ECHA
EUROPEAN CHEMICALS AGENCY

Technical Agreements for Biocides

Analytical Methods and Physico-Chemical Properties (APCP)

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Introduction

The Technical Agreements for Biocides (TAB) intends to provide in a concise format the general agreements of the Working Groups (WGs) which have not yet been included in any other BPR related guidance documents.

This document is intended to cover the technical/scientific WG agreements that have general relevance and to create a general database of questions where an agreement has already been reached. Only agreements of general relevance have been included.

The TAB is publicly available on the ECHA website and on the public S-CIRCABC Interest Group.

The answers presented in the document are those agreed by the APCP-WG. They are not the official view of ECHA or the Commission, nor are they legally binding.
It is not an authoritative source of information, and when in doubt, the original documents cited should always be consulted. The main sources for the TAB are the adopted minutes of the APCP-WG, and in all cases, a reference is given to the WG meeting or the Technical Meeting (TM) where the agreement was reached.

Procedure

TAB does not require a formal endorsement by the Biocidal Products Committee or the APCP-WG because the document records agreements made at the APCP-WG and included in their minutes. It is a living document that will be updated over time with new additions. Any suggestions on the need to change the content can be sent at any time to BPC-WGs@echa.europa.eu.

The text will be updated regularly by uploading a revised version in the Newsgroups of the BPC-WG S-CIRCABC site for a commenting period of 4 weeks for the WG members. After the commenting period, ECHA will revise the TAB if necessary, and publish it on the ECHA website.

The procedure does not involve discussions at the APCP-WG. However, the TAB entry may be discussed at the APCP-WG, if necessary.

1. Substance Information

1.1. Reference specification and reference source

1.1.1. Reference source under the Biocidal Products Regulation (BPR) (EU) No 528/2012

In summary, the following definitions have been agreed:

- A source is defined by the following information:
  - the applicant
  - the manufacturer
  - the manufacture location/plant location
  - the manufacturing process

- The specification is set by the applicants and should be in general derived from a 5-batch analysis. Quality control data might be used to refine or support the specification set by the applicant. In specific cases, it might be possible to refer to specifications set by other pieces of legislation e.g. the European Pharmacopeia or specifications set for food additives. Nevertheless, these specifications need to be supported by analytical data.

- Reference specification can be defined as the specification compared to the test substance used for the provided studies and adjusted by the experts of toxicology, ecotoxicology and chemistry taking into account the content of the different constituents in the (test) substance. Hence, it can be regarded as a scientific refinement of the specification.

  - The experts can narrow or expand the specification based on quality control data, the composition of the test substance or expert judgement based on the physico-chemical, toxicological and eco-toxicological properties of the substance. A sound scientific justification should always be provided when the reference specification deviates from the specification.

  - There should always be one reference specification for one application. This also applies for an application, which includes several applicants, e.g. task forces. In cases of several applicants with their own active substance dossier, the reference specification with the lowest purity is taken for the inclusion in the Union list.

  - Reference source is the combination of a source and the set reference specification considering the provided studies (including the composition of the test substance). Each applicant (including consortia and task forces) might have its own reference sources.

(WG II 2014, WG III 2014, WG II 2015)

1.1.2. Reference specifications based on other pieces of legislation, European Pharmacopoeia or EN norms NEW

The reference specification can also be set by referring to other pieces of legislation, e.g. food additives, European Pharmacopoeia or EN norms. In these cases, the reference has to be clearly identified with the exact title and year (date of issue). It has to be highlighted that also these reference specifications have to be confirmed by providing 5-batch analyses.

In cases where the substances are listed in the European Pharmacopoeia and the manufacturing sites are certified according to the procedure of the European Pharmacopoeia a 5-batch analyses is not required. As the requirement for a 5-batch analysis can be considered to be covered by the certification procedure for including the manufacturing site into the European Pharmacopoeia. Therefore, in such cases the submission of certificates of analysis together with proof that the manufacturing site is certified are considered sufficient.
(WG IV 2016 and WG I 2017)

1.1.3. More than one reference specification

More than one reference specification could be established due to the fact that more than one dossier for the same substance have been submitted and separately evaluated. The reference specification is one characteristic of the agreed reference source(s) therefore the reference source(s) is/are bond to their reference specification(s). Can a reference source of one dossier use the reference specification of another dossier of the same active substance?

