ECHA
EUROPEAN CHEMICALS AGENCY

Guidance on the data requirements and assessment of applications for renewal of approval of active substances under BPR

November 2020

Background

The renewal of approval of an active substance is based on the provisions of Biocidal Products Regulation (EC) No 528/2012 (BPR). Chapter III of the BPR addresses the procedure of renewal including conditions, which have to be met for a renewal to be granted. Specifically, articles 12, 13 and 14 of BPR refer to the conditions of renewal submission, the acceptance of applications and the evaluation of applications for renewal.
Supplemental information and further details on the submission of applications for renewal are specified in:

- Note agreed by the Member State competent authorities for biocidal products (CA-July17-Doc.5.3-Final)
- Practical Guide chapter on the renewal of the approval of active substance

This document includes guidance on data requirements and on the assessment of applications for renewal; it should be read in conjunction with the above documents and BPR.

Legal Notice

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List of abbreviations

Standard term / Abbreviation	Explanation
APCP	Analytical methods and Physico-Chemical Properties
AS	Active Substance
BPC	Biocidal Product Committee
BPR	Biocidal Products Regulation
CAR	Competent Authority Report
CLH	Harmonised Classification and Labelling
CMR	Carcinogen Mutagen Reproductive toxicant
eCA	evaluating Competent Authority
ECHA	European Chemicals Agency
ED	Endocrine Disruption
EU	European Union
GLP	Good Laboratory Practice
IUCLID	International Uniform Chemical Information Database
MSCA	Member State Competent Authority
PNEC	Predicted No Effect Concentration
PT	Product Type
RAC	Risk Assessment Committee
RAR	Renewal Assessment Report
RNL	Renewal
TAB	Technical Agreements on Biocides

1. Preparation and submission of the application

1.1. General

The objectives of the assessment for the renewal of approval of active substances should guide the preparation of the dossier and its assessment.
The objectives are the following and the assessment report should be revised as necessary to meet them:

1) Check if the active substance still meets the conditions of approval in accordance with BPR Article 12 (1, 2),
2) Assess mandatory endpoints or criteria that have not been previously assessed,
3) In light of new information and scientific and technical progress, consider possible change to the main conclusions and the reference values.

The applicant should start preparing the submission of the dossier for renewal of approval by considering any technical and scientific changes in the information requirements and the evaluation of active substances since the time of the initial approval or previous renewal. To this purpose, the BPC document "Applicability time of new guidance and guidance –related documents in active substance approval" should be considered. If applying new guidance would lead to generate new data, the applicant is advised to confirm this with the eCA at the pre-submission meeting(s). In particular, if studies on vertebrates are required (e.g. for ED assessment), the applicant should always confirm this with the eCA and the Agency as instructed in BPR Annex II and Article 62(2).

The applicant should ensure that the dossier allows to draw key conclusions on the renewal of the approval and in particular on the exclusion criteria. In this respect, the applicant should consider the information requirements of the Biocidal Products Regulation (annexes II and III). Any generation of new data should be finalised by the time of the submission of the dossier. The applicant should also identify any new information available on the active substance since the previous approval or review and include any relevant data in the renewal dossier; this relates in particular to the notifications of adverse or unexpected effects submitted under the provisions of Article 47 (1) when they are related to the active substance.

The applicant should search for information in the scientific literature or other publicly available information, to assess whether there is new information questioning or confirming the conclusions of the initial approval. The timeframe of the search should cover the time since the previous literature search and might need to be expanded for the endpoints not previously assessed (e.g. endocrine disruption).

When referring to open literature studies, the applicant (or the eCA in the Assessment Report) should bear in mind that the information on the test substance may be limited and this may prevent the comparison with the reference specifications. This should therefore, be taken into account when selecting the studies to consider for the assessment.
The reliability of the studies should be also considered and used in a weight of evidence approach, rather than for rejecting studies.

Moreover, the applicant needs to anticipate the generation of data on ED properties on their active substance, so that the necessary data is generated and included in the submission of the application.

The IUCLID dossier submitted by the applicant should include the Renewal Assessment Report (RAR) and the Renewal Document. Detailed instructions on the preparation of these documents are provided below.

