Guidance and Standard Operating Procedure for drafting Robust Study Summaries

This document is part of the work package 2 deliveries under contract ECHA/2021/46[1]

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[1] https://echa.europa.eu/about-us/procurement/closed-calls

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A) Purpose and Scope

The purpose of this Standard Operation Procedure (SOP) is to establish, within the work package 2 (WP2) of the ECHA RSS research project, a uniform procedure for authoring and reviewing the robust study summaries (RSS) using IUCLID. The procedures outlined in this SOP are mainly applicable to authors and reviewers of the RSS.

This SOP does not include procedures for comparing new RSS with the RSS submitted by industry.

B) Contents of this SOP

The procedures included in this SOP have been taken from 4 main sources:

1. ECHA's Practical Guide 3[2]
2. Feedback received from authors and evaluators in WP1
3. Literature findings of the WP1
4. Yordas' experience with RSS and respective OECD Test Guidelines and harmonised templates

Most of the information was taken from the ECHA's Practical Guide 3. The procedures laid down by ECHA's Practical Guide have been reviewed and adapted for this SOP by including the feedback that was received from authors, evaluators, researchers and NGOs from the surveys and interviews conducted during the WP1.

In addition, during the WP1 literature review, new reporting proposals available in literature for the reliably and relevance of assessments were identified and selected in an attempt to facilitate the regulatory assessment of study reports. Two of such proposals are **CRED** (Criteria for Reporting and Evaluating Ecotoxicity Data)[3] and **SciRap** (Science in Risk Assessment and Policy)[4]. CRED is mainly applicable to ecotoxicology endpoints and SciRap includes human toxicology and *in-vitro* endpoints in addition to ecotoxicology. CRED and SciRap criteria are applicable to full study reports and their main aim is to improve the quality of the data reporting in the reports, especially peer reviewed publications; however, RSS authors should work with the understanding that RSSs are essentially short summaries of the full study reports and therefore, should have same representative qualities of full study reports; and thus should fulfil many of the criteria applicable to full study reports. Therefore, many of the factors in the reporting checklist suggested by CRED and SciRap for full study reports can be applied to RSS to make them more transparent and useful for hazard assessment.

[2] How to report robust study summaries; V2; 2012. https://echa.europa.eu/documents/10162/13643/pg_report_robust_study_summaries_en.pdf/1e8302c3-98b7-4a50-aa22-f6f02ca54352
[3] Moermond et al. 2016. Environ Toxicol Chem. May;35(5):1297-309. CRED: Criteria for reporting and evaluating ecotoxicity data.
[4] SciRAP (Science in Risk Assessment and Policy). http://www.scirap.org/

C) General steps for authoring and reviewing RSS

1) Review the study report from which the RSS will be generated. In this step, the author of the RSS should get a general understanding of the study and its findings, such as the corresponding Test Guideline (e.g. OECD Test Guideline, relevant year of publication). Look at the version of the guideline cited in the report and download the relevant version. For example, if the version of the OECD guideline cited in the report is older, download it from the archive: https://www.oecd.org/env/ehs/testing/section4-health-effects-replaced-and-cancelled-test-guidelines.htm In case of publications, if any particular guidance is not cited, use the latest guideline version.

2) If a particular test guideline is cited in the study report, familiarise yourself with that test guideline. Where a test guideline is not applicable or not clear, familiarise yourself with the OECD harmonised template for that endpoint to check which test guidelines are applicable. The material and method section of the report should give an indication of the appropriate test guideline. If not already familiar with a method, authors must familiarise themselves with the test guideline before starting the RSS.

3) All authors and reviewers should read Section D (General aspects of RSS) and develop a good understanding of the general aspects of the RSS. This should be followed by reading relevant sections of Appendix 1 (i.e. endpoints you are writing or reviewing). Note: The endpoint specific section (Appendix 1) is divided into 6 main **Endpoint Groups**: 1) Physicochemical 2) Environmental fate 3) Aquatic 4) Terrestrial 5) Human 6) in vitro.
Some of these **Endpoint Groups** have general instructions, which should be read by an author first if their assigned RSS falls within one of these endpoint groups. This should be followed by instructions within the specific endpoint.

   When reading this SOP for the first time, it is advisable to keep IUCLID open and see the relevant IUCLID sections as you read through the instructions of this SOP.

4) Before submitting the RSS to the reviewer, check your RSS against points reported in Appendix 2 (SciRap) and/or Appendix 3 (CRED) (depending on your endpoint type) and make sure that the factors identified in SciRap and CRED are included in your RSS (as much as possible based on available information from the full report). These SciRap and CRED criteria were included in this SOP as a self-review mechanism for the authors to ensure that their RSS contains all the critical reporting parameters. Further instructions and notes on SciRap and CRED criteria are available at the beginning of Appendix 2 and 3, respectively.

5) Once the RSS is complete, run the validation assistant check in IUCLID, and once all the issues are resolved create a pdf or rtf file of your IUCLID RSS for review.

6) The reviewer will review the files and make any changes necessary in the RSS in accordance with the procedure laid out in this SOP and a final pdf or rtf file will be generated. If there are recurring mistakes by the author, then the author should be informed about it immediately. The reviewers can also add their comments on the draft files of the RSS.

D) General aspects of the RSS (common for all endpoints)

1) Many IUCLID fields have pre-existing templates. Whenever available, these templates should be inserted and filled as much as possible. However, it is not always possible to fill all required information within templates. Therefore, section D.3 Material and methods, D.4 Results and discussion and appendix 1 (endpoint specific information) should be treated as minimum information that is deemed necessary; hence, should be provided in all cases and 'no information available' be written if any of the information is missing and justify the reason for no information.

2) All RSS should be independent and self-contained. In most cases, no part of the RSS should rely on another RSS for the assessment. In other words, we should never cite an RSS in another RSS. However, several environmental fate and ecotoxicology endpoints are informed by physicochemical endpoints; therefore, the author should pay close attention to the report to see if these aspects have been considered in the report and any impact on interpretation due to a lack of such information should be discussed in RSS.

3) No prior knowledge on the test substance should be used when writing the RSS, in order to prevent advocacy, bias, and emotional factors in reporting information especially if the test substance is suspected to be environmentally hazardous, carcinogen or endocrine disruptor.

4) If trying to copy (Ctrl+C) and paste (Ctrl+V) large sections of the information from reports, do it preferably one sentence at a time. After pasting, read the pasted section to ensure it is relevant and decide if some irrelevant information can be cut to make it more succinct. Also, when you are pasting blocks of text from the full report be very careful not to bring over a reference to something that is not in the RSS.

   Note: When you are copying and pasting, it is always better to first paste it in Word or Google Doc file, edit it and then paste it in IUCLID.
   Note: This does not mean that the entire study report should be copy pasted in RSS. RSS is a summary of the study report.

5) **Important:** whenever you are not able to find within the full report a criterion listed in this SOP, do not leave the corresponding IUCLID field blank. Instead, write 'information not available in the report'. This is to highlight that a particular lack of information was due to the deficiency in the report and not the RSS.

Complete the following IUCLID fields for all RSS:

D.1 Administrative data

- *Endpoint (pick-list)*

  In most cases, 'Remark' will not be needed for this project. Remark is usually added when the endpoint in study is not a standard endpoint or deviates significantly from a standard endpoint.
  Note: The endpoints addressed are defined by the Test Guidelines used, if one has. Do not assume the study report author has got this correct.

- *Type of information (pick-list)*

  All studies requested for this project are standard experimental studies, so we do not anticipate any information to be filled in the 'Remark' section.

- *Adequacy (pick-list):*

  Pick 'key study' or 'supporting study' based on your best judgement.
  Note: Key study should be selected when a study is highly suitable (in terms of relevance and reliability) to cover the endpoint without a major reservation. Supporting study, should be selected for any other adequate study supportive to the key study. Studies with Klimisch score 3 and 4 are never used in isolation as a key study.

- *Robust study summary (checkbox)*

- *Study Period:*

  Write the experiment start and end date. Use an unambiguous format such as 'From 12 MAY 1999 to 15 AUG 2000'. If only year available, mention that date and month not available in the report (mostly the case with publications).

  Note: in-life period may have to be specified for some toxicology endpoints. (i.e., the phase in which the test system is alive/growing)

- *Reliability (pick-list):*

  For this project please rely on Klimisch criteria[5].

  Note: it is recommended that you fill this section in the end (after writing all other sections). This is because you will have a better idea about the deficiencies of the report once you have created the RSS from it.

- *Rationale for reliability incl. Deficiencies*

  There is an 'add remark' section below the picklist. Provide more details on why you think the chosen reliability score is appropriate. This may include brief statements such as soundness of method,

[5] Klimisch HJ et al.. (1997). "A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data". *Regulatory Toxicology and Pharmacology*. 25 (1): 1–5. doi:10.1006/rtph.1996.1076.

appropriateness of species for a given endpoint etc. Sometimes, even though reports state they are OECD compliant studies, they may contain noticeable deficiencies in the methodology. It would be appropriate to record those deficiencies here. This step is especially important for academic publications and old laboratory reports (pre-GLP i.e. before 1972) as well as reports which used a particular test guideline that has since been superseded or updated.
Note: Be aware of the difference between the term 'deficiency' and 'deviation'. On many occasions, these two terms may have different meanings. For example, poor reporting of analytical data or missing information on the test substance identification is a deficiency whereas the temperature deviation within an experiment outside ± 1 ℃ range in an OECD 202 test is a deviation from the Test Guideline. Clearly distinguish the two terms in this section while writing.

D.2 Data source

Enter the correct and complete bibliographic reference of the study report or publication

- *Reference* (including the year(s) when the study was performed)
  To create a new literature reference, click on 'Select' in the 'Reference' field under 'Data source'. The link will take you to the Literature reference inventory. In the pop-up window click on 'Create / New Literature reference'. Fill in the fields in the pop-up window and click Save. For publications, also include DOI number.
  For author's name in study reports, report the author's name (study director). If the author's name is not available, enter name of company or organisation.

D.3 Materials and methods

Note: All active fields in a given endpoint should be filled as far as possible. If you leave a field blank, provide a justification. Moreover, as stated earlier in this document, use the text template functionality wherever it is available and fill it as much as possible. It is not always possible to fill all required information within templates but indicate when some information is not available or not applicable. Section D.3 Material and methods should be treated as minimum information that is deemed necessary and it also provides some additional guidance on technical aspects of the information. 'No information available' should be written if any of the information is missing and the reason for no information should be justified.

Note: All preliminary studies such as dose range finding study and homogeneity and stability studies are important and hence a brief description of their study design must also be included in the material and method section. This is usually done in the 'study design' subsection for human toxicology and 'any other information on methods' for ecotoxicology endpoints. Please follow endpoint specific fields for this information when you are working on the RSS of your assigned endpoint.

- *Method/guideline followed* (pick-list or description if different from the pick-list), along with the organisation(s) (e.g. OECD, EPA, ISO etc, multiple guidelines may be cited if relevant)
    - Qualifier (pick-list)
    - Note deviation: GLP reports usually already mention any deviations from the guideline. For publications, if deviations are not described directly by authors, then check the materials and method section and compare with the guideline requirements.
    - Version of the guideline: usually indicated by the guideline publication year.

- *Principles of method if other than guideline:*
  At least provide the main principles of the test, a short description of test conditions, and parameters analysed.

- *GLP compliance (pick-list)*
  Always check if the GLP certificate in the QA section of the report is provided or not. If a certificate is not included, pay very close attention to the language used and GLP compliant option should only be selected if there is an unambiguous statement from a responsible person stating that the study was fully conducted to GLP at a GLP-certified facility. In some cases, part of a study may not be GLP, such as a dose range finding study may not be GLP but the main study is GLP. In the 'remark' box in this section, please clearly mention whether the certificate was included or if the GLP compliance is ambiguous. Also state here if part of a study is not GLP and whether or not that has any impact on the main study.

- *Type of test (some endpoints)*
  Sometimes, there are multiple methods available in a particular endpoint (e.g. boiling point can be measured using dynamic method, distillation methods or several other methods (see 'type of method' box in boiling point IUCLID template)). If yes, then report this in the RSS (e.g. in 'Type of method' field for boiling point; 'Type of study' field for skin sensitization or 'Test type' field for human acute tox etc in 'material and method' section). In such cases, see if there is a rationale for choosing a particular method in the report and write it in the 'justification' or 'remark' field. For publications, try to provide a rationale on the suitability of the method from your experience (if not discussed in the paper). Moreover, if the method is other than guidelines, then it is required to provide a justification for using Migration of Polycyclic Aromatic Hydrocarbons (PAHs) from plastic and rubber articles if this method is available. If a report/publication is old and performed prior to a published guideline, it should be specified.

- *Test material information*
  Information on test material identity. This section is mandatory. Go to the 'Test material information' section. To create a new substance record, select

'create' and provide name, composition, test material form, and details on test materials (insert IUCLID template function and add as many details as available). Substance should be described in sufficient detail to allow assessment; therefore, include full composition and if applicable other aspects of production/synthesis such as degree of ethoxylation etc. that can help in understanding the nature of the substance

In the composition table, provide 'type', 'reference substance', and 'concentration' as a minimum. If the substance is multi-constituent/UVCB, all components should be added in the composition table. In addition, 'test material form' must be filled and 'details on test material' should also be filled using the template function, if relevant (e.g. nanomaterial).