The following is agreed:

- The purity of the active substance should not be lower than the minimum purity indicated in the implementing regulation.
- The impurity profile remains the same (i.e. no new relevant or significant impurities are present).
- The limits of all significant but not relevant impurities as certified on the basis of a five batch analysis for the reference source cannot exceed by more than the following limits:

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Limits of significant but not relevant impurities in the technical specifications of the reference source	Acceptable maximum increase in the alternative source
≤6 g/kg	3 g/kg
>6 g/kg	50% of the certified limit

If one of these conditions is not met, the applicant has to submit an application for the assessment of technical equivalence.
(WG I 2016)

1.1.4. Reference specification for in situ generated substances

To set the reference specification for in situ generated active substances the following information should be provided:

- Generation process including the conditions and their variation.
- Information on the starting materials and reaction products (complete specification of the starting materials and possible maximum concentrations of the reaction products).
- Information on the equilibrium (individual constituents measured with validated methods on one batch of the equilibrium at a defined condition).
- Quality control data of the in situ generated active substance as an indicator for the level of variation of the composition at different conditions: pH, temperature, dilution. Further conditions of the equilibrium might be required for product authorisation.

(WG II 2014)

1.1.5. Number of reference sources

The CAR can include as many (reference) sources as complying with the reference specification. However, these sources must be included in the CAR for approval of the active substance. All sources, which are not included in the CAR but used for biocidal products, must apply for the assessment for technical equivalence to ECHA before they can be used for product authorisation.
(WG III 2016)

1.2. Substance composition and 5-batch analysis

1.2.1. GLP requirement for 5-batch analysis

The 5-batch analyses including the method development and validation of the method shall be conducted by a GLP certified laboratory. In cases the study was not (e.g. for dossiers submitted under the BPD) conducted under the GLP requirements, quality control data need to be presented to support the analysis.
(WG IV 2014 and WG V 2015)

1.2.2. Age of 5-batch analyses UPDATED

In general, the age of a 5-batch analysis shall not exceed 5 years based on the date of analysis; the date of manufacture of the batches shall also not exceed 5 years. In cases where the age of the 5-batch analysis is in the range of 5 to 10 years a justification has to be provided by the applicant (e.g. quality control data) to support the results of the 5-batch analysis and to proof that the batches are still representative for the manufacturing

process and that the proposed specification still applies. 5-batch analyses conducted more than 10 years ago cannot be accepted and shall be replaces by a new 5-batch analysis. (WG III 2014 and WG IV 2015)

1.2.3. **Quality control data (QC)** 

When submitting QC the following issues have to be considered:

- Period of monitoring/age of the data: not older than 5 years.
- Frequency of monitoring and data points: all batches of the time period (<5 years) that can be summarised with the number of data, the maximum and minimum of the measured values. However with the possibility to request all (raw) data.
- What should be monitored: minimum purity, the content of significant impurities and the content of the relevant impurities; in case this information is not measured and therefore not available, a new 5-batch analysis might be requested.
- Outliers: outliers should be considered carefully on a case-by-case basis; blending might be possible or discarding of those batches.
- Quality system: in-house methods or general production methods are acceptable, that need not to be fully validate and specific. Validation data of the analytical method must be available and might be requested from the applicant.

(WG III 2016)

1.2.4. **Certificates of analysis (CoA)** 

In general, the CoA should cover to blocks of information, administrative information and technical information.