1.2. Submission of dossier

In accordance with Article 13 (2), the applicant shall submit data on the active substance it has generated after the initial approval or the previous renewal of approval. The applicant should also submit its assessment on whether the conclusions of the initial or previous assessment on the active substance remain valid and any supportive information to substantiate this conclusion. The change of the reference product and its uses should normally be avoided in order to minimise the work needed; however, there might be situations where it is appropriate to replace the representative product or its uses considered in the previous approval by another one, which corresponds more to the products that are actually on the market.

The Applicant should include the following in the IUCLID dossier submission:

- For the endpoints where no new data or no revisions are provided, an assessment of why the conclusions of the initial assessment remain valid, and any supporting information (e.g. data requirements and/or guidance documents not changed since initial approval or previous re-approval; no new information is available nor from applicant neither from open literature search).
- For the endpoints where new data or re-assessment are provided, a justification for the new data or the reason for re-assessment. The justification could include among others:
    - information that has become available on the active substance since its approval, including the related study summaries,
    - data requested or answers to issues raised and left open at the time of the initial approval,
    - change of data requirements,
    - changes to scientific and technical knowledge, development of guidance documents,
    - necessity to amend and/or extend the conditions of approval, or to change the range of representative uses.

1.3. Template for draft risk assessment – Renewal Assessment Report (RAR)

The BPR template for draft risk assessment report, which is a combined CAR and CLH report template, should be used for the RAR (https://echa.europa.eu/support/guidance-on-reach-and-clp-implementation/formats). Notably, a proposal for harmonised classification and labelling is necessary under the renewal of approval if the active substance has not yet been classified. The parts of the assessment that have not changed since the initial approval have to be copied in the relevant sections of the new template. The parts where the evaluation of previously submitted studies and the risk assessment has changed, have to be highlighted. Any new studies/information or assessment have to be highlighted as well. The new studies have to be highlighted in the table of contents and in the reference list as well.
The Applicant should include the following in the RAR:

- For substances that meet the exclusion criteria, an assessment on whether at least one of the conditions set out in Article 5(2) is met and for which precise use(s) and a proposal for the appropriate risk mitigation measures to ensure that the exposure of humans, animals or the environment is minimised.
- For active substances approved before June 2018, or for which the assessment report was submitted before 1st September 2013, the endocrine disruption (ED) properties were not assessed in accordance with the criteria in Commission Delegated Regulation (EU) No 2017/2100 or the BPC could not reach a conclusion on ED properties. Assessment in the light of this new criteria is therefore essential in the context of the renewal, therefore the applicant should refer to the document CA-September18.Doc.7.5.a "Implementation of scientific criteria to determine the

endocrine-disrupting properties of already approved active substances" and the EFSA – ECHA guidance[1].
The applicant should provide either an assessment of ED properties, if not assessed previously, or a justified statement that the conclusions of the latest assessment are still valid. The applicant should also indicate whether they have generated or considered any new information for this purpose. The assessment of ED properties should be included in the relevant section of the RAR.
For CMR substances that meet the exclusion criteria, assessment of ED properties is still required in accordance with CA document CA-March18.Doc.7.3.a- Final.

- The new studies shall be included in the list of studies submitted for the renewal of approval of the AS indicating whether they are considered relevant[2] renewal data. The decision whether a given study is considered relevant renewal data for the purpose of Article 95 will be taken by the eCA when the evaluation is finalised.

RAR has to be attached in section 13 of IUCLID dossier.

1.4. Renewal Document

The applicant should provide a short overview on the application for renewal in a separate "RENEWAL DOCUMENT" (RNL DOC template in Appendix I). This document will serve as the basis of the discussion at the pre-submission meetings of the applicant with the eCA, since no RAR will be available at that time. The purpose of the RNL DOC is to provide a quick overview of the active substance approval and the new information and revisions that the applicant intends to submit at RNL. The document may undergo significant revision(s) pending on the outcome of the pre-submission meetings and with the agreement of the eCA.