- Details on test material (go to 'Specific details on test material used for the study' section, use IUCLID template functionality to fill in as much detail as possible). As a minimum, fill following details and any of the information is not available, write the reason (e.g. not provided in report or not relevant):
    - Source of test material
    - Lot/batch number
    - Expiry date
    - Purity and purity test date (also include name, isomers and concentration of impurities if the test substance in the study is different from the substance for which information is provided in the 'test material section' e.g. the test material is a solution or mixture containing the substance)
    - Storage condition of test material
    - Stability and homogeneity of test material in the vehicle/solvent
    - Stability of the test material in medium
    - Solubility and stability of the test substance in the solvent/vehicle under test conditions (e.g. in the exposure medium) and during storage
    - Reactivity of the test substance with the solvent/vehicle and with the incubation material used (e.g. plastic ware)
    - Treatment of test material prior to testing
    - Preliminary purification step
    - Final dilution (mention neat, if no dilution)
    - Dilution media (if applicable)
    - Form applied (if different from original form)

- *Statistics*
    - Basics of statistical method and statistical error estimates are mandatory. This should be done in the 'statistics' section.

D.4 Results and discussions

Note: All active fields in a given endpoint should be filled as far as possible. If you leave a field blank, provide a justification. Moreover, as stated earlier in this document, use template

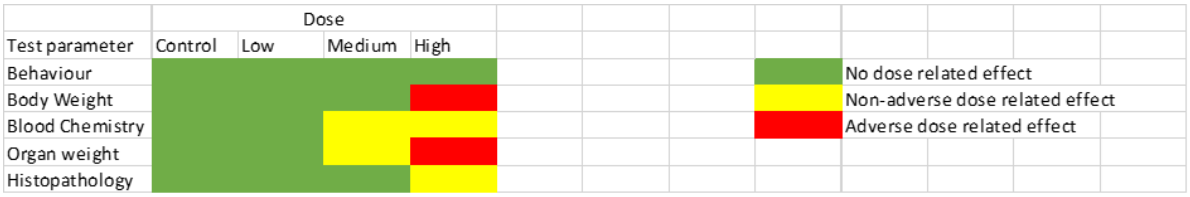
functionality wherever it is available and fill it as much as possible. It is not always possible to fill all required information within templates. Section D.4 Results and discussion should be treated as minimum information that is deemed necessary and it also provides some additional guidance on technical aspects of the information. 'No information available' should be written if any of the information is missing and the reason for no information should be justified.

Following aspects of study report must be conveyed in the RSS by inserting information in either **predefined boxes or in free text fields**:

- The summary of all observations (follow Results and Discussion sections within the endpoint specific details provided in Appendix 1)

- For human toxicology, there might be several categories of adverse effects reported in the report e.g. neuropathological effects, immunotoxic effects etc. They must all be reported in the RSS in their respective fields in IUCLID. Key adverse effects driving the NOAEL derivation should be identified, which should be done in the IUCLID Table in the 'Effect levels' in the results and discussion section by reporting all effects and selecting the 'key effect' box.

- 'Basis of effects' in the results section should never be left empty. Conclusions must be backed up by results provided within the RSS. A rationale on why an effect is adverse or non-adverse should be provided. If in doubt, draw up a matrix of parameter vs dose and identify whether a dose related effect was seen and if this was adverse or not (see table below).



- In the 'remarks' in the results section, any type of dose conversion should be reported OR any other information that may help in the evaluation of adverse effects.

- 'Any other information on results' section:

  Concentration/dose response relationship should be presented, in the tabular form for all major parameters. Table numbers should be assigned to all tables in this section. Note: Whenever possible, do not create tables in Word file and paste them in IUCLID because it can lead to formatting errors when converted to pdf. Instead, try to create tables directly in IUCLID (go into the rich text editor provided within this field of IUCLID, then go to Table option and create the table).

  The discussion on any significant deviations from the guideline
  Write anything unusual about the test and other relevant information which might have influenced the results.

D.5 Overall remarks, validity criteria fulfilled, interpretation, and conclusions

- *Overall remarks* (relevant for human endpoints; see appendix 1):
  Provide toxicological evaluation of all the findings of the study (adverse and non adverse effects, reversible and irreversible effects) explaining also the biological relevance of the effects observed in animals and if needed address human relevance. If it is a lab report, this information is discussed by the study director in the discussion and/or conclusion section. In the publication, this information could be found in the discussion section. Any Mechanistic information including adverse outcome pathways (AOP) related discussions should also be included in this section.

  If relevant include a summary of confounding factors that may affect the results of the study

  Discuss any significant deviations from the guideline.

- *Validity criteria fulfilled* (only applicable to some endpoints; check individual endpoints in Appendix 1):
  discuss whether or not the validity criteria have been fulfilled (state what the validity results were in the 'any other information on material and method' section).

- *Interpretation of results:* only applicable to some endpoints (check individual endpoints in Appendix 1):
  Where applicable, choose appropriate option from picklist

- *Conclusions:* check individual endpoints (Appendix 1)
  In general, write about which conclusions were derived from the underlying data with proper explanation.
  For example, in the conclusion section of repeated dose toxicity, one must clearly write the basis of conclusion such as "Rats ingesting up to 1000 mg/kg/day for 13 weeks survived the in-life portion of the study without clinically adverse effects. The only effects found at 250 mg/kg/day were very slight decrements in RBC parameters, but all were within the historical control and the effects were not observed at higher doses; hence, the effects were not considered adverse, and NOAEL was determined to be 1000 mg/kg".

D.6 Executive Summary

RSS authors should visit the OHTs website where predefined Executive Summaries are available for most of the selected endpoints. See fourth column in this web page: https://www.oecd.org/ehs/templates/harmonised-templates-health-effects.htm

If an OHT predefined Executive Summary is not available for an endpoint, then look into the study report carefully and for most GLP reports, a summary is already available. It should be read carefully to ensure it has all important details related to materials, methods, results and conclusion and If the 'summary' of the report covers basic aspects of materials, methods, results and conclusions, it should be copied and pasted as such. For academic papers, abstracts usually contain some unusable introductory information and miss key information, especially the test material information and study design.

Therefore, authors should make sure their executive summary follows a strict structure with the following elements: the test method used, the test material used, test species or cell type and source, critical elements of study design: exposure duration, doses, post exposure period (if any), parameters analysed, key observations (including EC50, NOEC, NOAEL if relevant) and overall conclusion.

Appendix 1: Endpoint specific information

1.1 Physicochemical Endpoints

1.1.1 Vapour pressure

1) **Administrative data**
   - Common to all endpoints. Refer to section D

2) **Data source**
   - Common to all endpoints. Refer to section D

3) **Materials and methods**
   - *Type of method*:
     description of the apparatus or reference to the standard or the test method (see section D)

   Important: In the **Test guideline section,** note any deviation from the guideline method used and reasons

4) **Results and discussion**
   - *Vapour pressure* (Table)
     Measured value of the vapour pressure for at least two temperatures
     Estimate of the vapour pressure at 20 or 25 ºC (if not measured)
     Temperature
     Report results in hPa. Convert to hPa if reported in other units.
   - *Transition/decomposition* (Table):
     If a transition (change of state, decomposition) is observed, the following should be noted:
     - nature of change;
     - temperature at which change occurs.

5) **Applicant's summary and conclusion**
   - Common to all endpoints. See section D

1.1.2. Partition coefficient (n-octanol/water)

Materials and methods
The information in this section is common to all endpoints (see section D) except for the following parts:

- *Type of method*
  After selecting the method from the picklist, provide a justification for the method chosen (if available), then go to 'any other information on material and methods' section and provide following information:

If it is Shake-flask method (EU A.8/ OECD TG 107):

- Equilibrium concentrations of the test substance in both phases;
- Relative volumes of the two phases;
- Analytical method(s).

If it is Calculation method (EU A.8):

- Identification of the method;
- Working principle of the method;
- Reference to the method;
- Information on source chosen to justify Kow values of fragments being manipulated;
- applicability of the method.

If it is HPLC method (EU A.8/OECD TG 117):

- Column(s) used;
- Mobile phase (composition, buffer, pH);
- Reference substances with respective Kow values from the literature;
- Concentrations measured.

If it is Slow-stirring method (OECD TG 123):

- Label purity of labelled chemicals and molar activity (where appropriate);
- sampling times;
- Description of the test vessels and stirring conditions;
- Number of replicates;
- Temperature during the experiment;
- Volumes of 1-octanol and water at the beginning, during and remaining after the test;
- Determined concentrations of the test substance in 1-octanol and water as a function of time;
- Description of the test vessels and stirring conditions (geometry of the stirring bar and of the test vessel, vortex height in mm, and when available: stirring rate) used;
- Analytical methods used to determine the test substance (its repeatability and sensitivity) and the method limit of quantification;
- Sampling times;
- pH of the aqueous phase and of the buffers used, when pH is adjusted for Ionisable molecules;
- Number of replicates;
- Demonstration of mass balance;
- Temperature and standard deviation or the range of temperature during the experiment;
- The regression of concentration ratio against time.

- Select partition coefficient type, in general is always “octanol-water”

- Details on methods
  Composition and concentration of buffers
  Concentration of the stock solution
  Any other information on the analytical method

Important: In the **Test guideline section,** note any deviation from the guideline method used and reasons

Results and discussion

- *Partition coefficient* (Table)
  Type (Pow or LogPow)
  Partition coefficient value
  Temperature, pH
- *Details on results*
  Consider giving standard deviation of partition coefficient
  Provide any further details

Applicants summary and conclusion

Provide main conclusion
Provide a brief executive summary

1.1.3 Water solubility

Materials and methods

- *Type of method*
  Chose the type of method from picklist
  After selecting the method from the picklist, go to 'any other information on material and methods' section and provide following information:
  If it is Column Elution method:
  - Concentrations, flow rates and pH for each sample;
  - Mean and standard deviations of five samples at least;
  - Average for each of two successive runs at least;
  - Nature and loading of support material;
  - Solvent used.

  If it is Flask method:
  - pH of each sample;
  - Individual analytical determinations and the average;
  - Average of the values for different flasks.

- Analytical methods
  Picklist
- Details on the methods
  Provide details on the methods including analytical method, method validation data and all relevant chromatograms

- Any other information on material and method

Description of the apparatus and dimensions or reference to the standard or the test method applied;
Results from preliminary test (if any);
Water temperature during saturation process;

Important: In **Test guideline section,** note any deviation from the guideline method used and reasons

Results and discussion

- *Water solubility (Table)*
  Enter mean water solubility or range if reported
  indicate the temperature and pH conditions
  If necessary, copy this block of fields for each temperature and pH conditions at which the water solubility was determined.
  If the pH value was measured with another test substance concentration than the given water solubility concentration, specify the concentration with unit in field 'Details on remarks'.

Applicants summary and conclusion

Provide main conclusion
Provide a brief executive summary

1.1.4 Flammability

Material and methods

- *Any other information on material and method*
  Description of the apparatus and dimensions or reference to the standard or the test method applied;
  Test temperature;
  Tested concentrations.

Important: In **Test guideline section,** note any deviation from the guideline method used and reasons

Results and discussion

- Fill relevant details in the Tables (depending on the substance type)
- Indicate lower and upper explosion limits in % volume;

Applicant's summary and conclusion

Interpretation of results
Provide main conclusion
Provide a brief executive summary

1.2 Environmental fate

General comments on environmental fate

If measurements were made on multiple time-points, please include results of all time points, not just the last time point. Use the table provided in the results section of IUCLID. There is time field available in that table.

1.2.1 Stability (Hydrolysis as function of pH)

Materials and methods

- **Study Design**

  Analytical monitoring: yes/no

  Details of sampling:

  - Sampling intervals
  - Sampling method
  - Sample storage
  - Any other useful information/observation on sampling

  Details on analytical methods:

  Divide this section into 3 main parts

  (1) Pre-treatment of samples- such as centrifugation, filtration, digestion, cleanup, C14 measurement etc.

  (2) Identification and quantification- separation method (HPLC, GC etc), conditions (solvent, mobile phase etc), detection method (e.g. UV, ICP, MS etc), detection limit, reproducibility, linearity, calibration details etc

  (3) If relevant: Identification and quantification of transformation product

  Buffers: pH, molarity, composition

  Details on test conditions:

  Divide this section into several parts

  (1) Test system: type, material, volume of flask, lighting, any other useful information such as measures to exclude oxygen etc. Amount of substance applied

  (2) Test medium: kind of water, volume, preparation, renewal, any co-solvent

  (3) Other test conditions: pH adjustment

  (4) dissolved oxygen information

  Duration of test: Use the table to fill the information: pH, temperature, initial concentration

  5) Amount of substance applied, solvent used, method of extraction, nominal concentration, sampling times

  Number of replicates (very important)

  Positive control, negative control (if available)

- **Any other information on materials and methods**

  Validity criteria defined in the study report

Results and discussion

Preliminary test results (tier 1)
Test Performance: Report on any unusual observations during test
Transformation Products (important):
picklist; if yes, fill the tables on identity and details on hydrolysis

Identity of transformation products: use table. Include CAS/EC numbers

Dissipation DT50 of parent compound for the different pHs and temperatures tested. If applicable, the extrapolated results for 25℃.

Total recovery of test substance (in %) for the different pHs and temperatures, if available in radiolabelled experimental setup
Results of reference substance (if applicable)
Note: if labelled substance is used, then mass balance during and at the end of the studies is also required
Note: OECD compliant tests are conducted in tiered fashion (refer to guideline). In such cases, clearly distinguish the different tiers both in methodology and results.