The administrative information shall include:

- Header (Certificate of analysis)
- Name and address of the supplier or manufacturer
- Name and address of the manufacturer
- Name and address of the manufacture location/site
- Name and address of the testing laboratory
- Date, printed names and signature(s) of analysts
- Date, printed names and signature(s) of approver
- Date of analyses
- Lot/Batch number and size
- Date of Manufacture
- Product code or number
- Expiration date of the analysed substance

The technical information shall include:

- IUPAC-, CAS-, ISO- (if available) and general name of the substance analysed

- EC- and CAS-number of the substance analysed
- Appearance of the test material (e.g. powder including particle size)
- Stability and storage statement
- Name of the test, used analytical instruments and method applied (including analytical, physical and physico-chemical tests)
- Test result (which should include the chemical composition of the substance, at least the content of the active substance and relevant impurities.)
- Acceptance criteria (e.g. product specification)

(WG IV 2015)

1.2.5. For a substance that is not stable as such, should the Annex I inclusion be for a dry form, or should the water content and/or stabilizers be included? Does it matter whether the substance is not stable as the dry form?

The dry form will be listed on Annex I. Where testing cannot be performed using the dry form, this will affect the testing approach but not the content of the Annex I inclusion.
The applicant has to provide an explanation on why data on the dry form cannot be generated. The CAR should give clear information on what the actual tested substance was.
(TM V 2007)

1.2.6. How to derive the theoretical dry weight specification? Calculation method

The dry weight composition needs to be calculated and included in the CAR. For Union list inclusion, it was agreed that the REACH guidance for identification and naming needs to be followed and the purity should refer to the dry matter. For the Union list inclusion, the actual content of the substance is to be considered.

Following considerations need to be taken into account:

- 5-batch analyses are to be performed on the technical concentration and not on the dry material since the data should reflect what it is actually manufactured. Meanwhile the purified material is to be used for determination of the physico-chemical properties.

- The dry weight can be calculated with the method of calculations:

$$CDWn\ (\%) = \frac{Cn(concentration\ in\ TK)\ (\%)}{\Sigma\ Cn\ (concentration\ in\ TK\ without\ solvent)(\%)} * 100\ \%$$

CDWn = dry weight concentration of constituent "n"

OR

$$content\ active\ (TC, dry)\left(\frac{g}{kg}\right) = \frac{measured\ value\ (TK)\left(\frac{g}{kg}\right)}{sum\ of\ measured\ values\ except\ solvent\ in\left(\frac{g}{kg}\right)} * 1000\frac{g}{kg}$$

- Solvents and additives. Additives are constituents of substances, which do not contribute to the naming of the substance, but they have to be considered for the substance composition. Therefore, a change of an additive triggers a technical equivalence assessment. Solvents, which are not needed for stabilisation of the substance or can be removed without affecting the substance composition, should be not considered for the substance composition.

(WG II 2014, WG III 2014)

1.2.7. **Iodate in biocidal products: use as redox agent** UPDATED

Iodate in biocidal products: use as redox agent
Iodate (IO_3^-) and iodide (I^-) can be present as co-formulants in biocidal products containing iodine as active substance (a.s.). The function of these substances, usually designated as stabilisers within biocidal products, is not always adequately described. Therefore, further explanation is needed on the status of these two compounds within the scope of iodine containing product authorisations.

In the context of this document, the following two cases are explained for iodate (and iodide) present as co-formulants in true products:

1.
Biocidal products formulated with: IO_3^- + I_2 , but no I^- present
The biocidal product is formulated with iodine (a.s.) and iodate (co-formulant) but no iodide is present. Iodine reduces over time, to a certain extent, to the degradation product iodide. Iodate and iodide (re)form iodine by a redox-reaction, which results in a stable iodine concentration in the biocidal product. A concentration increase of iodine in the biocidal product might be temporarily observed. It should be noted that no impact on the efficacy is expected. Therefore, iodate is regarded as a co-formulant acting as redox agent.

2.
Biocidal products formulated with: IO_3^- + I^- + I_2
The biocidal product is formulated with iodate, iodide (co-formulants) and iodine (a.s.). Several chemical reactions may occur in parallel and can be described as:
a) Iodine (I_2) is reduced to iodide ($2I^-$);
b) Iodate and iodide react in a redox reaction to iodine.

Iodate and iodide (re)form iodine by a redox-reaction, which results in a stable iodine concentration in the biocidal product. A slight concentration increase of iodine in the biocidal product might be temporarily observed due to involvement of iodate and iodide in this reaction. It should be noted that no impact on the efficacy is expected. Therefore, iodate and iodide are regarded as co-formulants acting as redox agents.

