidance on the efficacy evaluation of products in PT22 which was endorsed and published as transitional guidance on 12-8-2014. Until *Volume II Efficacy Part B/C: Efficacy Assessment and Evaluation* is finalised this section can be found at the ECHA website under Transitional Guidance.

Resistance and cross-resistance
According to the BPR (Article 19(1)(b) criterion ii and common principles point 50 and 75 in Annex VI) biocidal products should cause no unacceptable effects on the target organisms, including unacceptable resistance or cross resistance. This criterion is relevant for biocides of all product types.

Where relevant, an evaluation on the possibility of the development by the target organism of resistance or cross-resistance to an active substance in the biocidal product shall be made.

Where the development of resistance or cross-resistance to the active substance in the biocidal product is likely, the evaluating body shall consider actions to minimise the consequences of this resistance. This may involve modification of the conditions under which an authorisation is given. However, where the development of resistance or cross-resistance cannot be reduced sufficiently, the evaluating authority shall conclude that the biocidal product does not satisfy criterion (ii) under point (b) of Article 19(1).

Guidance on the assessment of resistance and cross-resistance is currently not included in *Volume II Efficacy Part B/C: Efficacy Assessment and Evaluation*, but some general guidance can be found in the TNsG on Product Evaluation Chapter 6.

4. HUMAN HEALTH

4.1. Information requirements for active substances and biocidal products

Starting points for the evaluation of dossiers for biocidal products as regards the effects on humans are presented in the Common Principles (Annex VI to BPR 528/2012). In summary, in each of the areas where risk assessments have been carried out, the evaluating body shall combine the results for the active substance together with the results for any substance of concern to produce an overall assessment for the biocidal product itself. This shall also take account of any cumulative or synergistic effects. For biocidal product containing more than one active substance, any adverse effects shall also be considered together to produce an overall assessment for the biocidal product itself.

The information requirements regarding the human health risk assessment are explained in Volume III - Part A for which 1.1 (November 2014) is the current version. The information requirements are two-tiered. The core data set (CDS) is mandatory for all product types and has always to be submitted. The additional data set (ADS) must be submitted when required by the intrinsic properties of the active substance or biocidal product, when required by the foreseen use and route of exposure, or when the initial risk assessment must be refined. It is self-evident that the ADS should focus on the information requirements needed for the specific case.

The Ctgb follows the BPR regarding information requirements and has not defined additional requirements. Note that the assessment report for the active substance contains at least the CDS. A letter of access to the relevant active substance dossier(s) is therefore often sufficient, unless additional information requirements are listed in the BPR opinion and/or product specific parameters are necessary. Not also that the Ctgb highly value the purpose of article 62 of the BPR, i.e. to avoid animal testing. Therefore the applicant should have submitted a written request to the Agency to allow them to check whether such tests have already been submitted in connection with a previous application.

In addition to information requirements presented in Volume III - Part A the working group on Human Health (BPC WG HH) adopted the document "Dermal absorption of PT21 active substances" in November 2016. The publication date on the ECHA website was 9-12-2016 and Ctgb implemented the document from 9-12-2016.

The document on dermal absorption PT21 describes the practical ways forward in performing and interpreting dermal absorption studies on antifouling products.
At the moment the protocols as given in OECD guidelines 427 (*in vivo*) and 428 (*in vitro*), supported by OECD Guidance Document No. 28 for the conduct of skin absorption studies, are considered appropriate. Furthermore, the general principles as indicated in e.g. ECHA Guidance Vol III Part A: Information requirements and EFSA Guidance on dermal absorption (2012) are followed. However, some of the recommended procedures or general principles are difficult to apply to film-forming antifouling paints. In this document the practical ways forward in performing and interpreting dermal absorption studies on antifouling products, not supported by the protocols and the general principles as indicated are recommended.

4.2. Information requirements for substances of concern

Some biocidal product may contain at least one substance of concern (SoC) regarding the human health, i.e. a co-formulant that triggers the human health classification of the biocidal product. The SoC guidance for human health toxicology is described in CA-Nov14-Doc.5.11 – SoC guidance_final.doc which is available on the CIRCABC Public Biocides Regulation Page (Circabc public > categories > European Commission> Health and Food

Safety>Biocides – BPR 528/2012 – Public > Library > Documents finalised at CA meetings). In general, the risk assessment should be performed using a pragmatic approach based on expert judgement e.g. based on "the worst case exposure scenario for respiratory exposure to the product as a value in mg/m3 product per day and the content of the co-formulant in percentages of the product be used". In the Netherlands a full quantitative risk assessment needs to be performed for substances for which community workplace exposure limits exists, (see SER lijst and Arbeidsomstandighedenregeling).