Any other information on results:
Replicate data in tabular forms
If hydrolysis rate is determined in the study: a) concentrations versus time data at each pH and Temperature for test substance and hydrolysis product (if relevant); b) results of Arrhenius equation for the temperature 20 C/25 C, with pH, rate constant [h-1 or day-1], half-life or DT50, temperatures [C] including confidence limits and the coefficients of correlation (r2) or comparable information; c) proposed pathway of hydrolysis

Applicants' summary and conclusions

Validity criteria fulfilled?
Conclusions and executive summary

1.2.2 Biodegradation in water (screening)

Materials and methods

- *Oxygen conditions*

Pick aerobic or anaerobic. In the remarks, add any additional information on how aerobic or anaerobic conditions were provided such as method of aeration etc
If relevant, the oxygen uptake of the inoculum blank (mg 02/L) after 28 d or oxygen depletion in the inoculum blank after 28 d and the residual concentration of oxygen in the test bottles;

- *Inoculum or test system*

  Picklist (select appropriate option). If it is not clear whether the inoculum was adapted or not, select ‘adaptation not specified’. Read the report carefully before selecting not specified.

- *Details on inoculum*

  source of inoculum
  sampling site(s)
  concentration and any pre-conditioning treatment – any ageing to be mentioned specifically) duration of test;
  storage of inoculum (length and condition)
  final sludge or other inoculum concentration
  Any filtration used during sludge preparation (if yes, name, type and size)

- *Duration of test*

- *Initial test substance concentration*

  Select unit
  If concentration unit is not in the list, then choose ‘other’ and specify in the free text field
  Select the appropriate option from the list named ‘based on’. If you pick initial concentration based on parameters other than ‘test material’, then a further explanation in remark will be useful in which actual test material amount/concentration added should be specified followed by equivalent concentration in COD, DOC, or ThOD etc.

- *Parameter followed for biodegradation estimation*

  Picklist. Select appropriate option

- *Details on analytical methods*

  Can be mainly divided into three sections:
  1) Pre-treatment: Any pre-treatment of samples after collection. Here, discuss things like digestion, extraction, centrifugation, and any clean-up of samples, C14 measurement. If there is no pre-treatment of the collected sample, mention ‘no pre-treatment’ or ‘not specified’ whichever is applicable.
  2) Quantification of parent compound: All details on the method used for analysis of parent substance. Includes name of method, instrument used (e.g. HPLC, GC MS etc), solvents use, detection limits, linearity, calibration, precisions, reproducibility etc.
  3) Quantification of transformation products: In most reports, this won’t be applicable. Hence, mention that transformation products were not measured. If measured, discuss the methodology as mentioned in the report.
  Note: if there is no information on analytical methods at all. Mention ‘no details in report’ in such cases.

Note: Full details of radioactive labelling should be provided (if applicable) in the study design section. This should include specific activity of the compound and also a certificate of analysis.

- *Details on study design*

  Should cover five major aspects:
  1) Test conditions (such as composition of medium, test temperature, pH,
  2) Test system (e.g. type of flask, volume etc)
  3) Sampling: How samples were collected, what days etc
  4) Control and blank
  5) Statistical method
  Note: in the case of poorly soluble test substances, provide methods of preparation of test solutions/suspensions

  For five points discussed above, use either the predefined template provided in IUCLID or write your own, making sure it covers all five areas described above.

- *Reference substance*

  Identity of reference substance(s) used;

- *Any other information on materials and methods*

  Validity criteria defined in the study report
  Parameter followed for degradation estimation method of calculating measured concentrations (arithmetic mean, geometric mean, etc.)
  Details on any preliminary study design

Results and discussion & Applicant's Summary and conclusion (including interpretation of results)

- *Preliminary study:*

  Write not applicable if there was no pre-study. E.g. adsorption of test material on wall

- *Degradation %*

  Include time, parameter (picklist),
  Select the key result (usually the results on the last observation day)
  In the 'value' field, if no information is entered, then select the reason for no value from the dropdown in 'remarks on results'.

- *BOD5 / COD results*

  Same as above

- *Results with reference substance:*

  Also indicate whether results with reference substance are valid.

- *Any other information on results*

  Not everything is applicable below. Pick and write depending on the report.

a) Degradation results presented preferably with tables of percentage degradation against time for the test and reference substances, the lag phase, degradation phase, the 10-d window and slope;

b) If no full table then at least indication of the duration of the lag phase, the degradation phase and location of the 10-d window within the test period;

c) Replicate values of the degradation % of the test chemical at the degradation rate at the plateau, in the end of test, and/or after 10-d window, where applicable, as appropriate;

d) Degradation % of the reference compound by day 14 (if relevant also after 7 days);

e) Degradation % within 14 days in a toxicity test (if relevant) containing both the test substance and a reference compound specific chemical analytical data, if available;

f) Assessment of inhibition and, if observed, quantitative estimation of the effect(s) observed at different concentrations

g) any inhibition phenomena or unusual observations or other information affecting the results;

h) if relevant, inorganic carbon (IC) content of the test substance suspension in the mineral medium at the beginning of the test and total carbon (TC) content
i) if relevant, total CO2 evolution in the inoculum blank at the end of the test.

- *Applicant's summary and conclusion:*

  Always check if the validity criteria were met. This is usually provided as a statement in the GLP reports. For publications, check the validity criteria in the OECD guideline and compare it to the results in publication. If validity criteria were not met then results are not reliable.

  Interpretation of results

  Key conclusion

1.2.2. Biodegradation in water / sediment (Simulation)

Materials and methods

- *Oxygen conditions*

  Pick aerobic or anaerobic. In the remarks, add any additional information on how aerobic or anaerobic conditions were provided such as method of aeration etc

If relevant, the oxygen uptake of the inoculum blank (mg 02/L) after 28 d or oxygen depletion in the inoculum blank after 28 d and the residual concentration of oxygen in the test bottles;

- *Inoculum or test system*
  Picklist (select appropriate option).

- *If water study: provide following information in the 'details on source and properties of surface water':*
  Temperature, pH, conductivity, DO, redox potential, hardness, storage conditions, nutrients, appearance of sample, details on collection, DOC/TOC, BOD, microbial biomass, filtration, filter information (if used)

- *If sediment study: provide following information in the 'details on source and properties of sediment'*:
  pH, redox potential, storage conditions, details on collection, organic carbon, CEC, biomass, sieving, bulk density, textural information, depth of collection, appearance, dry weight in g/l of the suspended solids, TOC concentration or weight loss on ignition as a measure of the content of organic matter;

- *Details on inoculum:*
  Use IUCLID template functionality to provide information

- *Duration of test*
- *Initial test substance concentration*
- *Parameter followed for biodegradation estimation:* picklist
- *Details on analytical methods:*
  Can be mainly divided into three sections:
  1) Pre-treatment: Any pre-treatment of samples after collection. Here, discuss things like digestion, extraction, centrifugation, and any clean-up of samples, C14 measurement. If there is no pre-treatment of the collected sample, mention 'no pre-treatment' or 'not specified' whichever is applicable.
  2) Quantification of parent compound: All details on the method used for analysis of parent substance. Includes name of method, instrument used (e.g. HPLC, GC MS etc), solvents use, detection limits, linearity, calibration, precisions, reproducibility etc.
  3) Quantification of transformation product

- *Details on study design:*
  Details on test conditions (test temperature, pH, continuous darkness: yes/no, etc.).
  Amount of test substance applied, test concentration and reference substance concentration, solubilising agent if relevant
  Sample storage
  Method of application of the test substance

Solvent use
Volume of surface water used and sediment (if used)
If dark conditions are not to be maintained, information on the "diffuse light" conditions
Information on the method(s) used for establishing sterile controls (e.g. temperature, time and number of autoclavings)
Information on controls and blank system used
Details on sampling: (e.g. frequency, method and sterility)
Delay between collection and use in the laboratory

- Statistical *methods details*
- Reference substance
- Any other details on method: Validity criteria

Results and discussion & Applicant's Summary and conclusion (including interpretation of results)

- *Percentage of recovery*
- *half-life* or DT50, DT75 and DT90 for the test substance and, where appropriate, for major transformation products including confidence limits
- *Details on transformation*

  where appropriate, identification, molar concentration, and percentage of applied of major transformation products, a proposed pathway of transformation

- Where appropriate, identification, molar concentration, and percentage of applied of major transformation products, a proposed pathway of transformation
- Where applicable, an assessment of transformation kinetics for the test substance and characterisation of non-extractable (bound) radioactivity or residues in soil
- Where applicable, degradation % and time interval of degradation of the reference compound

- *Any other information on results*:
  - averages of the results observed in individual replicates, for example, length of lag phase, degradation rate constant and degradation half-life
  - categorise the system as either non-adapted or adapted as judged from the appearance of the degradation curve and from the possible influence of the test concentration

- *Applicant's summary and conclusion:*

  Always check if the validity criteria were met. This is usually provided as a statement in the GLP reports. For publications, check the validity criteria in the OECD guideline and compare it to the results in publication. If validity criteria were not met then results are not reliable.

  Interpretation of results

Key conclusion

1.2.3 Bioaccumulation (aquatic/sediment)

Materials and methods

- *Test material*
  - Follow the general instructions (Section D)
  - Radiolabelling: picklist. If yes, provide details on specific activity as well as the position of the label and whether isotopic dilution has been performed.
- *Sampling and analysis*

  Details of sampling:
  - Sampling intervals
  - Sampling method
  - Sample storage
  - Any other useful information on sampling

  Details on analytical methods:

  Divide this section into 2 main parts

  (1) Pre-treatment of samples- such as centrifugation, filtration, digestion, clean-up etc.

  (2) Identification and quantification- separation method (HPLC, GC etc), conditions (solvent, mobile phase etc), detection method (e.g. UV, ICP, MS etc), detection limit, reproducibility, linearity, calibration details etc

- *Test Solutions*

  Vehicle

  Indicate whether vehicle was used to emulsify or mix the experimental test material to enhance its solubility (if aqueous study), or prior to spiking food (if dietary study)

  Details on preparation of test solutions

  Insert appropriate template from IUCLID and fill details

- *Test organisms*

  Species

  Details: Divide into 2 main parts:

  1) Test organism: common name, strain, source, age, length, weight, lipid content, housing, feeding (type, amount, frequency)

  2) Acclimation: acclimation period, condition, food given during acclimation and frequency

- *Study design*

  Route of exposure

  Test type

  Water/sediment type

  Duration (uptake and depuration)

- *Test conditions*
  - *Hardness, temperature, pH, DO, TOC, Salinity, conductivity*
  - *Details on test conditions:*
    - Use the template function in the IUCLID to fill as many as possible details on the test system (Note: it is not necessary to fill all details. The information you provide depends on how much is available in the test report.
    - If aquatic study, at a minimum try to include:
      - basic test system details such as test vessel material, size, volume, aeration, number of organisms/vessel, replicate vessels numbers, biomass loading, water properties such as chemistry, volume, source. Also include pH adjustment, photoperiod and light intensity.
    - If aquatic dietary study: additionally include:
      - Stability of substance in food
      - Nominal concentration of substance in food
      - Spiking technique, amount of (lipid) vehicle used in food Spiking process (if used)
      - Test substance concentration measurement in diet
      - Detail on solvent/carrier oil (if used)
      - Food type employed (proximate analysis, grade or quality, supplier, etc.), feeding rate during uptake phase, amount of food administered and frequency (including any adjustments based on sampled fish weight)
      - Time at which fish were collected and euthanized for chemical analysis;
      - Frequency of faecal matter removal from the tank.
      - Detail on whether uneaten food was removed after feeding
    - If test is sediment test, some additional details on test conditions are required such as sediment mass volume, aeration, type of flow through, sediment-water ratio (use IUCLID template functionality to fill as much details as possible)
- *Nominal and measured concentration*
- *If available: positive control*
- *Any other information on materials and methods*
  - Validity criteria
  - Details on range finding study (if available)

Results and discussion

- Fill tables as per the information available in the report (include data for all concentrations in BAF table)
- *Details on results*

Any additional effects observed in fish including any adverse effects including mortalities

- *Any other information on results*

  Summary tables (including all measured data), showing growth, i.e. fish weight vs. time, uptake and depuration of the test chemical in the fish; Fish weight data should be tabulated and linked to individual fish chemical concentration;

  tabulated test substance concentration data in fish (Cf, linked to individual fish) and water (Cw) (with mean values for test group and control, standard deviation and range, if appropriate) for all sampling times.

  In addition:

  For aqueous exposure: lipid content of fish, method used, lipid normalisation factor, kinetic BCF, , derived uptake and depuration rate constants k1 and k2

  For sediment: measured lipid concentrations in food, tabulated fish lipid contents data, mean values for test group and control at test start, end of uptake and end of depuration, raw dietary BMF, lipid and growth-corrected BMF, tissue-specific results if applicable. Metabolites and their accumulation pattern

Applicants' summary and conclusions

Validity criteria fulfilled?

Conclusions and executive summary

1.3 Aquatic toxicity

General instructions on aquatic toxicology

Always add comments in the 'basis of effect' section in the 'results and discussion' table.

Measured concentration must be reported in the results and discussion table if available. If not available, then a statement should be made clearly indicating that measurement of concentration was not performed. In addition, measured data should also be reflected as % of nominal concentration too. The method of mean measured endpoints (e.g. geometric, arithmetic, time-weighted etc) should also be clear.

Tabulated raw data for each dose group should preferably be provided (in 'any other details on results' section) and add images of plots (including slopes) of the effect curves in the 'illustration' subsection of the 'Overall remarks' section.

If measurements were made at multiple time-points, please include results of all time points, not just the last time point. Use the table provided in the results section of the IUCLID. There is time field available in that table.

1.3.1 Short-term toxicity on fish

Materials and methods

- *Sampling and analysis*

  Analytical monitoring: picklist

  Details of sampling:
  - Concentrations
  - Sampling method
  - Sample storage
  - Any other useful information on sampling

  Details on analytical methods:

  Divide this section into 2 main parts

  (1) Pre-treatment of samples- such as centrifugation, filtration, digestion, clean-up etc.