For both co-formulants, the risk assessment of the biocidal product should take into

account the maximum theoretical concentration of all iodine sources (meaning iodine and iodate and/or iodide that can be converted to iodine equivalents). However, in case unacceptable risks have been identified as a result of the consideration of total dietary intake of iodine (including co-formulants) due to the use of biocidal products, it is not considered appropriate to take risk management decisions in isolation with respect to the biocidal product.

Conclusion
Within the scope of applications for authorisation of iodine containing products, iodate and iodide as above explained are considered co-formulants with the function redox agents.
(BPC-24)

1.2.8. How much information on the isomeric ratio should be required?

The exact chemical identity and composition of the substance must be known. This includes detailed information about isomers and their ratio.
(TM III 2006)

1.2.9. Minor concentration isomers (<10% w/w) UPDATED

According to REACH guidance for identification and naming of substances, a mono-constituent substance is a substance in which one constituent is present at a concentration of at least 80% w/w and which contains up to 20% w/w of impurities. A substance as manufactured that contains an individual isomer of at >80% w/w are considered as a mono-constituent substance. All other isomers present in the substance at <10% w/w are generally considered impurities, unless it can be demonstrated that these isomers contribute to the efficacy of the substance. Isomers that are present at <10% w/w and make a contribution to efficacy of the substance can be considered as "minor isomers" in order to differentiate them from general process impurities. However, the information about the efficacy of each individual isomer might not always be available or difficult to generate. In such cases, the eCA should consult the working group members case by case to decide on the most appropriate name. ISO names can only be used if the isomeric composition described in ISO definition of the substance is met. Consistency with other legislations (REACH, CLH, and PPP) should be taken into account for the naming of active substances.
(TM II 2011, WG IV 2017)

1.2.10. Redefinition of active substances NEW

In case where an active substance require a redefinition according to Article 13 of Commission Delegated Regulation (EU) No 1062/2014, the following procedure was agreed:

- The eCA and applicant discuss and agree on the redefinition of the substance.
- The eCA initiate an early working group discussion (APCP) for the redefinition.
- The applicant is invited to the early WG discussion.

- During the early working group discussion, member states, applicant and ECHA can exchange their views and agree/disagree on the redefinition of the active substance.
- In case of disagreement, the active substance is not redefined.
- In case of agreement, the eCA informs officially ECHA about the redefinition after the working group meeting.
- ECHA updates the Registry.
- ECHA publishes the invitation to take over the role of participant.

(WG III 2016)

1.2.11. **Commodity Chemicals** 

A binding definition of and selection for commodity chemicals is not available, hence so-called "commodity chemicals" are treated as other types of substances. Independent of the type of substances, sufficient information needs to be provided to characterise the composition of the substance and its identity. Therefore, a special treatment of commodity chemicals is regarded as not appropriate and the mandatory information about substance identification shall be decided by the evaluating member state (eCA) on a case-by-case basis. However, the eCA shall initiate an e-consultation for getting agreement about the required analytical information and whether the available results are sufficient to characterise the active substance. In cases where reduced information is sufficient or an alternative approach for setting the reference specification is acceptable, this procedure is also to be followed if an application for the assessment of technical equivalence will be submitted to ECHA. Further, active substances supplied by alternative suppliers, listed on the Article 95 list, must be approved as technically equivalent. It is the responsibility of the applicant for biocidal product authorisation that the used source is traceable.
(WG II 2017)

1.3. Technical equivalence and chemical similarity

1.3.1. **Chemical similarity checks for the evaluation of multiple dossiers of the same active substance**

For the evaluation of multiple dossiers of the same active substance, the assessment of chemical similarity is not regarded as necessary when the applicants provided their own complete and compliant data packages, which allow individual evaluations of the substance. Hence, the applications refer to their own reference sources. Therefore, a chemical similarity check is not necessary as sufficient information is provided to support the approvals of the active substance. However, in such cases more than one reference specification might be acceptable. It has to be noted that a combined CAR and list of endpoint needs to be provided by the eCA.
(WG II 2014)

2. Physico-chemical properties and physical hazards

2.1. General issues

2.1.1. Can data on physico-chemical properties be put into classes? For example, can water solubility be expressed verbally, based on threshold values: very slightly soluble – slightly soluble – moderately soluble – readily soluble?