4.3. Information requirement for disinfection by-products

DBPs at present will not be part of the product authorisation of DBP forming active substances (e.g. reactive chlorinated/brominated substances, peroxides etc.).

In January 2017 the final guidance on Disinfection By-Products was made available on the ECHA website.
This document summarises background information and provides a strategy for the human health risk assessment of DBPs. This document provides a scientific and pragmatic strategy for the risk assessment of disinfection by-products (DBPs) in the context of authorisation of halogenated biocidal products in swimming-pool water under European legislation.
The risk assessment is based on a set of known marker DBPs, using consensus health-based limit values and published, modelled or measured DBP concentrations under described conditions.
Measurements of concentrations of DBPs after biocide use in swimming-pools are needed to perform the risk assessment. Relevant concentration data may be gathered from available literature. Where needed actual measurements should be performed. Simulation studies or modelling can be used to derive realistic worst case formation levels.

It is recommended that industry parties coordinate activities to refine the risk assessment.

The present guidance focuses on PT2 in swimming-pool water for which human exposure was considered most relevant while discussing the exposures to DBPs (PT2 swimming water, PT11/12). Other PTs for which a DBP-assessment may be needed are PT1, PT4 and PT5, followed by PT3, PT11 and PT12. It is recommended to further investigate the applicability of the present guidance to these PTs.

The guidance should be used by EU member states (CAs and applicants) from January 2019.

Ctgb will inform the applicant that in case there are no concentration data gathered from available literature available actual measurements or simulation data or modelling approaches should be made available by the applicant to be used in the assessments for product authorisations over 2 years. From January 2019 the data for PT2 (swimming water) and the risk assessment based on these data are compulsory. Moreover, the applicants are asked to further investigate the applicability of the present guidance to other human exposure scenarios in PT2 and other PTs and submit data.

4.4. Human health risk assessment

In general the Guidance on the BPR: Volume III Human health, Part B Risk Assessment (active substances) plays a key role in the Human Health risk assessment. This Guidance provides technical advice on how to perform the hazard and exposure assessment and risk characterisation for biocidal active substances with respect to Human Health risk assessment. The latest version is available on the ECHA's website. The applicant must apply the most recent version which is currently 2.0 (April 2015) and includes all additional agreements as published in the Technical Agreements on Biocides (TAB). The TAB is

available on ECHA's website as well. Various updates of the Guidance are expected in the near future. These updates concerns textual and explicatory changes as well as inclusion of agreements presented.

Instructions for the evaluation of toxicity studies are given in the Guidance on the BPR: Volume III Human Health, Part B&C Assessment & Evaluation (Guidance on the BPR: Volume III Human Health, Part B&C Assessment & Evaluation). This Guidance provides technical advice on how to perform the hazard assessment and exposure assessment and risk characterisation for biocidal active substances and products with respect to human health risk assessment

Studies are evaluated by using criteria. This evaluation leads for each study and for each sub-aspect to a toxicologically based endpoint, and finally to the toxicological profile of a substance. In Chapter 1 of the Guidance on the BPR: Volume III Human Health, Part B&C Assessment & Evaluation the hazard identification is described. In chapter 2 the hazard characterisation is described.

Besides the guidances on the BPR and the document with TAB agreements there are also relevant CA documents that should be used for the assessment of the completeness of the dossier and the derivation of endpoints and limit values. A list of CA documents is available on the CIRCABC Public Biocides Regulation Page (Circabc public > categories > European Commission > Health and Food Safety>Biocides – BPR 528/2012 – Public > Library > Documents finalised at CA meetings) . The relevant CA document for the assessment of the completeness of the dossier and the derivation of endpoints and limit values is presented below :

CA-July13-Doc.6.2.b – Final- approach _dermal_absorption.doc

The estimation of human exposure is a fundamental element of the risk assessment process and requires quantification of the levels of exposure for both users of the biocidal product and others who may be exposed following its use.