  (2) Identification and quantification- separation method (HPLC, GC etc), conditions (solvent, mobile phase etc), detection method (e.g. UV, ICP, MS etc), detection limit, reproducibility, linearity, calibration details etc

  Note: If there is no information on analytical methods at all, mention 'no details in report' in such cases.

- *Test solutions*

  Vehicle: yes/no

  Details on test solution

  This is especially important for 'difficult to test substances'. How the test substance solution was prepared, including identification of vehicle, method, concentration of vehicle in final test medium, solvent control information etc. Also include any visual observations about the test solutions e.g. particles observed in suspension, at the surface, clear and colourless solutions etc.

- *Test Organisms*

  Species: picklist. If species is not in the list, select 'others' and provide the name in the textbox.

  Details on test organisms: This section can be divided into two subsections.

  1) Test organisms: information on organisms such as common name, strain, source, Age, weight, length, life-stage, method of breeding, brood maintenance.
  2) Acclimation: duration, conditions, type and amount of food

- *Study design*

  Test type: Picklist

  Water media: picklist

  Limit test: yes/no

  Exposure duration

- *Test condition*

  Hardness, temperature, pH, dissolved oxygen, salinity, conductivity
  Nominal and measured concentration
  Details on test conditions: This could be divided into 4 subsections

  1) Test system: test vessel, material, headspace, aeration technique, if flow-through then renewal rate, number of organisms per vessel, number of vessels per concentration (replicates), loading rate
  2) Parameters measured
  3) Other test conditions: pH adjustment, light/dark cycle, light intensity
  4) Test concentrations: list all concentrations, spacing factor for concentration, justification of dose, any dose range finding study (brief details on methodology)

  Positive control details (generally not needed, but include this information if reported in the report)
- *Any other information on materials and methods*

  Any information on preliminary study conducted
  Control parameters (such as mortality) was measured or not
  Note the validity criteria utilised in the study

Results and discussion

- *Effect concentrations*

  Fill all details in the table, checkbox the 'key result'. Basis of effects- Select from picklist.
  Report EC50 on multiple time points if available
  Report all ECx (e.g. EC50, EC25) available, making sure the basis is clear e.g. nominal or measured
- *Details on results*

  Note important things about results such as mortality in control, any behavioural abnormalities in treatment and control group, observations on body weight and length
  Any other sublethal effect
- *Positive control results*
- *Statistics*

  Indicate the parameters analysed, the statistical method used and the statistical test performed. Also add a comparative statement between solvent control and procedural control and which data is used as study control.
- *Any other information on results:*

  Report tabulated data on all dose groups

Applicant's summary and conclusions

- Validity criteria fulfilled
  Validity criteria are usually listed in lab reports. If working with publication or if lab report does not list validity criteria then please check OECD guideline
- Conclusion
  List key conclusions

1.3.2 Long-term toxicity on fish

Materials and methods

- *Sampling and analysis*

  Analytical monitoring: picklist

  Details of sampling:

  - Concentrations
  - Sampling method
  - Sample storage
  - Any other useful information on sampling

  Details on analytical methods:

  Divide this section into 2 main parts

  (1) Pre-treatment of samples- such as centrifugation, filtration, digestion, clean-up etc.

  (2) Identification and quantification- separation method (HPLC, GC etc), conditions (solvent, mobile phase etc), detection method (e.g. UV, ICP, MS etc), detection limit, reproducibility, linearity, calibration details etc

  Note: If there is no information on analytical methods at all, mention 'no details in report' in such cases.

- *Test solutions*

  Vehicle: yes/no

  Details on test solution

  This is especially important for 'difficult to test substance'. How the test substance solution was prepared, including identification of vehicle, method, concentration of vehicle in final test medium, solvent control information etc. Also include any visual observations about the test solutions e.g. particles observed in suspension, at the surface, clear and colourless solutions etc.

- *Test Organisms*

  Species: picklist. If species is not in the list, select 'others' and provide the name in the textbox.

  Details on test organisms:

  This section depends on the type of long-term test. Use the IUCLID predetermined template. As a minimum:

  If 'adult fish' test:

  a) Test organisms: information on organisms such as common name, strain, source, age, weight, length, life-stage, method of breeding, Feeding schedule, food name frequency and amount.
  b) Acclimation: duration, conditions, type and amount of food

  If 'early life-stage reproduction' or 'embryo/egg' test:

  a) Test organism: species, strain, source
  b) Number of fish from which eggs were collected

c) Number of eggs / replicate
d) Method of egg collection and handling of eggs
e) Post hatch feeding: source of food, amount, frequency

- *Study design*

  Test type: picklist
  Water media: picklist
  Limit test: yes/no.
  Exposure duration
  Post Exposure observation

- *Test condition*

  Hardness, temperature, pH, dissolved oxygen, salinity, conductivity

  Nominal and measured concentration

  Details on test conditions:

  This could be divided into 4 subsections

  1) Test system: test vessel, material, headspace, aeration technique, if flow-through then renewal rate, number of organisms per vessel, number of vessels per concentration (replicates), loading rate
  2) Parameters measured
  3) Other test conditions: pH adjustment, light/dark cycle, light intensity
  4) Test concentrations: list all concentrations, spacing factor for concentration, justification of dose, any dose range finding study (brief details on methodology)

- *Any other information on materials and methods*

  Any information on preliminary study conducted
  Control parameters (such as mortality) was measured or not
  Note the validity criteria utilised in the study

Results and discussion

- *Effect concentrations*

  Fill all details in the table, checkbox the ‘key result’. Basis of effects- Select from picklist.
  Report ECx / NOEC on multiple time points if available
  Report all ECx / NOEC available, making sure the basis is clear e.g. nominal or measured

  Endpoints to include here are mortality, days to hatch, numbers of larvae hatched each day, numbers hatched, length and weight of surviving animals, morphological abnormalities, behavioural effects.

- *Details on results*

  Use IUCLID template function for this parameter

Note important things about results such as mortality in control, any behavioural abnormalities in treatment and control group, observations on body weight and length, hatching success and post-hatch survival, abnormal appearance and behaviour, individual weights at the end of the test, etc.
Any other sublethal effect.

- *Statistics*
  Indicate the parameters analysed, the statistical method used and the statistical test performed. Also add a comparative statement between solvent control and procedural control and which data is used as study control.

- *Any other information on results:*
  Report tabulated data on all dose groups

Applicant's summary and conclusions

- *Validity criteria fulfilled*
  Validity criteria are usually listed in lab reports. If working with publication or if lab report does not list validity criteria then please check OECD guideline

- *Conclusion*
  List key conclusions

1.3.3 Short-term toxicity on aquatic invertebrates

Materials and methods

- *Sampling and analysis*
  Analytical monitoring: picklist
  Details of sampling:
  - Concentrations
  - Sampling method
  - Sample storage
  - Any other useful information on sampling

  Details on analytical methods:
  Divide this section into 2 main parts
  (1) Pre-treatment of samples- such as centrifugation, filtration, digestion, clean-up etc.
  (2) Identification and quantification- separation method (HPLC, GC etc), conditions (solvent, mobile phase etc), detection method (e.g. UV, ICP, MS etc), detection limit, reproducibility, linearity, calibration details etc
  Note: If there is no information on analytical methods at all, mention 'no details in report' in such cases.

- *Test solutions*
  Vehicle: yes/no

Details on test solution

This is especially important for 'difficult to test substances'. How the test substance solution was prepared, including identification of vehicle, method, concentration of vehicle in final test medium, solvent control information etc. Also include any visual observations about the test solutions e.g. particles observed in suspension, at the surface, clear and colourless solutions etc.

- *Test Organisms*

  Species: picklist.

  If species is not in the list, select 'others' and provide the name in the textbox.

  Details on test organisms:

  This section can be divided into three subsections.

  1) Test organisms: information on organisms such as common name, strain, source, Age, weight, length, life-stage, method of breeding, Feeding schedule, food name frequency and amount.
  2) Acclimation: duration, conditions, type and amount of food
  3) Culturing condition

- *Study design*

  Test type: picklist

  Water media: picklist

  Limit test: yes/no.

  Exposure duration

  Post exposure observation period (if relevant)

- Test condition

  Hardness, temperature, pH, dissolved oxygen, salinity, conductivity

  Nominal and measured concentration

  Details on test conditions:

  This could be divided into 5 subsections

  1) Test system: test vessel, material, headspace, aeration technique, if flow-through then renewal rate, number of organisms per vessel, number of vessels per concentration (replicates), loading rate
  2) Parameters measured
  3) Test concentrations: list all concentrations, spacing factor for concentration, justification of dose, any dose range finding study (brief details on methodology)
  4) Other test conditions: pH adjustment, light/dark cycle, light intensity
  5) What parameters were measured

Positive control information (generally not needed, but include this information if reported in the report)

- *Any other information on materials and methods*

  Any information on preliminary study conducted
  Control parameters (such as mortality) was measured or not
  Note the validity criteria utilised in the study

Results and discussion

- *Effect concentrations*

  Fill all details in the table, checkbox the 'key result'. Basis of effects- Select from picklist.
  Report EC50 on multiple time points if available
  Report all ECx (e.g. EC50, EC25) available, making sure the basis is clear e.g. nominal or measured
- *Details on results*

  Note important things about results such as mortality in control, any behavioural abnormalities in treatment and control group, observations on body weight and length
  Any other sublethal effect
- *Positive control results*
- *Statistics*

  Indicate the parameters analysed, the statistical method used and the statistical test performed. Also add a comparative statement between solvent control and procedural control and which data is used as study control.
- *Any other information on results:*

  Report tabulated data on all dose groups

Applicant's summary and conclusions

- *Validity criteria fulfilled*

  Validity criteria are usually listed in lab reports. If working with publication or if lab report does not list validity criteria then please check OECD guideline
- *Conclusion*

  List key conclusions

1.3.4 Long-term toxicity on aquatic invertebrates

Materials and methods

- *Sampling and analysis*

  Analytical monitoring: yes/no
  Details on sampling:

  Concentrations from which samples were collected, sampling method, sample storage conditions
  Details on analytical monitoring:

  This section could be divided into two sub-sections:

  1) Pre-treatment: Any pre-treatment of samples after collection. Here, discuss things like digestion, extraction, centrifugation and any clean-up of samples. If there is no pre-treatment of the collected sample,

mention ‘no pre-treatment’ or ‘not specified’ whichever is applicable.

2) Quantification of substance: All details on the method used for analysis of substance. Includes name of method, instrument used (e.g. HPLC, GC MS etc), solvents use, detection limits, linearity, calibration, precisions, reproducibility etc.

Note: If there is no information on analytical methods at all, mention ‘no details in report’ in such cases.

- *Test solutions*

  Vehicle: yes/no

  Details on test solution

  This is especially important for ‘difficult to test substances’. How the test substance solution was prepared, including identification of the vehicle, method, concentration of vehicle in final test medium, solvent control information etc. Also include any visual observations about the test solutions e.g. particles observed in suspension, at the surface, clear and colourless solutions etc.

- *Test Organisms*

  Species: picklist. If species is not in the list, select ‘others’ and provide the name in the textbox.

  Details on test organisms:

  This section can be divided into two subsections.

  1) Test organisms: information on organisms such as common name, strain, source, Age, weight, length, life-stage, method of breeding, Feeding schedule, food name frequency and amount.
  2) Acclimation: duration, conditions, type and amount of food

- *Study design*

  Test type: picklist

  Water media: picklist

  Limit test: yes/no

  Exposure duration

- *Test condition*

  Hardness, temperature, pH, dissolved oxygen, salinity, conductivity

  Nominal and measured concentration

  Details on test conditions:

  This could be divided into 4 subsections

  1) Test system: test vessel, material, headspace, aeration technique, if flow-through then renewal rate, number of organisms per vessel, number of vessels per concentration (replicates), loading rate
  2) Parameters measured

3) Other test conditions: pH adjustment, light/dark cycle, light intensity
4) Test concentrations: list all concentrations, spacing factor for concentration, justification of dose, any dose range finding study (brief details on methodology)

Positive control details (generally not needed, but include this information if reported in the report)

- *Any other information on materials and methods*

  Any information on a preliminary study conducted

  Control parameters (such as mortality) was measured or not

  Note the validity criteria utilised in the study. Also add a comparative statement between solvent control and procedural control and which data is used as study control.

Results and discussion

- *Effect concentrations*, making sure the basis is clear e.g. nominal or measured

  Fill all details in the table, checkbox the 'key result'. Basis of effects- Select effect parameter such as inhibition of reproduction, mortality or growth inhibition, which the effect concentration relates to
- *Details on results*

  Note important things about results such as mortality in control, any behavioural abnormalities in treatment and control group, observations on body weight and length
- *Positive control results*
- *Statistics*: Indicate the parameters analysed, the statistical method used, and the statistical test performed.
- *Any other information*: Report tabulated data on all dose groups

Applicant's summary and conclusions

- Validity criteria fulfilled

  Validity criteria are usually listed in lab reports. If working with the publication or if lab report does not list validity criteria then please check OECD guideline
- Conclusion

  List key conclusions

1.3.5 Algal growth inhibition test

Materials and methods

- *Sampling and analysis*

  Analytical monitoring: yes/no

  Details on sampling:

  Concentrations from which samples were collected, sampling method, sample storage conditions

  Details on analytical monitoring:

This section could be divided into two sub-sections:

1) Pre-treatment: Any pre-treatment of samples after collection. Here, discuss things like digestion, extraction, centrifugation, and any clean-up of samples. If there is no pre-treatment of the collected sample, mention 'no pre-treatment' or 'not specified' whichever is applicable.

2) Quantification of substance: All details on the method used for the analysis of substance. Includes name of method, instrument used (e.g. HPLC, GC MS etc), solvents use, detection limits, linearity, calibration, precisions, reproducibility etc.