At the submission of dossier, the final RNL DOC should be submitted in Section 13 of IUCLID dossier as Appendix to RAR and include a reference list of all new studies providing their section in the RAR.

1.5. 5-Batch analysis and reference specifications of the active substance

The applicant must provide a new 5 batch analysis in accordance with the APCP WG instructions. Hence, a new 5-batch analysis must be provided where the batches are older than 10 years; quality control data must be provided where the age of the batches is between 5 and 10 years.
For active substances that were approved without reference specifications or reference sources, a reference specification should be set at renewal.
For the rest of the substances, in principle, the reference sources of the active substance and the reference specifications will remain the same as in the initial approval. In exceptional situations, the reference specifications would be adapted if justified by safety concerns linked to the previous reference specifications.
In case the renewal applicant does not support a reference source, no five batch analysis is required for the alternative source supported at the renewal. The renewal applicant can only use alternative sources that are assessed as technical equivalent. Consequently, no new or updated reference specification will be established at renewal.

[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7009395/pdf/EFS2-16-e05311.pdf

[2] CA-Sept20-Doc.7.1.b document on Relevant Renewal Data under Article 95 proposes the following criteria: Data which was not provided in the initial AS/PT approval or previous renewal; and which was submitted in the context and for the purpose of the most recent AS/PT renewal; and which was considered relevant by the eCA for the purpose of the most recent AS/PT renewal.

The alternative sources that have previously been assessed as technically equivalent will not need to be re-assessed following the renewal of the active substance as the set reference specification will not be changing during the renewal.

1.6. Pre-submission meetings

Pre-submission meetings between the prospective applicant and the eCA shall take place in order to provide clarifications in particular on issues raised and left open at the time of the initial approval or that might lead to identify the substance as meeting the exclusion or substitution criteria. The discussion shall be based on the Renewal Document.

If the initial approval of the substance for a given AS/PT was granted based on derogation criteria, the eCA and the applicant are encouraged to initiate at the pre-submission meetings, the discussion whether the exclusion criteria are still met and if this is the case, whether the derogation conditions could still be satisfied.

Detailed discussion is needed on parts of the assessment not addressed in the initial approval, previous renewal or review of the approval, e.g. assessment of endocrine disrupting properties. Applicants should anticipate and discuss with the eCA well before the deadline on the need to generate new data to investigate ED properties. The discussion should start sufficiently in advance (i.e. several years) of the submission to avoid delays due to missing data.

Pre-submission meetings should take place between the prospective applicant and the eCA as early as possible, preferably 3 years before the deadline of submission. Such anticipation would ensure a good preparation and dialogue between the prospective applicant and the eCA, with the view to facilitate the renewal process on the active substance.

2. Evaluation by the eCA of the application for renewal

The eCA shall make an independent, objective and transparent assessment in the light of current scientific and technical knowledge. It shall take into account the renewal dossier, and, where appropriate, the dossiers submitted for the approval, subsequent reviews and renewals of the approval. Notably, no "validation" step is foreseen in the BPR for the applications for renewal[3]: once the application is accepted by ECHA, the eCA shall start assessing the application.

Decision on full evaluation
Article 14 (1) indicates that the eCA is responsible for deciding within 90 days whether, on the basis of an assessment of the available information and the need to review the conclusions of the previous evaluation, a full evaluation is necessary. Article 14 (1) also states that the decision shall be taken in the light of current scientific knowledge. Therefore, the eCA should carefully consider the following:

- whether the dossier submitted meets the data requirements for the applicant as specified in the present document;
- In case an assessment of endocrine disruption properties is included, whether the data available are sufficient to support this assessment or whether additional information could be necessary later during the evaluation (e.g. for non-target organisms).

The eCA should consider also that under the full evaluation, request for further data is possible since the evaluation is done in accordance with Article 8 (1, 2, 3), whereas under the limited evaluation request of further data is not foreseen. It should be noted that Article 8(2) of the BPR is applicable in case of full evaluation. In particular, the eCA may require the applicant to

[3] The "Validation" step in R4BP is a task item for the eCA to accept/reject the application if the fee is (non) submitted and to decide whether the full evaluation should be undertaken or not. This step is not relevant to the validation procedure described in article 7 par. 4.

provide sufficient data to permit a determination of whether an active substance meets the exclusion or substitution criteria.