For each of the identified populations that are likely to be exposed to the biocidal product, it needs to be defined what type of exposure is expected. The type of exposure expected for each of the identified exposed populations should be characterised as primary (direct) or secondary (indirect). **Primary exposure** to biocidal products occurs to the individual who actively uses the biocidal products, i.e. the user. The user may be a professional at work or a non-professional. Professional users differ from non-professional users in a number of aspects and a distinction between the two is necessary in exposure assessments.

Secondary exposure is exposure that may occur during or after the actual use or application of the biocidal product. There can be three main categories that need to be considered as being potential source of secondary (indirect exposure). These are environmental sources from the point of view of treated areas with biocidal products (e.g. a room fumigated with a biocidal product, swimming pool treated with disinfectants), treated articles and dietary exposure sources (covering potential of exposure via consumption of food where residues of biocidal products may be present).

Not all tasks that may be carried out with biocidal products are covered with suitable experimental exposure data or databases/approaches. In such cases suitable information on exposure is required (to be provided by industry to the evaluating CA) to build a risk assessment to indicate appropriate safety for humans during use. The general principles for drawing up exposure estimates are given in the Guidance on the BPR: Volume III Human

Health, Part B&C Assessment & Evaluation (Guidance on the BPR: Volume III Human Health, Part B&C Assessment & Evaluation) available on the ECHA website at Guidance on biocides legislation. This Guidance provides technical advice on how to perform the hazard assessment and exposure assessment and risk characterisation for biocidal active substances and products with respect to human health risk assessment. The Guidance on Exposure Assessment (Chapter 3) should be read together with the Biocides Human Health Exposure Methodology (also available on the ECHA website Guidance on biocides legislation in which the actual estimation of exposure, additional technical guidance on types of generic models, calculations and default parameters are provided. Furthermore the Ad hoc Working Group on Human Exposure supports the Biocidal Products Committee and its Working Groups (especially the Working Group on Human Health) with issues related to human exposure to biocides, including among others:

- Technical or scientific matters as well as generic or specific methodological issues
- Harmonisation of the approach for assessing human exposure to biocides
- Implementation of the strategies of biocides exposure assessment
- Identification of the needs to revise the existing guidance documents on human exposure to biocidal products and contribution to the revision, where appropriate

As a result, opinions of the human exposure expert group and the recommendations of the ad hoc working group on human exposure were developed and available on the ECHA Ad hoc Working Group – Human Exposure webpage (see ECHA website Ad hoc Working Group - Human exposure).

In general, for many applications of biocidal products, harmonised assessment approaches have been agreed, which should be followed when appropriate for the application to be assessed. Besides these harmonised approaches, other models for exposure assessment exist and may be used in cases where no suitable harmonised approach exists In addition the excel file containing default exposure data for all PTs developed under the BPD 98/8/EC present on the ECHA website can be used in cases where no default exposure data are available (Excel file containing default exposure data).

Thus, when choosing a model for exposure estimation, the following ranking shall be observed:

1. Recommendations of the Ad hoc Working Group on Human Exposure (HEAd-hoc)
2. Opinions of the Human Exposure Expert Group (HEEG) (see ECHA website: HEEG opinions)
3. Models and defaults formerly presented in the Technical Notes for Guidance (TNsG) and the respective User Guidance
4. Other Models, e.g., generic models, ConsExpo, RISKOFDERM, etc.

Any deviation from this ranking should be justified.

Besides the guidances on the BPR and the document TAB agreements there are also relevant CA documents that should be used for the risk assessment. A list of CA documents is available on the CIRCABC Public Biocides Regulation Page (Circabc public > categories > European Commission > Health and Food Safety>Biocides – BPR 528/2012 – Public > Library > Documents finalised at CA meetings) . The relevant CA documents for the risk assessment are presented below (documents related to the BPR from 2013-) :

- CA-May16-Doc.5.4.a - Final- User categories of anticoagulant rodenticides about common understanding and adaptation to national situations in case of mutual recognition
- CA-Sept13-Doc.6.2a - Final.Rev1-sensitisers_PPE.doc about authorisation of biocidal products classified as skin sensitisers requiring PPE for non-professional

users

Because for a lot of scenarios there are models/default values missing ECHA recently asked KNOELL consultancy to perform a survey helping drafting a practical manual for the exposure assessment of disinfectant active substances and biocidal products for PT1-5. Although the project performed by KNOELL consultancy has been finished the manual is not available yet.