Note: If there is no information on analytical methods at all, mention 'no details in report' in such cases.

- *Test solutions*

  Vehicle: yes/no

  Details on test solution

  This is especially important for 'difficult to test substance'. How the test substance solution was prepared, including identification of vehicle, method, concentration of vehicle in final test medium, solvent control information etc. Also include any visual observations about the test solutions e.g. particles observed in suspension, at the surface, clear and colourless solutions etc.

- *Test Organisms*

  Species: picklist. If species is not in the list, select 'others' and provide the name in the textbox.

  Details on test organisms:

  This section can be divided into two subsections.

  1) Test organisms: information on organisms such as common name, strain, source, Age, weight, length, life-stage, method of breeding, Feeding schedule, food name frequency and amount.
  2) Acclimation: duration, conditions, type and amount of food

- *Study design*

  Test type: picklist

  Water media: picklist

  Limit test: yes/no

  Exposure duration

- *Test condition*

  Hardness, temperature, pH, dissolved oxygen, salinity, conductivity

  Nominal and measured concentration

Details on test conditions:

Use the IUCLID template option for this. This could be divided into 5 subsections

1) Test system: test vessel, material, headspace, aeration technique, if flow-through then renewal rate, number of organisms per vessel, number of vessels per concentration (replicates)
2) Growth media information: composition of media
3) Parameters measured: e.g cell lumbers or chlorophyll content
4) Other test conditions: pH adjustment, light/dark cycle, light intensity
5) Test concentrations: list all concentrations, spacing factor for concentration, justification of dose, any dose range finding study (brief details on methodology)

Positive control details

- Any other information on materials and methods

  Any information on preliminary study conducted
  Control parameters (such as mortality) was measured or not
  Note the validity criteria utilised in the study

Materials and methods

- *Test species*; include the scientific name of the species (if the name has changed, include both the new name and the name specified in the test report)
- *Initial cell concentration;*
- *Test conditions* (temperature, lighting, test medium, pH, test system, solubilising agent, etc.);
- *Test duration/total exposure duration* test design (e.g. test concentrations, number of controls, number of replicates);
- *Controls conditions (pH, etc.);*
  Include information on all types of controls (solvent, negative, positive etc). Positive control should be reported in field ‘Reference substance (positive control) field and other control should be included in ‘Details of test conditions’ field.

Results and discussion

- Effect concentrations EC50 / NOEC, making sure the basis is clear e.g. nominal or measured
  Fill all details in the table, checkbox the ‘key result’. Basis of effects- Select effect parameter such as biomass, cell number, growth rate etc
- Details on results
  Note important things about results. Use IUCLID template functionality. Things such as unusual observations such as unusual cell shape, cell colour, flocculation, adherence, and aggregation of cells. Growth trend in control and treatment, any precipitation or lack of solubility noted etc.
- Positive control results

- Statistics: Indicate the parameters analysed, the statistical method used, and the statistical test performed. Also add a comparative statement between solvent control and procedural control and which data is used as study control.
- Any other information: Report tabulated data on all dose groups

Applicant's summary and conclusions

- Validity criteria fulfilled
  Validity criteria are usually listed in lab reports. If working with publication or if lab report does not list validity criteria then please check OECD guideline
- Conclusion
  List key conclusions

1.3.6 Toxicity to microorganisms

Materials and methods

- *Sampling and analysis*
  Analytical monitoring: yes/no
  Details on sampling:
  Concentrations from which samples were collected, sampling method, sample storage conditions
  Details on analytical monitoring: This section could be divided into two sub-sections:
  1) Pre-treatment: Any pre-treatment of samples after collection. Here, discuss things like digestion, extraction, centrifugation, and any clean-up of samples. If there is no pre-treatment of the collected sample, mention 'no pre-treatment' or 'not specified' whichever is applicable.
  2) Quantification of substance: All details on the method used for analysis of substance. Includes name of method, instrument used (e.g. HPLC, GC MS etc), solvents use, detection limits, linearity, calibration, precisions, reproducibility etc.

  Note: If there is no information on analytical methods at all, mention 'no details in report' in such cases.

- *Test solutions*
  Vehicle: yes/no
  Details on test solution
  This is especially important for 'difficult to test substance'. How the test substance solution was prepared, including identification of vehicle, method, concentration of vehicle in final test medium, solvent control information etc. Also include any visual observations about the test solutions e.g. particles observed in suspension, at the surface, clear and colourless solutions etc.

- *Test Organisms*
  Species: picklist. If species is not in the list, select 'others' and provide the name in the textbox.
  Details on inoculum:
  STP where inoculum was collected; method of cultivation; Indicate laboratory culture origin and initial biomass concentration when appropriate
  Indicate suspended solid concentration in final test medium pre-treatment and preparation of inoculum

- *Study design*
  Test type: picklist
  Water media: picklist
  Limit test: yes/no concentration is tested.
  Exposure duration

- Test condition
  Hardness, temperature, pH, dissolved oxygen, salinity, conductivity
  Nominal and measured concentration
  Details on test conditions:
  This could be divided into 3 subsections

  1) Test system: test vessel, material, headspace, aeration technique, if flow-through then renewal rate, number of organisms per vessel, number of vessels per concentration (replicates)
  2) Parameters measured
  3) Test concentrations: list all concentrations, spacing factor for concentration, justification of dose, any dose range finding study (brief details on methodology)

  Positive control details

- Any other information on materials and methods
  Any information on preliminary study conducted
  Control parameters was measured or not
  Note the validity criteria utilised in the study

Results and discussion

- *Effect concentrations* such as EC10, EC50, NOEC (along with time of measurement), making sure the basis is clear e.g. nominal or measured
  Fill all details in the table, checkbox the 'key result'. Basis of effects- Select effect parameter from the picklist
- *Details on results*
  Note important things about results. Use IUCLID template functionality. Things such as unusual observations such as any precipitation or lack of solubility noted, adsorption, blank control O2 uptake, etc.
- *Positive control results*

- *Statistics*: Indicate the parameters analysed, the statistical method used, and the statistical test performed. Also add a comparative statement between solvent control and procedural control and which data is used as study control.
- *Any other information*: Report tabulated data on all dose groups

Applicant's summary and conclusions

- Validity criteria fulfilled
  Validity criteria are usually listed in lab reports. If working with a publication or if lab report does not list validity criteria then please check OECD guideline
- Conclusion
  List key conclusions

1.4 Terrestrial toxicity

General instructions on terrestrial toxicology

Always add comments in the 'basis of effect' section in the 'results and discussion' table.

Measured concentration must be reported in the results and discussion table if available. If not available, then a statement should be made clearly indicating that measured concentration was not reported in the report.

Tabulated raw data for each dose group should preferably be provided (in 'any other details on results' section) and add images of plots (including slopes) of the effect curves in the 'illustration' subsection of the 'Overall remarks' section

If measurements were made on multiple time-points, please include results of all time points, not just the last time point. Use the table provided in the results section of the IUCLID. There is a time field available in that table.

1.4.1 Toxicity to soil microorganisms - Nitrogen transformation test

Materials and methods

- Sampling and analysis
  Analytical monitoring: yes/no
  Details on sampling:
  Concentrations from which samples were collected, sampling method, sample storage conditions
  Details on analytical monitoring: This section could be divided into two sub-sections:
  1) Pre-treatment: Any pre-treatment of samples after collection. Here, discuss things like digestion, extraction, centrifugation, and any clean-up of samples. If there is no pre-treatment of the collected sample, mention 'no pre-treatment' or 'not specified' whichever is applicable.

2) Quantification of substance: All details on the method used for analysis of substance. Includes name of method, instrument used (e.g. HPLC, GC MS etc), solvents use, detection limits, linearity, calibration, precisions, reproducibility etc.

- Test substrate

  Vehicle
  Details on preparation and application of test substrate: Important to include details on soil amendment, Application method for test substance, Vehicle (name, concentration, prior evaporation).

- Test organisms: soil / other
- Exposure duration
- Test temperature
- Moisture content of soil (at the start and end of test)
- Organic carbon and nitrogen content of soil
- Details on test condition: Use the IUCLID template function and fill as much detail as possible. As a minimum
  - Nitrogen content of test substance
  - Details on test system: amount of soil, replicates, container
  - Soil incubation method
  - Source and properties of substrate: details such as soil history, texture, contamination, composition, pH, initial nitrate concentration, microbial mass, water holding capacity, cation exchange capacity etc
  - Pre-incubation of soil (if available)
  - Details of amendment and type of soil with organic substrate (source, composition, carbon content, nitrogen content, sieve size);
  - Test conditions (moisture, temperature, lighting);
  - Test duration, sampling times test system (e.g. sealed containers);
  - Test design (concentrations tested, number of controls, number of replicates, etc.);
  - Method for the application of the test substance to soil (use of carrier);
  - Method for extraction of nitrate from soil;
  - Analytical procedure and equipment used to analyse nitrate.
  - Parameters of study
  - Vehicle control (yes/no)

- Any other information on materials and methods

  Any information on preliminary study conducted
  Control parameters was measured or not
  Note the validity criteria utilised in the study

Results and discussion

- Observations: nitrate production (mg nitrate/ kg dry weight soil/day) (preferably in a tabular form), variation between the replicates in treated and control samples;
- EC50, EC25 or EC10 values with the confidence interval, the dose response curve and data on statistical treatment of the results.
- Statistics: Indicate the parameters analysed, the statistical method used, and the statistical test performed.

Applicant's summary and conclusions

- Validity criteria fulfilled
  Validity criteria are usually listed in lab reports. If working with publication or if lab report does not list validity criteria then please check OECD guideline
- Conclusion
  List key conclusions

1.4.2 Toxicity to soil microorganisms – Carbon transformation test

Materials and methods

- Sampling and analysis
  Analytical monitoring: yes/no
  Details on sampling:
    Concentrations from which samples were collected, sampling method, sample storage conditions
  Details on analytical monitoring: This section could be divided into two sub-sections:
    1) Pre-treatment: Any pre-treatment of samples after collection. Here, discuss things like digestion, extraction, centrifugation, and any clean-up of samples. If there is no pre-treatment of the collected sample, mention 'no pre-treatment' or 'not specified' whichever is applicable.
    2) Quantification of substance: All details on the method used for analysis of substance. Includes name of method, instrument used (e.g. HPLC, GC MS etc), solvents use, detection limits, linearity, calibration, precisions, reproducibility etc.

- Test substrate
    Vehicle
    Details on preparation and application of test substrate: Important to include details on soil amendment, Application method for test substance, Vehicle (name, concentration, prior evaporation).

- Test organisms: soil / other
- Exposure duration
- Test temperature
- Moisture content of soil (at the start and end of test)
- Organic carbon and nitrogen content of the soil
- Details on test condition: Use IUCLID template function and fill as much detail as possible. As a minimum

- Details on test system: amount of soil, replicates, container
- Soil incubation method
- Source and properties of substrate: details such as soil history, texture, contamination, composition, pH, initial nitrate concentration, microbial mass, water holding capacity, cation exchange capacity etc
- Pre-incubation of soil (if available)
- Details of amendment and type of soil with organic substrate (source, composition, carbon content, nitrogen content, sieve size);
- Test conditions (moisture, temperature, lighting);
- Test duration, sampling times test system (e.g. sealed containers);
- Test design (concentrations tested, number of controls, number of replicates, etc.);
- Method for the application of the test substance to soil (use of carrier);
- method for measuring the respiration rate (e.g. either mean CO2 released or mean O2 consumed)
- Parameters of study
- Vehicle control (yes/no)

- Any other information on materials and methods
  Any information on preliminary study conducted
  Control parameters was measured or not
  Note the validity criteria utilised in the study

Results and discussion

- observations: respiration rate (mg CO2/ kg dry weight soil/h or mg O2/ kg dry weight soil/h) (preferably mean and individual and in a tabular form), variation between the replicates in treated and control samples;
- EC50, EC25 or EC10 values with the confidence interval, the dose response curve and data on statistical treatment of the results.
- Statistics: Indicate the parameters analysed, the statistical method used, and the statistical test performed.

Applicant's summary and conclusions

- Validity criteria fulfilled
  Validity criteria are usually listed in lab reports. If working with publication or if lab report does not list validity criteria then please check OECD guideline
- Conclusion
  List key conclusions

1.4.3 Toxicity to terrestrial plants (seedling emergence)

Materials and methods

- Sampling and analysis
  Analytical monitoring: yes/no
  Details on sampling:
  Concentrations from which samples were collected, sampling method, sample storage conditions

Details on analytical monitoring: This section could be divided into two sub-sections:

1) Pre-treatment: Any pre-treatment of samples after collection. Here, discuss things like digestion, extraction, centrifugation, and any clean-up of samples. If there is no pre-treatment of the collected sample, mention 'no pre-treatment' or 'not specified' whichever is applicable.
2) Quantification of substance: All details on the method used for analysis of substance. Includes name of method, instrument used (e.g. HPLC, GC MS etc), solvents use, detection limits, linearity, calibration, precisions, reproducibility etc.

- Test substrate

  Vehicle

  Details on preparation and application of test substrate: Application method for test substance, Vehicle (name, concentration, prior evaporation, and method of application)

- Test organisms

  Species: picklist. If not listed, select other and provide details

  Within the test organisms block: provide other details i.e.

  plant families, scientific and common names, source, and history of the seeds; rationale for selection of mono- and di-cotyledon species tested; seed storage, treatment and maintenance, seeds season collected, batch/lot number and supplier of seeds.