If the applicant fails to submit the information agreed upon at the pre-submission meeting or requested by the eCA during evaluation, the eCA will indicate this data gap in the RAR. It may then not be possible to propose the renewal of the approval of the active substance due to lack of evidence that the conditions in Article 4 of the BPR are met.

The eCA may consult the Agency / or the MSCAs about the decision to undertake or not full evaluation. If other MSCAs than the eCA are aware of data relevant for the renewal, they should inform the eCA. They can also communicate to the eCA their views and related justifications on the need to review the conclusions of the previous evaluation. Such communication should preferably occur before the deadline for making applications for the renewal of the AS.

The eCA and the applicant should have a common understanding of how the decision to undertake full evaluation is taken. To this purpose, clear criteria should be set.

Possible option/criterion for decision to undertake a full or limited evaluation

The eCA should conduct a full evaluation unless all the following conditions are met (based on the information provided by the applicant):

- The original or previous assessment report contains an assessment of the substitution and exclusion criteria including ED properties of the active substance according to the criteria in Commission Delegated Regulation (EU) No 2017/2100, and there are no new data that could question the validity of the key conclusions of this assessment,
- The new data available (including the post-approval data of the initial/previous approval) is limited and is not expected to impact either the key conclusions of the exclusion and substitution criteria, assessment on hazards, risks or efficacy or the conditions of the approval,
- There is no need for re-assessment of data considered in the previous assessments or any re-assessment is not expected to impact either the key conclusions of the assessment on hazards, risks or efficacy or the conditions of the approval.

As key conclusions are regarded the conclusions relevant to the assessment of exclusion criteria, setting of reference values relevant to risk characterisation and outcome of efficacy and exposure assessment if essential for the approval or conditions connected with the approval. Full evaluation shall not include extensive re-evaluation of all endpoints but focus on the assessment of the key conclusions.

In case the eCA identifies any need to revise the harmonised classification, especially on the exclusion criteria, it should prepare the CLH dossier submission preferably in advance of the RAR, in order to be able to take into account the RAC opinion on the harmonised classification in the final RAR.

The eCA shall establish whether the exclusion criteria set out in Article 5(1) are met.
Where those criteria were known to be met before the submission, the applicant must have indicated for which precise use(s) the renewal under derogation considering the conditions of Article 5(2) is requested, and the eCA shall assess the appropriateness of risk mitigation measures for the related use(s), as provided by the applicant.
If previous approval of the substance was granted based on derogation criteria, the eCA for the renewal should check whether the exclusion criteria are still met, and, if this is the case, whether the derogation conditions could still be satisfied.
The assessment of ED properties is required in accordance with CA document CA-March18.Doc.7.3.a- Final.

If the conditions for full evaluation are not met, the eCA shall prepare a recommendation on the renewal of approval to be sent to ECHA and the applicant. The recommendation shall include the RAR and the draft BPC opinion. The RAR section of Overall Summary and Conclusions shall include the main outcome of the assessment, whereas reference shall be made to the initial or previous Assessment Report for the endpoints without any new information or changes in the conclusions of the assessment. For those endpoints where new

information or revised assessment has been considered, the assessment in the RAR shall include the details indicated in the combined CAR/CLH report template. The new studies and/or revised assessment of the RAR have to be highlighted in the table of contents and in the studies in the reference list as well.

Currently, for most active substances, the assessment of ED properties is missing. Therefore, in the first renewal approval it is expected that the full evaluation will be undertaken in order to include the ED assessment. In the subsequent renewals of approval, the need for full evaluation may become less frequent.

2.1. Assessment of data available from article 95 applications

New data on an active substance (e.g. recent *in vivo* toxicity studies), not available at the time of the original AS/PT approval, may have been submitted in the context of Article 95 applications under the BPR. The eCA should therefore investigate whether there is data available in Article 95 applications which could be relevant in an overall Weight of Evidence approach, together with other data, for risk assessment and classification and labelling. Since the Article 95 data relates normally to an alternative source, the eCA would only be able to consider these data if the corresponding source of the active substance has been assessed by ECHA as technically equivalent to the reference source.