The TM agreed that this should not be done, except for volatility and with respect to classification and labelling criteria.
Instead of verbal descriptions, actual values should be used in the report, avoiding terms like "high" or "low" as far as possible.
(TM I 2006)

2.1.2. Use of literature 

The 'Guidance on Biocidal Products Regulation; Volume I: Identity/physico-chemical properties/analytical methodology – Part A: Information requirements' includes already criteria for the use of literature: "Public literature data can be used in the assessment if the following conditions are fulfilled:
a.
The data comply with the BPR Annex II, III introduction points 5-9.
b.
The identity, purity and the impurities of the substance have to be defined in the publication and to be comparable with the substance addressed in the application.
c.
The reporting of the study allows evaluation of the quality of the study. If conditions a - c are met the applicant can claim that adequate data is publicly available. Providing that the quality of public data fulfils the criteria, it can be used as key studies."

The criteria have further specified as follows:

- Journals can be used if
  - The exact method is given
  - The purity of the test substance is indicated
  - The results are given and discussed
- Handbooks can be used for none critical endpoints (density, melting- and boiling point)
- Safety Data Sheets (SDS) are not accepted

Further, it was highlighted if different literature sources have conflicting results/data for an endpoint a test and study on this endpoint has to be submitted.
Literature referring to analytical methods can be used as long as it includes complete and sufficient information on the validation and its parameters.
(WG III 2017)

2.2. Surface tension

2.2.1. What is the trigger for the surface activity?

The trigger value for surface activity has been set to 60 mN/m at 20 ºC. This value is in accordance with the cut-off value of 60 mN/m as stated in point A.5 of COUNCIL REGULATION (EC) No 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). In this regulation, it is stated "Considering that distilled water has a surface tension of 72.75 mN/m at 20 ^{0}C, substances showing a surface tension lower than 60 mN/m under the conditions of this method should be regarded as being surface-active materials." The method described is based on OECD test guideline 115.
(TM III 2011, TM IV 2012)

2.3. Flammability and auto-flammability

2.3.1. Can the studies on flammability and auto-flammability be waived?

Either a scientific sound justification needs to be provided or the tests must be conducted.
(WG IV 2015)

2.4. Storage stability

2.4.1. Consideration about the storage stability tests

A degradation of content of the active substance by more than 10% should be assessed on a case-by-case basis as the request of further information depends on the active substance and the product. Hence, the setting of maximum degradation limits are regarded as not appropriate. In general, if a decrease of the active substance content by more than 10% should be assessed it requires further efficacy data, information on the degradation products and information on the toxicity and eco-toxicity of these degradation products.
Overdosing is not acceptable and there are no criteria on overdosing available.
Due to the complexity of the different groups of UVCB substances, the assessment should be done case by case. It has to be highlighted that for UVCB substance not only the analytical data should be considered but also other parameters such as the analytical finger-print, physico-chemical properties, toxicity and eco-toxicity data may be used along with efficacy data after storage.
(WG I 2016)

2.4.2. Accelerated storage stability 

The following conclusions have been made with regard to the accelerated storage stability:

1. The accelerated storage stability test under test conditions is negative but no complete shelf-life study is available:

- An accelerated storage stability test at lower temperature can be provided. In case this test is acceptable, a lower storage temperature shall be indicated on the product label of the biocidal product.

- Further information and tests can be provided for demonstrating that the biocidal product is still efficacious and the degradation products are not influencing the hazard and risk characterisation of the biocidal product.

- A provisional product authorisation can be issued if one of the above-mentioned options is met. The provisional authorisation, which should be based on intermediate data from the two years shelf life study, can be granted up to two years or until the complete shelf life study has been evaluated.

2. In case the degradation of the active substance exceeds 10% in the accelerated storage stability test and no long-term storage stability test or another acceptable accelerated storage test is available, degradation products have to be identified and quantified. The hazard and risks have to be assessed for degradation products.