- Study design and test conditions tab

  Provide following details in these sections:

  - Exposure duration
  - Test temperature
  - Moisture content of soil (at the start and end of test)
  - Organic carbon and nitrogen content of soil
  - substrate type: soil/substrate characteristics (e.g. texture, pH), when natural soil also its suitability for testing, nutrient medium if used
  - test conditions: test facility and test system (e.g. pot dimension, amount of soil), application of test substance (e.g. method/equipment/calibration for methods, auxiliary substances used), growth conditions (e.g. light intensity, photoperiod, max/min temperatures, watering schedule and method, fertilisation, pollination when included)
  - test duration/total exposure duration
  - test design: test concentrations/exposure rates including chemical verification, number of seeds per pot, of plants per dose, of replicates (pots) per exposure rates, type and number of controls, stage of plant development at the start of test

- Any other information on materials and methods

  Any information on preliminary study conducted

  Control parameters was measured or not

Note the validity criteria utilised in the study

Results and discussion

- Effect concentrations
  EC50, ER50, E(R)C10, NOEC and LOEC (necessary for long term), dose-response relationships
- Details on results
  Use template function and provide details on seedling emergence related results. description of the rating scale used to judge visual injury, if visual rating is provided
- Positive control data if available
- Statistical details
- Any other information
  table of all endpoints for each replicate, test rate/concentration and species observations of endpoints (mortality, emergence, biomass measurements, shoot height, etc.) as a percentage of the controls,

Applicant's summary and conclusions

- Validity criteria fulfilled
  Validity criteria are usually listed in lab reports. If working with publication or if lab report does not list validity criteria then please check OECD guideline
- Conclusion
  List key conclusions

1.4.4 Long term toxicity on terrestrial invertebrates (Earthworm, OECD 222)

Materials and methods

- Sampling and analysis
  Analytical monitoring: yes/no
  Details on sampling:
  Concentrations from which samples were collected, sampling method, sample storage conditions
  Details on analytical monitoring: This section could be divided into two sub-sections:
  1) Pre-treatment: Any pre-treatment of samples after collection. Here, discuss things like digestion, extraction, centrifugation, and any clean-up of samples. If there is no pre-treatment of the collected sample, mention 'no pre-treatment' or 'not specified' whichever is applicable.
  2) Quantification of substance: All details on the method used for analysis of substance. Includes name of method, instrument used (e.g. HPLC, GC MS etc), solvents use, detection limits, linearity, calibration, precisions, reproducibility etc.

- Test substrate
  Vehicle
  Details on preparation and application of test substrate: Application method for test substance, Vehicle (name, concentration, prior evaporation, and method of application)

- Test organism
  Species: picklist
  Group: picklist
  Details on test organism: provide source, age, weight of organism and acclimation
  Study design: Provide all details including study type, substrate type, exposure duration
  Test conditions: provide details such as temperature, pH, moisture, properties of soil (source, sampling depth, collection procedure, soil texture, storage, pre-treatment, water holding capacity, organic carbon, stability, and homogeneity of test substance in soil). Also provide information on replicates, test concentrations, spacing factor, nominal/measured concentrations, and reference substance; method and auxiliary substances used for application of test substance, temperature, duration of light-dark cycles, light intensity, feeding regime

- Any other information on materials and methods
  Any information on preliminary study conducted
  Control parameters was measured or not
  Note the validity criteria utilised in the study

Results and discussion

- observations in the controls (number of juveniles, mortality, etc.)
- observations: % adult mortality, % changes in body weight and average live weight of live adults (where applicable) at the end of the adult exposure period of the test, number of juveniles at end of test, obvious or pathological symptoms or distinct changes in behaviour

- results obtained with the reference test substance
- the LC50, the NOEC and LOEC and (recommended) ECx (e.g. EC50, EC10) for reproduction and other endpoints, dose-response relationships, description of statistical analysis performed

Applicant's summary and conclusions

- Validity criteria fulfilled
  Validity criteria are usually listed in lab reports. If working with publication or if lab report does not list validity criteria then please check OECD guideline
- Conclusion
  List key conclusions

1.5 Human Toxicology

General instructions on human toxicology

Use "insert existing template" functionality wherever it is available

If the full study report includes the historical control data on histopathology, please include this information in the ‘any other information on results’ section. If data values for historical control are not available but instead a statement on historical control data, it must be included in the RSS.

For all repeated dose toxicity studies, full dose-response data should be provided in the ‘any other information on results’ and not just the NOEL values. This information will be provided in tabular form for all major parameters and a Table number should be assigned to each table.

Note: Do not create tables in Word file and paste them in IUCLID because it leads to formatting errors when converted to pdf. Instead, create tables directly in the IUCLID.

For all types of repeated dose toxicity, always include any secondary effects or non-treatment related effects, if identified by the study director. These effects should be reported by selecting “effects observed, non-treatment related” from picklists available for parameters in the ‘Results of Examination’ section.

Wherever relevant, brief study design of a preliminary study (e.g. dose range finding study): provide details such as species, route of exposure, dose, exposure duration, number of groups, replicates, GLP status, parameters, results.

1.5.1 Skin sensitization

1.5.1.1 in vivo

Materials and methods

test type: LLNA or non-LLNA

Test substance and control test substances:

- identification data (e.g. CAS number, if available; source; purity; known impurities; lot number)
- physical nature and physicochemical properties (e.g. volatility, stability, solubility)
- if formulation, composition and relative percentages of components

Test animals

- species/strain/sex
- no. of animals per sex per dose
- age and weight at the study initiation
- control group and treatment
- for LLNA source of CBA mice
- Environmental conditions of animals

Study design: in-vivo (non-LLNA)

- Fill tables for Induction and challenge. Please also provide justification for the choice of vehicle in the remark section. Note all concentrations used. Also mention any pre-treatment that may have been conducted
- No of animals per dose
- Details on study design: give details on any preliminary study; Also provide full details on induction and challenge during main study: add details such as exposure duration, number of exposures, number of doses, frequency, duration. identify the endpoint to measure effect
- Details on controls

Study design: in-vivo (LLNA)

- Vehicle
- Concentration
- Number of animals/dose
- Details on stud design: pre-screening study detail (if relevant). Any other important information on study design. Justification for dose selection. Identify the endpoint to measure effect
- Positive control
- statistical methods

Any other information on material and methods

- criteria for considering studies as positive or negative
- Additional things that should be discussed:
    - if a concurrent PC was not included, the date and laboratory report for the most recent periodic PC and a report detailing the historical PC data for the laboratory justifying the basis for not conducting a concurrent PC

Results and discussion

- Positive control data
- Fill the appropriate tables
- Any other information on results:
    - data should be summarised in tabular form, showing for each animal the skin reactions at each observation point (e.g., number of animals with skin grades of 0, 1, 2, and 3 at each observation time)
    - narrative description of the nature and degree of effects observed
    - any histopathological findings
    - provide additional information that may be needed to adequately assess data for reliability and use, including the following, if available:
        - whether the substance was a skin irritant at the tested concentrations
        - incidence of skin scores greater than 1 for test and control groups
        - description, severity, time of onset and duration of clinical signs and/or lesions at the site of contact at each dose level
        - results of rechallenge

For the LLNA study results, provide the following additional information:

- time course of onset and signs of toxicity, including dermal irritation at site of administration, if any, for each animal
- time of animal sacrifice and time of ATP measurement for each animal
- a table of individual mouse BrdU or RLU values and SI values for each dose treatment group
- mean and associated error term (e.g. SD, SEM) for BrdU labelling index/mouse or RLU/mouse for each treatment group and the results of outlier analysis for each treatment group
- calculated SI and an appropriate measure of variability that takes into account the inter-animal variability in both the test substance and control groups
- dose response relationship
- statistical analyses, where appropriate

Overall remarks, attachments

- Provide toxicological evaluation of the findings of the study, their biological relevance and if needed human relevance. If relevant, include a summary of confounding factors that may affect the results of the study.
- Discuss any significant deviations from the guideline.

Applicant's summary and conclusions

- Give a brief commentary on the results, with a dose-response analysis and a conclusion as to whether the test substance should be considered a skin sensitiser. Provide information related to classification and labelling under interpretation of results, and the conclusion of the study under conclusions.

1.5.1.2 OECD 442C specific information

Test chemicals

- Treatment of test chemical prior to testing
- Solubility properties
- Stability of test chemicals
- Storage conditions

Methods

- Details of the test system (picklist)
- Details on the study design:
    - Test solution preparation
    - Incubation time
    - HPLC details
    - Peptide details such as supplier, lot, purity
    - Peptide detection wavelength
- Vehicle used
- Positive control

Results

- Positive control results
- Parameter
- Value
- Concentration at which results are reported
- Vehicle and controls validity met?
- Remarks on results (necessary)
- Outcome

Applicant summary and conclusion

- GHS criteria
- Conclusions

1.5.1.3 OECD 442D specific information

Material and Methods

- Type of study (from picklist): e.g. KeratinoSens; LuSens; hCLAT etc
- Details on test system (picklist): cell line used. If not in list, select others and mention the name
- Details on study design should be as detailed as possible:
    a) full details on preparation of test solution such as stocks, dilutions, prep of positive control, all types of solvents used for material and controls;
    b) Details on the dose range finding study: highest concentration, solubility information (in solvent and media), cytotoxicity details, Final concentration selected and why;
    c) Application details: Number of replicates in test and control, all concentrations, duration of exposure, application method
    d) Acceptance criteria
    e) Seeding and incubation details and washing details
    f) Details on luminometer used
    g) Cytotoxicity determination method name and details, stats applied

- Positive, negative, solvent control details

Results

- Positive control details are mandatory
- In the results table: always correctly identify the key results and checkmark it
- Identify the experimental group in which the key results were obtained
- Is it the mean value or an individual run?
- Selecting the correct unit of the results are mandatory
- Report cell viability at the concentration
- Select all the validity criteria for all controls
- Outcome of the predictive model (picklist)
- Any other effects, other than key results should be reported in ‘other effects’ free textbox

Summary and conclusion

- Interpretation of result is mandatory (picklist)
- Conclusions and study summary should be fulfilled as described in the general section of this SOP

1.5.2 Repeated dose toxicity

Materials and methods

Limit test

Yes/No.

Test animals

- species/strain/sex
- no. of animals per sex per dose
- Details on test animals or test system
  This subsection could be divided into three parts
  1) Test animals: describe the source, age and weight at initiation, fasting period before the study, acclimatisation
  2) Food and water: describe food and water regimen (e.g. ad libitum or once or twice a day, whichever is applicable), also describe the quality of food and water- usually there are statements in reports that the food and water was bpa or oestrogen free etc
  3) Environmental conditions: Temperature, Humidity, Air change per hour, photoperiod of the animal room

Administration/exposure

- route of administration – oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapour, gas, particulate), other
- vehicle: if other than water, please provide justification. Justification should ideally be present in the report. If not given in the report, then see stability and homogeneity section and check if substance was homogeneously dispersed or soluble in the vehicle. If you are not able to find any justification of the vehicle, mention that it is not available in the report and record this issue as a deficiency in the RSS, in the ‘rationale for reliability’ as a side note.
- Details on oral exposure
  This section should be divided into two parts:
  1) Diet preparation: How often diets were prepared, how much substance was mixed with how much food, how the prepared diet was stored
  2) Vehicle: How much substance in how much vehicle, lot/batch number of vehicle, purity of vehicle
- Analytical verification of doses: yes/no
- Details on analytical verification
  Very brief description of method, note the difference between nominal and measured concentrations, focus on conclusion of two properties: homogeneity and stability
- duration and frequency of test/exposure period
- doses/concentration levels, rationale for dose level selection
- No of animals/sex per dose

- Control animals
- Details on study design:
  Within this section, discuss following -
  basis of dose selection,
  fasting period before sampling,
  are there any satellite groups, if yes, rationale
  Recovery period in satellite groups
  Brief study design of preliminary study: e.g. provide dose, exposure duration, number of groups, replicates, GLP status, parameters, results.

- Positive control: Usually not the case. Mention yes/no. If yes, provide name, CAS, batch number, purity

Examinations

- Observations and examinations performed and frequency
  Click on ‘insert existing template’. This will create 14 subsections within this section. All the keywords in subsections of this existing template are standard toxicology parameters; hence, the fastest and most accurate way is to do ctrl F with these keywords in the report and note whether each of these parameters were performed or not. Fill as many details as possible. Mention ‘not specified in the rest’
- Sacrifice and pathology: specify whether gross pathology and histopathology was performed
- Statistics: Note down all the statistical parameters, p values

For inhalation studies

- type of inhalation exposure and test conditions (e.g. exposure apparatus)
- method of exposure (“whole body”, “oro-nasal”, or “head only”), exposure data
- analytical verification of test atmosphere concentrations
- Form of test material (e.g. gas, vapour, aerosol, dust, mist etc). This could be reported in “Details on inhalation exposure” section
- particle size (for studies with aerosols, indicate mass median aerodynamic diameter and geometric standard deviation or give other specifications)
- type or preparation of particles (for studies with aerosols)

For dermal studies

- area covered (e.g. 10% of body surface)
- occlusion (e.g. semi-occlusive)
- total volume applied
- removal of test substance (e.g. water or solvent)

Statistical methods

Results and discussion

- Within each parameter listed under this heading, select the appropriate option. If no effects occurred, select "No effects observed". Don't leave any parameter blank, i.e.,

if a particular parameter was not evaluated, please write ‘not examined’. If a particular parameter was evaluated (described in the method of report) but no results were reported in the results section, then write ‘not specified’. If ‘effect observed, treatment related’ or ‘no effects observed’ are selected, then please give justification on why this was decided in the ‘description (incidence and severity)’.

- For each of the parameters listed in this section, ‘incidence and severity’ is very important. Ideally, a brief summary of the dose response relationship of the parameter in question, whether the effects were adverse or non-adverse and whether effects were reversible or irreversible (if analysed in satellite). If the data in the report is very extensive and not possible to summarise, then simply write ‘please see Any other information on results incl. table’ and provide detailed tables with proper headings in the ‘Any other information on results incl. tables’.