The Article 95 data that is deemed relevant for the active should be considered by the eCA. The eCA should consider whether this data could have consequences for the harmonised classification of the active substance.

2.2. Assessment of data on the AS requested in the BPC opinion

The data requested under point 2.5 in BPC opinion of initial approval or previous renewal should be provided in the application for renewal and should be considered by the eCA.

2.3. Assessment of data on the AS submitted at Product Authorisation

The data on the active substance submitted in Product Authorisation applications should also be considered by the eCA if it is deemed relevant for the active substance (i.e. test substance meeting the reference specification or produced by a technically equivalent alternative source).

In practice, the identification of those data requires the support of the MSCAs who have evaluated the applications for product authorisation.

The eCA should provide in a separate reference list, the studies and information included in the RAR which originate from applications for product authorisations. The list should be placed below the applicant's reference list in the RAR.

As regards the use of data on the active substance obtained either from article 95 or Product Authorisation submissions, or requested in BPC opinion, it is noted that this data can also contribute to the risk assessment.

2.4. Section specific considerations for the eCA

2.4.1. Efficacy

Apart from situations where new (eco)-toxicological information would lead, compared to the previous approval, to significantly reduced safe doses for the reference product and that would

be below the efficacious dose for the corresponding use, no efficacy assessment is deemed to be necessary at this stage. Evaluation of efficacy data, when needed, will be done for the renewal of product authorisations and new product authorisations.

However, in case no biocidal product is authorised on the EU market at the time of the renewal of the active substance, the efficacy of the reference product should be confirmed with reference to the applicable relevant guidance. This situation could require the submission of new information.

In case there are aspects not covered by previous legal requirements at the time of the first/previous approval, efficacy of the reference product should be confirmed with reference to the applicable relevant guidance. For example, regarding the use of the substance in treated articles presented in the reference use, efficacy should be confirmed with reference to the applicable relevant guidance that the reference biocidal product is efficacious in treated articles, so that the articles fulfil claims made.

All information available related to the development of resistance should be provided. When a guidance on the assessment of resistance development will be available, it will provide specific data requirements.

2.4.2. Analytical Methods and Physical-Chemical Properties (APCP)

The CLP Regulation has fully entered into application in 2015 and physical hazards have to be addressed according to its requirements.
Furthermore, new guidance, e.g. entries in the TAB, must be applied for renewal if applicable in accordance with the general rules of application of guidance.

2.4.3. Human Health

The CLP Regulation has fully entered into application in 2015 and human health hazards have to be addressed according to its requirements.

The following elements should be considered in the evaluation of human health hazards, exposure assessment and risk characterisation under the application of renewal of approval of an active substance.

- Old, non GLP experimental studies should not be invalidated because they have not been conducted under GLP. It should be checked if biological effects and parameters recorded in the old studies address sufficiently the assessment needs in light of the current scientific knowledge. Deviations from new guidelines that are taken into account to conclude on the validity of the results should be clearly mentioned. Attention should be paid to the setting of the high dose; the eCA has to confirm that the available studies have appropriate dose setting and not too low or overly toxic doses.
- Further to a quality check of the studies against current standards, old studies often lack investigating parameters/endpoints that shall be carefully addressed according to the new data requirements (such as toxicokinetic data, potential neurotoxic and immunotoxic effects or genotoxicity by way of micronuclei formation in short term studies and endocrine sensitive parameters in reproductive studies). In these cases, the whole dossier should be checked by the eCA to verify whether these endpoints have been investigated elsewhere before a consideration of conducting new studies is undertaken. The repeat or duplication of studies using vertebrate animals should only be considered as the last resort.
- Changes in the exposure assessment. Any new recommendation of the ad hoc working group on exposure assessment and Guidance Documents relevant to exposure scenarios should be taken into account in the assessment of the exposure.
- New legal requirements, e.g. ED assessment.

2.4.4. Environment

The CLP Regulation has fully entered into application in 2015 and environmental hazards have to be addressed according to its requirements.