In addition to the technical advices on how to perform the hazard assessment presented in Volume III - Part B&C the working group on Human Health adopted one important document in November 2016. The working Group on Human Health (BPC WG HH) adopted the document "ADI and ARfD derivation for biocidal active substances". The publication date on the ECHA website was 9-12-2016 and Ctgb implemented the document from 9-12-2016.
The document on ADI and ARfD describes that always an ADI and ARfD should be derived if appropriate information is available, unless it is not scientifically justified (e.g. highly reactive substances where no residues are expected). At the moment the ECHA Guidance Vol III Part B&C (2017) describes that only an ADI and ARfD (if necessary) should be derived if residues in food and feed are expected due to the use pattern of a biocidal product.

4.5. Exposure via environmental sources and Risk assessment

As stated in the Guidance on the BPR: Volume III Human Health, Part B&C Assessment & Evaluation (Guidance on the BPR: Volume III Human Health, Part B&C Assessment & Evaluation) indirect exposure of humans via the environment may occur by consumption of food (e.g. fish, crops, meat and milk) and drinking water, inhalation of air and ingestion of soil.

There are three more specific areas where estimation of risk via exposure needs to be addressed for specific product types and specific guidance is currently under development. It should however be noted that for use scenarios from additional product types (that are not listed below) dietary exposure may be less likely but still has to be considered on a case-by-case basis.

1. Estimating Dietary Risk from Transfer of Biocidal Active Substances into Foods Non-professional Uses.
2. Estimating Transfer of Biocidal Active Substances into Foods – Professional Uses.
3. Estimating Livestock Exposure to Biocidal Active Substances

In the WGIII 2016 meeting has been decided that the Draft Guidance on Estimating Dietary Risk from Transfer of Biocidal Active Substances into Foods – Non-professional Uses together with the Guideline on Risk characterisation and assessment of Maximum Residue Limits (MRL) for biocides- EMA/CVMP/90250/2010 already available on the ECHA ad hoc Working Group – Art food webpage (Artfood) and on the EMEA website (Guideline on Risk characterisation and assessment of MRLs for biocides)) respectively should be used for a preliminary assessment of the transfer of biocidal active substance residue into food and feed if relevant and possible. This preliminary assessment could be included as an annex to the CAR, clearly indicating that the assessment is an eCA proposal. The Guidance on Estimating Transfer of Biocidal Active Substances into Foods – Professional Uses and the Guidance on Estimating Livestock Exposure to Active Substances used in Biocidal Product are not yet agreed upon by the Artfood members and cannot be used by an eCA, yet.

As a result, the following provision should be included in section 2.4 of the BPC opinion on a case by case basis: "An assessment of the risk in food and feed areas may be required at

product authorisation where use of the product may lead to contamination of food and feeding stuffs".

The Ctgb assesses human health risks entirely according to the latest agreed versions of the Guidances. As long as there is no agreed guidance, the conclusion on dietary risk assessment will not affect the approval of the active substance. Having a preliminary exposure estimation to residues in food and feed and dietary risk assessment at the active substance approval phase would serve the purpose of providing useful information for the product authorisation phase.

If it is concluded that evaluation is not possible using the information available in the dossier, it may be necessary to postpone the exposure estimation to residue and the dietary risk assessment to product authorisation stage.

Besides the guidances on the BPR and the document TAB agreements there are also relevant CA documents that should be used for the dietary risk assessment. A list of CA documents is available on the CIRCABC Public Biocides Regulation Page (Circabc public > categories > European Commission > Health and Food Safety > Biocides – BPR 528/2012 – Public > Library > Documents finalised at CA meetings. The relevant CA document for the dietary risk assessment is presented below:

CA-July13-Doc.5.1.i – FCM_Biocides.doc about the regulation of the use of biocides in food contact materials.

5. ENVIRONMENT

5.1. Information requirements for active substances and biocidal products

The information requirements regarding the environmental risk assessment are explained in Volume IV - Part A for which 1.1 (November 2014) is the current version. The information requirements are two-tiered. The core data set (CDS) is mandatory for all product types and has always to be submitted. The additional data set (ADS) must be submitted when required by the intrinsic properties of the active substance or biocidal product, when required by the foreseen use and route of exposure, or when the initial risk assessment must be refined. It is self-evident that the ADS should focus on the information requirements needed for the specific case.