- Effect levels:
  Checkmark the ones that drive NOAEL. Fill all other details required in the table. Basis of effect’ means the parameter that led to the NOAEL determination and if the endpoint is not listed, select the ‘other’ and provide details.

- Target organs: Fill all the details. There could be multiple target organs. Provide all information

- ‘Any other information’:
  As indicated in the general section of human tox RSS full dose-response data should be provided in the ‘any other information on results’ and not just the NOAEL values. In your tables, segregate the data according to sex. All tables should have proper headings in this section. There is no limit on how many tables you can include. Just to give you some idea, the following tables may be included:
  Tabulated data for organ weights (with proper heading) along with all doses and severity
  Tabulated data for histopathology (with proper heading) along with all doses and severity
  Tabulated data on the frequency of findings (with proper headings) along with all doses and severity
  Historical control data, if available

Overall remarks, attachments

- Provide toxicological evaluation of all the findings of the study (adverse and non-adverse effects, reversible and irreversible effects) also explaining the biological relevance of the effects observed in animals and if needed address human relevance. If it is a lab report, this information is discussed by the study director in the discussion and/or conclusion section. In the publication, this information could be found in the discussion section.
- If relevant include a summary of confounding factors that may affect the results of the study
- Discuss any significant deviations from the guideline.

Applicant's summary and conclusions

- Provide information related to classification and labelling, interpretation of results, and the conclusion of the study under the section conclusions.

1.5.3 Genetic Toxicology

1.5.3.1 *In vitro*

Materials and methods

Method

- Target gene (report only if it is necessary to characterise the system). For example, it is not required in Ames test
- Species/strain: Fill the table. Add rows for each tester strain
- Cytokinesis block (if used)
- Metabolic activation along with details such as type and composition of activation system, source, method of preparation, concentration, volume, QC
- Test concentration along with justification of top dose (whether the top dose was due to cytotoxicity or solubility).
- Vehicle/solvent: also provide justification of the vehicle
- Controls: provide details of all controls in the table
- Details of test system and experimental condition
  Use template function. And provide all the critical information needed in this section. As a minimum, try to cover at least following parameters (also provide chromosome aberration/gene mutation specific details in the template, if relevant)-
    - Replications
    - Cell density (except ames test)
    - How test substance was added
    - Details on slide preparation
    - Number of metaphase analysed
    - Method of cytotoxicity measurement
- Evaluation criteria must be clearly defined
- Statistics

'Any other information on materials and methods

- Tabulated data for dose selection

Results and discussion

- Test results: provide details in table
- Additional information: Provide additional details that can help in interpretation results. Use 'insert existing template' functionality and fill details that are available in the report. Also consider providing historical control data
- 'Any other information':
    - Tabulated data for interpretation of results on each dose

Overall remarks, attachments

- Provide toxicological evaluation of the findings of the study. If relevant include a summary of confounding factors that may affect the results of the study and analysis of equivocal results. Discuss any significant deviations from the guideline.

Applicant's summary and conclusions

- Provide information related to classification and labelling and the conclusion of the study under the conclusions section

1.5.3.2 *In vivo*

Materials and methods

- type of genotoxicity,
- type of study (in vivo mammalian chromosome aberration test etc.)

Test animals

- species/strain/sex
- no. of animals per sex per dose
- age and weight at the study initiation
- Environmental conditions

Administration/exposure

- Route
- Vehicle: name, justification, concentration, amount, lot number, purity
- Details on exposure: Preparation of dosing solutions; diet preparation
- Duration of exposure
- Post exposure duration (if any)
- Doses/concentration (in the table)
- Number of animals/sex/dose
- Control animals (select appropriate)
- Positive control: name, justification, route, dose/concentration

Examinations

- Tissue and cell type
- Tissue and slide preparation:
  This section could be broken into 4 parts: 1) Criteria dose selection 2) Treatment sampling time 3) Slide preparation 4) Method of analysis
- Evaluation criteria: Criteria that are used to judge the substance as a positive
- Statistics

Any other information

- If oral study: actual doses (mg/kg bw/day) and conversion factor from diet/drinking water test substance concentration (ppm) to the actual dose, if applicable

Results and discussion

- Test results: Fill in the table including the validity of the controls

- Additional information: 1) Range finding study: Dose range, solubility clinical signs toxicity, Harvest times etc. 2) Definite study: Report types of structural aberrations (for CAB assay), MN induction (MN assay), Ratio of PCE/NCE by dose level/sex
- Any other information: add tabulated data on all dose groups

Overall remarks, attachments

- Provide toxicological evaluation of the findings of the study explaining also the biological relevance of the effects observed in animals and if needed address human relevance. If relevant include a summary of confounding factors that may affect the results of the study. Discuss any significant deviations from the guideline.

Applicant's summary and conclusions

- Provide information related to classification and labelling, interpretation of results, and the conclusion of the study under section conclusions.

1.5.4 Toxicity to Reproduction/Fertility

Materials and methods

Test type

- (one generation, two generation, extended one-generation reproductive toxicity study (EOGRTS), screening, combined, other). Note: different test types have different reporting requirements. These requirements are listed in their respective OECD Guideline. Therefore, not everything listed in sections below may be required. Familiarise yourself with the test guideline before writing RSS so that you are aware what information listed below is relevant for your RSS.

Test animals

- species/strain/sex
- number of animals per sex per dose
- age and weight at the study initiation

Administration/Exposure

- Route of administration
- Details on exposure: 1) Preparation method of dosing solution 2) Diet preparation 3) Vehicle information including name, lot number, purity, supplier etc
- Details on mating: how the mating was performed, M/F ratio/cage, length of cohabitation, proof of pregnancy etc
- Analytical verification of doses: yes/no
- Details on analytical verification: provide name of method, instruments, standardisation, method details, concentrations, vehicles, sample sprep, storage etc. Stability and homogeneity of dose formulation
- Duration of exposure
- Frequency of treatment

- Doses (Table)
- animals/sex/dose
- Control animals
- Details on study design
  Dose selection rationale; Fasting period before blood sampling; details (rationale, etc.) of the administration of the test substance conversion from diet/drinking water test substance concentration (ppm) to the achieved dose (mg/kg body weight/day), if applicable; details of food and water quality (including diet composition, if available); if available, brief study design of preliminary study

Examinations

- Note all observations made for parental animals and offsprings. Use ‘insert existing template functionality

Statistical methods

Results and discussion

- Describe the relevant findings (from relevant generations i.e. Po, P1, F1, F2, depending on the study) from the IUCLID fields. Within each parameter listed under these fields, select the appropriate option. If no effects occurred, select "No effects observed". Don't leave any parameter blank, i.e. if a particular parameter was not evaluated, please write ‘not examined’. If a particular parameter was evaluated (described in the method of report) but no results were reported in the results section, then write ‘not specified’. If ‘effect observed, treatment related’ or ‘no effects observed’ are selected, then please give justification on why this was decided in the ‘description (incidence and severity)’.

- NOAEL/NOAEC (NOEL/NOEC) and LOAEL/LOAEC (LOEL/LOEC) for both males and females of P, F1 and F2 generations, as appropriate

- The lowest relevant NOAEL/NOAEC (NOEL/NOEC and LOAEL/LOAEC LOEL/LOEC for parental systemic toxicity, reproduction (fertility effects) and offspring effects

- Actual dose received by dose level by sex if known

- Present results preferably in tabular form by sex and generation for each test group with statistical results, as appropriate (tables should be inserted in ‘any other information on results’ (see next section ‘any other information’)):

  If assessed, the following results should be reported:

  Note: If any of the information listed below is not reported in the report, it needs to be cross-checked with the test guideline whether that information is required by the guideline. Proper justification should be available in the report if a parameter is required by the guideline but is missing from the report. Record that justification in the RSS. If no justification is provided for a missing

parameter (if required by guideline), then this is a deviation from the guideline. And should be recorded in the deviation from guideline section.

- food consumption, water consumption if available, food efficiency (body weight gain per gram of food consumed, except for the period of cohabitation and during lactation), and test material consumption (for dietary/drinking water administration) for P and F1 animals
- absorption data (if available)
- body weight data for P animals
- body weight data for the selected F1 animals postweaning
- time of death during the study or whether animals survived to termination. Nature, severity and duration of clinical observations (whether reversible or not, organs examined at necropsy, others (e.g. anogenital distance)
- haematology, urinalysis, and clinical chemistry data including TSH and T4
- phenotypic analysis of spleen cells (T-, B-, NK-cells)
- bone marrow cellularity
- toxic response data
- number of P and F1 females with normal or abnormal oestrous cycle and cycle duration
- time to mating (precoital interval, the number of days between pairing and mating)
- toxic or other effects on reproduction, including numbers and percentages of animals that accomplished mating, pregnancy, parturition and lactation, of males inducing pregnancy, of females with signs of dystocia/prolonged or difficult parturition
- duration of pregnancy and, if available, parturition
- numbers of implantations, litter size and percentage of male pups
- number and percent of post-implantation loss, live births and stillbirths
- litter weight and pup weight data (males, females and combined), the number of runts if determined
- number of pups with grossly visible abnormalities
- toxic or other effects on offspring, postnatal growth, viability, etc.
- data on physical landmarks in pups and other postnatal developmental data
- data on sexual maturation of F1 animals
- data on functional observations in pups and adults, as applicable
- body weight at sacrifice and absolute and relative organ weight data for the P and adult F1 animals
- necropsy findings
- detailed description of all histopathological findings
- total cauda epididymal sperm number, percent progressively motile sperm, percent morphologically normal sperm, and percent of sperm with each identified abnormality for P and F1 males
- numbers and maturational stages of follicles contained in the ovaries of P and F1 females, where applicable
- enumeration of corpora lutea in the ovaries of F1 females
- statistical treatment of results, where appropriate
- haematology, urinalysis and clinical chemistry data including TSH and T4
- phenotypic analysis of spleen cells (T-, B-, NK-cells)

- bone marrow cellularity
- toxic response data
- Endocrine findings

- **If the study is EOGRTS and if following Cohort 2 parameters are reported, please record in RSS:**
  - detailed description of the procedures used to standardise observations and procedures as well as operational definitions for scoring observations
  - list of all test procedures used, and justification for their use
  - details of the behavioural/functional, neuropathological and morphometric procedures used
  - short justification explaining any decisions involving professional judgement
  - detailed description of all behavioural/functional, neuropathological and morphometric findings by sex and dose group, including both increases and decreases from controls
  - brain weight
  - any diagnoses derived from neurological signs and lesions, including naturally occurring diseases or conditions
  - images of exemplar findings
  - low-power images to assess homology of sections used for morphometry
  - statistical treatment of results, including statistical models used to analyse the data, and the results, regardless of whether they were significant or not
  - relationship of any other toxic effects to a conclusion about the neurotoxic potential of the test chemical, by sex and dose group
  - impact of any toxicokinetic information on the conclusions

- **If the study is EOGRTS and if following Cohort 3 parameters are reported, please record in RSS:**
  - serum IgM antibody titres (sensitization to SRBC or KLH), or splenic IgM PFC units (sensitization to SRBC)
  - performance of the TDAR method should be confirmed as part of the optimisation process by laboratory setting up the assay for the first time, and periodically (e.g. yearly) by all laboratories

- ‘Any other information’:

  As indicated in the general section of human tox RSS full dose-response data should be provided in the ‘any other information on results’ and not just the NOAEL values. In your tables, segregate the data according to sex. All tables should have proper headings in this section. There is no limit on how many tables you can include. Tables should be included for as many parameters as possible listed above in the results and discussion section.
  In addition, provide historical control data in this section.

Overall remarks, attachments

- Provide toxicological evaluation of the findings of the study explaining also the biological relevance of the effects observed in animals and if needed address human relevance.

- If relevant include a summary of confounding factors that may affect the results of the study.
- Discuss any significant deviations from the guideline.

Applicant's summary and conclusions

- Provide information of the reproductive and offspring toxicity in relation to parental toxicity and (proposal of) classification for reproduction (fertility) and the main conclusions under the section 'conclusions'.
- Provide all information not obtained during the study, but useful for the interpretation of the results, e.g., similarities of effects to any known neurotoxicants.
- For EOGRTS studies with cohort 2, include a discussion of the overall interpretation of the data based on the results, including a conclusion whether the chemical caused developmental neurotoxicity and the NOAEL.
- For EOGRTS studies with cohort 3, include a discussion of the overall interpretation of the data based on the results, including a conclusion whether the chemical caused developmental immunotoxicity and the NOAEL.

1.5.5 Developmental Toxicity/Teratogenicity

Materials and methods

Test type

- (developmental toxicity, screening, combined, other). Note: different test types have different reporting requirements. These requirements are listed in their respective OECD Guideline. Therefore, not everything listed in sections below may be required. Familiarise yourself with the test guideline before writing RSS so that you are aware what information listed below is relevant for your RSS.