The following elements should be considered in the evaluation of environmental hazard, exposure assessment and risk characterisation under the application of renewal of approval of an active substance.

- Old, non GLP experimental studies should not be invalidated because they have not been conducted under GLP. It should be checked if biological effects and parameters recorded in the old studies address sufficiently the assessment needs in light of the current scientific knowledge. Deviations from new or updated guidelines that are taken into account to conclude on the validity of the results should be clearly mentioned.
- Changes in the exposure assessment. Any new recommendation of the ad hoc working group on exposure assessment and Guidance Documents relevant to exposure scenarios should be taken into account in the assessment of the exposure.
- New legal requirements, e.g. ED assessment.
- Scientific knowledge influencing the assessment of relevant endpoints (e.g. new interpretation of data resulting in a necessary revision of PNEC derivation).
- Data requested during the active substance approval.

Appendix I

Renewal Document, RNL DOC

In this document, the applicant should describe shortly the status prior to evaluation and preparation of the Draft Renewal Assessment Report, with the purpose to:
- early in the process identify data gaps that need to be fulfilled at dossier submission,
- identify areas on which the subsequent evaluation must be focussed,
- justify why new information is needed in specific sections,
- explain why the conclusions of previous assessment(s) of the active substance remain valid in other section or, where relevant, why no new information is submitted.

In case the substance meets the exclusion criteria, the applicant should include:
- the reasons for renewal of approval,
- why he considers that the derogation criteria would be met,
- for which exact uses renewal by derogation is requested,
- why there are no appropriate alternatives to the active substance.

The document should be prepared and shared with the eCA at the pre-submission meeting(s) of the applicant with the eCA in order to describe the status of the dossier. At that time, new studies might be still ongoing or need to be generated. The RNL DOC should be revised at the time of dossier submission and included as Appendix I in Section 13 of IUCLID dossier.

1. BACKGROUND
[Brief overview with dates and decisions related to the approval, early reviews or subsequent renewals of the active substance (including on other Product Types than the one of which the renewal is now applied for) including listing of any specific provisions/restrictions; intended uses included in the assessment for the approval; details of the application for renewal of the approval; brief overview of the Biocidal Products authorised on the market, for which uses, and in which Member States.]

2. THE ACTIVE SUBSTANCE AND THE BIOCIDAL PRODUCT
[Identification of additional data needed for the re-assessment, such as batch no. and purity of test substance used for (old and new) toxicological and environmental studies, and justification for deviations from the profile of the active substance of the application for renewal; identification of the reference specification; information on the representative product if changed from previous approval.
In case an ED assessment is needed, include a data gap analysis for the investigation of ED properties and a justification on the strategy to be followed to provide relevant ED data on the active substance.]

3. SPECIFIC CONCLUSIONS BASED ON PREVIOUS EVALUATION
[Brief overview, section by section, of data available for the approval, early reviews or subsequent renewals of the active substance and the conclusions of the previous evaluation; assessment by section of whether the conclusions of the initial or previous assessment of the active substance remain valid; identification of potential data gaps; guidance on what will be expected from the re-submission, with a view on new test methods and development of guidance since the approval or subsequent renewals.]
- Efficacy
- Identity, physical/chemical/technical properties and methods of analysis
- Human Health
- Environment
- Classification and Labelling

4. LIST OF NEW STUDIES
[List of new studies addressing data gaps identified in the previous sections that need to be finalised and included in dossier submission]

5. IDENTIFIED AREAS FOR WHICH UPDATED RE-ASSESSMENT IS NEEDED IN DOSSIER FROM APPLICANT AND IN EVALUATION BY eCA.

[A list of areas proposed to be addressed that might have led to restrictions in the previous assessment, and/or for which there have been scientific and technical developments and implementation of new guidance documents since the previous assessment.]

6. CONCLUSION ON THE EXTENT OF THE EVALUATION

Based on the identification of the new evaluations that need to be performed and considering the criteria included in the "Guidance on the data requirements and assessment of applications for renewal of approval of active substances under BPR", it is proposed that a full evaluation shall / shall not be performed.