The Ctgb follows the BPR regarding information requirements and has not defined additional demands. Note that the assessment report for the active substance contains at least the CDS. A letter of access to the relevant active substance dossier(s) is therefore often sufficient, unless additional information requirements are listed in the BPR opinion and/or product specific parameters e.g. leaching behaviour (PT06-10) are necessary.

5.2. Information requirements for substances of concern

Some biocidal product may contain at least one substance of concern (SoC) regarding the environment, i.e. a co-formulant that triggers the environmental classification (H400, H410, H411, H412, H413 and/or H420) even without the active substance. SoCs must be included in the risk assessment and their risks are assessed analogue to the active substance. Therefore, the SoC requires the same core data set as the active substance and depending on the physical-chemical properties, the intended use, and possible higher tier risks assessment one or more information items from the additional data set. It is preferable to refer to an existing dossier if the SoC is notified and/or authorised within the BPR and/or REACH. A valid Letter of Access to the relevant dossier is self-explanatory. Alternatively, endpoints derived using quantitative structure activity relationships (QSARs), taken from public resources (e.g. scientific literature), and/or determined experimentally will be accepted as well, but needs to be evaluated by the Ctgb.

5.3. Information requirement for disinfection by-products

Guidance on DBPs is agreed at WG I 2016, but not yet adopted at CA level. This means that DBPs at present will not be part of the product authorisation of DBP forming active substances (e.g. reactive chlorinated/brominated substances, and peroxides).

5.4. Environmental risk assessment

The Guidance on the BPR: Volume IV Environment, Part B Risk Assessment (active substances) plays a key role in the environmental risk assessment. This Guidance provides technical advice on how to perform the hazard and exposure assessment and risk characterisation for biocidal active substances with respect to environmental risk assessment. The latest version is available on ECHA's website. The applicant must apply the most recent version which is currently 1.0 (April 2015) and includes all additional agreements as published in the Technical Agreements on Biocides (TAB). The TAB is available on ECHA's website as well. Various updates of the Guidance are expected in the near future. These updates concerns textual and explicatory changes as well as inclusion of agreements presented.

Emission scenario documents (ESDs) are used to estimate the initial release of substances from biocidal products (or treated materials) to the environment. ESDs for several product types were developed in the EUBEES I and II projects. In addition, ESDs for some product types were developed by the OECD. All finalised ESDs for biocides are available on ECHA's

website, where the ESDs are presented per product type in separate folders. In these folders, relevant additional guidance and information is also presented. For the majority of the intended uses the active substances are released to the sewer. Here, SimpleTreat is used to calculate distribution over air, sewage sludge, and the aqueous phase, and the amount of active substance that is removed by degradation during sewage treatment. Further distribution into the environment is calculated according to the Guideline based on SimpleTreat outcomes (concentrations in air, sludge, and effluent). The version to be applied is 3.1, but it may be expected that version 4.0 will be adopted soon. More information on SimpleTreat is available on the website of the National Institute for Public Health and the Environment (RIVM). Version 4.0 is downloadable from the RIVM-website, version 3.1 is included in the EUSES model which can be downloaded here.

The Ctgb assesses environmental risks entirely according to the latest agreed versions of the Guidance, ESD, and SimpleTreat. Where applicable, the risk assessment will be adapted to the specific Dutch situation regarding intended use, national legislations, and/or a specific emission pattern. These adaptations are explained in the NL specific evaluation manual and does not require additional data. Note that the number of agreed ESDs is limited and scenarios for some applications are not available. There are several options how to deal with missing ESDs:

- It may be possible that the intended use has been assessed in a Competent Assessment Report (CAR) or Product Authorisation Report (PAR). In that case the applied methods has more or less been agreed by the BPC Working Groups and are therefore preferable;
- An existing ESD can be applied as a worst-case surrogate;
- If the concerning product has several applications, emission from the foreseen intended use may be covered by another use regarding consumption and emission routes;
- Emission to the environment can be assessed qualitatively if emission to the environment is negligible due to the foreseen use and risk mitigation measures that prevent unacceptable emission to the environment;
- Propose a new scenario in the Product Assessment Report

Questions regarding scenarios to be applied can be send to the Ctgb service desk.