3. The OECD guideline and the Manual on development and use of FAO and WHO specifications for pesticides states that the decrease should not be more than 5%, whereas a 10% threshold for degradation was agreed and applied previously under the BPD. It was agreed that the 10% threshold should also be applied under the BPR.

(WG II 2017)

2.5. Corrosive to metals 

A substance or a mixture that is corrosive to metal under normal conditions is a substance or a mixture liable to undergo an irreversible electrochemical reaction with metals that leads to significant damage or, in some cases, even to full destruction of the metallic components. The corrosive to metal property is a quite complex property, since it is a substance (or mixture) related as well as a material (metal) related property. This means a corrosive substance or mixture leads to corroded material (metal), according to a number of external conditions. From the material side, many types of corrosion processes may occur, according to configurations, liquid or fluid media inducing the corrosion process, nature of metal, potential passivation occurring by oxide formation during corrosion.

Following parameters are helpful to evaluate corrosive properties before testing:

- melting points for solids
- chemical nature of the substances and mixtures under evaluation (e.g. strong acids)
- pH values (liquids)

The following substances and mixtures should be considered for classification in this class:

- substances and mixtures having acidic or basic functional groups
- substances or mixtures containing halogen

- substances able to form complexes with metals and mixtures containing such substances

Corrosivity to metals is so complex that the evaluation of a mixture cannot be extrapolated from similar behaviour of components of a mixture. However, if one component of a mixture is corrosive to metals the mixture is likely to be corrosive to metals as well. Testing the actual mixture is therefore highly recommended.

No test is required if the product is:

- halogen-free
- no acid
- no base
- no complexing agents
- pH-neutral

All above mentioned points **must be fulfilled**.

The following aspects are important:

- The interaction or reactions of ingredients play a role, i.e. the possible reaction products are to be considered and also if whether buffers or stabilizers are used. Products containing stabilizers must be tested over the whole period of four weeks, since the stabilizer can already be consumed after one week, which then cannot be recorded with a test period of only one week.

- Properties and reactions of the individual substances are known.

- Water content of organic substances: drop formation may occur during testing and the increase of concentration, causing localized corrosion.

- The classification criteria of the corrosion rate of 6.25 mm/a are not met, but the criteria of pitting corrosion!

Waiver examples which **are not acceptable**:

- No applicable. The products are not transported or stored in steel or aluminium containers.

- Not applicable because the products do not contain substances classified as corrosive to metals.

- The commercial packaging types which are in contact with the biocidal product do not include metal containers.

(WG II 2018)

3. Analytical Methods

3.1. General

3.1.1. Do the analytical methods used to support environmental studies need to be validated?

Analytical methods have to be validated in order to ascertain that the method is suitable for the purpose. In case that a specific method is not validated a scientific sound justification need to be provide to conclude whether the method is acceptable for the purpose.
(TM I 2004)

3.1.2. Stereo isomers 

The analytical method for the active substance shall be specific or highly specific to analyse each individual stereo isomer of the substance. Therefore, the stereo isomers should be analysed by chiral chromatographic method. In case of racemic mixtures, an analysis of the optical rotation may be acceptable.
(WG IV 2015)

3.2. Analytical methods for residues

3.2.1. Is there any flexibility for the delivery of the confirmatory analytical methods for residues?

TM I 2012 accepted to leave the applicants some more time for the development of confirmatory methods for residues and/or their validation, in some specific cases granting the permission to provide the information to the RMS 6 months before product authorisation.
The TM also accepted to allow applicants not to submit confirmatory methods for residues in air when same methods are sufficiently validated in soil and water, as these matrices that are more complex.
(TM I 2012)

3.2.2. Monitoring methods for relevant impurities 

In cases where relevant impurities or metabolites, generated during product storage, are present in the biocidal product, a fully validated and specific analytical method is required. Additionally, the following applies:

- In cases where relevant impurities are present or metabolites are generated during storage a determination of the content of the relevant impurities/metabolites before and after the storage stability test is required.

- In cases where no relevant impurities are present or metabolites are generated during storage, no determination of the content of relevant impurities/metabolites is required before and after the storage stability test.

(WG V 2015)