Test animals

- species/strain/sex
- no. of animals per sex per dose
- age and weight at the study initiation

Administration/Exposure

- Route of administration
- Details on exposure: 1) Preparation method of dosing solution 2) Diet preparation 3) Vehicle information including name, lot number, purity, supplier etc
- Details on mating: how the mating was performed, M/F ratio/cage, length of cohabitation, proof of pregnancy etc
- Analytical verification of doses: yes/no
- Details on analytical verification: provide name of method, instruments, standardisation, method details, concentrations, vehicles, sample sprep, storage etc. Stability and homogeneity of dose formulation.
- Duration of exposure
- Frequency of treatment

- Doses (Table)
- animals/sex/dose
- Control animals
- Details on study design
  Dose selection rationale; Fasting period before blood sampling; details (rationale, etc.) of the administration of the test substance conversion from diet/drinking water test substance concentration (ppm) to the achieved dose (mg/kg body weight/day), if applicable; details of food and water quality (including diet composition, if available); if available, brief study design of preliminary study

Examinations

- Note all observations made for parental animals and offsprings. Use ‘insert existing template functionality
- statistical methods

Results and discussion

- Describe the relevant findings (from relevant generations i.e. maternal and foetus) from the IUCLID fields. Within each parameter listed under these fields, select the appropriate option. If no effects occurred, select "No effects observed". Don't leave any parameter blank, i.e. if a particular parameter was not evaluated, please write ‘not examined’. If a particular parameter was evaluated (described in the method of report) but no results were reported in the results section, then write ‘not specified’. If ‘effect observed, treatment related’ or ‘no effects observed’ are selected, then please give justification on why this was decided in the ‘description (incidence and severity)’.

- NOAEL (NOEL) (C)and LOAEL (LOEL) (C) maternal toxicity
- NOAEL (NOEL) and LOAEL (LOEL) developmental toxicity
- actual dose received by dose level by sex if available
- present maternal and fetal (or offspring) data with dose levels preferable in tabular form for each test group with statistical results, as appropriate (tables should be inserted in ‘any other information on results’ (see next section ‘any other information’)):

  For dams (per dose)

  - number of pregnant and non-pregnant dams
  - number of dams with abortions, early deliveries, stillbirths, resorptions and/or dead
  - foetuses mortality and day of death
  - clinical signs: description, severity, time of onset and duration
  - haematological and clinical biochemistry findings if available
  - mean number of implantations, live foetuses (pups), resorptions (early and late), dead
  - foetuses, abortions, and stillbirths per litter (with implants)
  - pre and post implantation loss: number and percent
  - number of corpora lutea
  - duration of pregnancy

- body weight, body weight change and gravid uterine weight, including optionally,
- body weight change corrected for gravid uterine weight
- other organ weight changes if available
- histopathological findings: nature and severity
- necropsy findings including uterine weight
- endocrine findings, if examined
- immunological findings, if examined
- neurological findings, if examined

For foetuses/offspring (per dose)

- mean number and percent of live offspring
- sex ratio
- mean foetal/pup body weight by sex and with sexes combined
- external, soft tissue and skeletal malformations and other relevant alterations [Also refer to appropriate test guideline to make sure the results follow the guideline]
- number and percent of foetuses and litters with malformations (including runts) and/or variations as well as description and incidences of malformations and main variations (and/or retardations)
- Anogenital distance for rodent foetuses

- criteria for categorisation of external, soft tissue, and skeletal malformations and other relevant alterations

- 'Any other information':

  As indicated in the general section of human tox RSS full dose-response data should be provided in the 'any other information on results' and not just the NOAEL values (for both maternal and foetus). In your tables, segregate the data according to sex. All tables should have proper headings in this section. There is no limit on how many tables you can include. Tables should be included for as many parameters as possible listed above in the results and discussion section.
  In addition, provide historical control data in this section

Overall remarks, attachments

- Provide toxicological evaluation of the findings of the study also explaining the biological relevance of the effects observed in animals and if needed address human relevance. If relevant, include a summary of confounding factors that may affect the results of the study. Discuss any significant deviations from the guideline.

Applicant's summary and conclusions

- Provide information of the reproductive and offspring toxicity in relation to parental toxicity and (proposal of) classification for reproduction (fertility) and the conclusion of the study under section conclusions

1.5.6 Carcinogenicity

Materials and methods

Test type

- (e.g. lifelong bioassay, initiation/promotion, transgenic, neonatal mouse or other)

Test animals

- species/strain/sex
- number of animals per sex per dose
- age and weight at the study initiation

Administration/Exposure

- Route of administration
- Details on exposure: 1) Preparation method of dosing solution 2) Diet preparation 3) Vehicle information including name, lot number, purity, supplier, etc.
- Details on mating: how the mating was performed, M/F ratio/cage, length of cohabitation, proof of pregnancy, etc.
- Analytical verification of doses: yes/no
- Details on analytical verification: provide name of method, instruments, standardisation, method details, concentrations, vehicles, sample sprep, storage etc. Stability and homogeneity of dose formulation.
- Duration of exposure
- Frequency of treatment
- Post exposure duration
- Doses (Table)
- animals/sex/dose
- Control animals
- Details on study design
  Dose selection rationale; Fasting period before blood sampling; details (rationale, etc.) of the administration of the test substance conversion from diet/drinking water test substance concentration (ppm) to the achieved dose (mg/kg body weight/day), if applicable; details of food and water quality (including diet composition, if available); if available, brief study design of preliminary study

Examinations

- Note all observations made during the study. Use ‘insert existing template functionality
- statistical methods

Results and discussion

- Describe the relevant findings (from relevant generations i.e. maternal and fetus) from the IUCLID fields. Within each parameter listed under these fields, select the appropriate option. If no effects occurred, select "No effects observed". Don't leave

any parameter blank, i.e. if a particular parameter was not evaluated, please write 'not examined'. If a particular parameter was evaluated (described in the method of report) but no results were reported in the results section, then write 'not specified'. If 'effect observed, treatment related' or 'no effects observed' are selected, then please give justification on why this was decided in the 'description (incidence and severity)'.

- Results shall be presented preferably in tabular form with statistical results, as appropriate (tables should be inserted in 'any other information on results' (see next section 'any other information')):
    - mortality and time to death (indicate number died per sex per dose and time to death) clinical signs
    - body weight gain
    - food/water consumption
    - ophthalmoscopic examination
    - clinical chemistry
    - haematology
    - urinalysis
    - organ weights
    - necropsy findings: nature and severity
    - histopathological findings: nature and severity
        - non neoplastic histopathological findings,
        - neoplastic histopathological findings,
    - tumour incidence data by sex, dose and tumour type
    - toxic response data by sex and dose
    - time to tumours (for dermal route and skin tumours: give mean time until appearance of tumour or time until appearance of first tumour or other measure)
    - statistical results (unless already described with specific test results above)

- 'Any other information':

    As indicated in the general section of human tox RSS full dose-response data should be provided in the 'any other information on results' and not just the NOAEL values. In your tables, segregate the data according to sex. All tables should have proper headings in this section. There is no limit on how many tables you can include. Tables should be included for as many parameters as possible listed above in the results and discussion section.
    In addition, provide historical control data in this section

Overall remarks, attachments

- Provide toxicological evaluation of the findings of the study explaining also the biological relevance of the effects observed in animals and if needed address human relevance. If relevant, include a summary of confounding factors that may affect the results of the study. Discussion can also include:
    - any modelling approaches;
    - dose-response relationships;
    - historical control data;
    - consideration of any mode of action information;
    - BMD, NOAEL or LOAEL determination;

Applicant's summary and conclusions

- Provide information related to classification and labelling and the conclusion of the study under section conclusions

1.6 In vitro skin corrosion and irritation

1.6.1 OECD 431 or 439

Test chemicals

- Treatment of test chemical prior to testing
- Solubility properties
- Stability of test chemicals
- Storage conditions

Methods (in vitro test system)

- Details on test system: RhE model used including batch number (and details such as production date, shipping date, testing date, other QC information
- Cell type
- Justification for test system
- Vehicle
- Control samples
- Amount applied: both test substance and controls
- Duration of treatment
- Post exposure incubation if any
- Number of replicates
- Any other information (or could also be reported in 'Details on the test system'):
    - pass (if applicable) used for quantifying MTT formazan, and linearity range of measuring device;
    - Description of the method used to quantify MTT formazan;
    - Description of the qualification of the HPLC/UPLC-spectrophotometry system, if applicable;
    - Volume and number of Washing steps etc
    - Test acceptance criteria (very critical)

Results

- Irritation/corrosion parameter (most likely mean % viability)
- Number of experiments
- Value
- Control validity
- Is there any indication of irritation? OR not?
- Does the controls and test data meet the acceptability criteria?

Applicant summary and conclusion

- GHS criteria
- Conclusions

Appendix 2: SciRap criteria

Note 1: the checklist provided below does not specify at what IUCLID location a criterion should be reported. Therefore, you must make sure that these criteria have been included in the RSS at the correct location within IUCLID. If you have followed section E of this SOP while writing RSS, then most of the criteria listed below will automatically be at the correct location in the IUCLID.

Note 2: In most cases (especially publications), you will not be able to fulfil all the criteria listed in the checklist because some of these parameters will not be available in the full report. In those cases, it is better to write 'information not available in the report' instead of leaving the field blank in the IUCLID.

2.1 in-vivo human toxicology

Endpoints
The main endpoint investigated

Test substance
Name/CAS
Source, purity, batch number
Basis of dose selection
Stability and homogeneity in vehicle
Stability under storage conditions

Vehicle
Type/characteristics
Justification for vehicle chosen (if other than water)

Animals
Species, strain, source
Number, sex, age and life stage
Body weight at the start of the study
Acclimatisation period
Method of individual identification

Housing conditions
Temperature, humidity, Light/dar cycles
Number of animals/sex/cage(for F0, F2, F2 as relevant)
Cage material, bedding material
Water bottle material
Any cage enrichment information

Feed
Type and source
Contaminant information
Phytoestrogen content
Frequency and method of feeding

Drinking water
Source
Contamination (if any)

Administration of test substance
Animals/sex/dose/group
Dose selection rationale
Method for determining group size
Dose levels
Number of dose groups
Method for dose conversion (if not in mg/kg)
Method of animal assignment
All control information
Route of administration and rationale
Administration method
Duration and frequency of treatment
Any post exposure duration

Methods
How many samples from and from which group
Age and life-stage at termination
Sufficient details on method
Control data in sufficient detail
All instrumentations
Method of euthanization

Statistics
Details on the statistical methods
Assumptions of statistical methods

Observations
Body weight data
Food and water consumption
Time and cause of death for animals dying prematurely
Clinical observations
All types of effects (including adverse, secondary etc)
Data by sex and treatment group
Data should be reported along with standard deviation and statistical significance
Control data + historical control data
Dose response relationship (not just NOAEL)
Potential mechanistic information
Relevance to humans

Additional information on reproductive toxicity
Vaginal smear data before treatment
Parturition
Randomization procedures to select pups for culling
Day of culling
Number of animals/sex/litter after culling.
Method for individual identification of offspring.
Litter of origin for all offspring

Statistical unit, i.e. if it is the litter or the individual pup
For endpoints measured in offspring it should be clear if littermates are subjected to the same tests/analyses.

SciRap checklist reference: http://www.scirap.org/Page/Index/9ced3317-ab2b-4617-86f4-f2d3b86a419f/reporting-checklist

Appendix 3: CRED criteria

Note 1: the checklist provided below does not specify at what IUCLID location a criterion should be reported. Therefore, you must make sure that these criteria have been included in the RSS at the correct location within IUCLID. If you have followed section E of this SOP while writing RSS, then most of the criteria listed below will automatically be at the correct location in the IUCLID.

Note 2: In most cases (especially publications), you will not be able to fulfil all the criteria listed in the checklist because some of these parameters will not be available in the full report. In those cases, it is better to write 'information not available in the report' instead of leaving the field blank in the IUCLID.

3.1 Ecotoxicology

Endpoints
The main endpoint investigated

Material and Methods
Test guideline, version, year, organisation
GLP: yes/no
Description of all types of controls
Control(s) mortality, growth, morbidity and other parameters
Are validity criteria properly defined (if applicable)?

Test substance
Full identification (name, cas)
Make it clear whether the salt or base is being tested
Source, purity, composition

Test organisms
Scientific name
Body weight, age, life-stage, length
Strain, sex, source
Culture conditions

Exposure
Exposure type (static, flow-through etc)
Open/closed
Test media type and source
Temperature, pH (including time of measurements)
Hardness, alkalinity, conductivity, DO
Light source, intensity and cycle
Feed composition and schedule
Material and volume of test apparatus
If sand and sediment (full characteristics such as TOC, particle size etc)
Stock solution information (clearly state concentration of substance and solvent)
Both nominal and measured concentration
How many time concentrations were measured?
Analytical methods (incl LOD and LOQ)
Exposure duration
Total test duration
Any post exposure gap?
Are results based on nominal or measured concentrations
Biomass per litre

Statistics
Number of replicates
Unit of measurement
Number of animals/replicate (if unit of measurement is not individual animal)
Statistical method used

Results
Results for each concentration not just NOEC
Statistically significant result clearly distinguished than others
Significance value (i.e. 0.05 or less)
Mean +- SEM/SD values
Raw data tables

3.2 Environmental fate (criteria written by Yordas to be similar to CRED)

Endpoints
The main endpoint investigated

Material and Methods
Test guideline, version, year, organisation
GLP: yes/no
Description of all types of controls
Control(s), blanks and reference substance
Are validity criteria properly defined (if applicable)?

Test substance
Full identification (name, CAS)
Make it clear whether the salt or base is being tested
Source, purity, composition

Inoculum (for biodegradation endpoint)
Nature and sampling site
Concentration
Any pre-conditioning treatment

Exposure (for biodegradation)
aerobic/anaerobic
Duration
Pre-treatment details (if any): e.g. radioactive labelling, digestion, extraction etc
Analytical methods (incl. LOD and LOQ)
Test media composition and condition (e.g. pH, temp)
Test equipments (culture apparatus), nature, number, replicates etc
Measurement equipments (e.g. respirometer)
Sampling method and time
All control and reference substance details
Parameter followed for biodegradation estimation

Test organisms (for bioaccumulation endpoint)
Scientific name
Body weight, age, life-stage, length
Strain, sex, source
Culture conditions

Exposure (for bioaccumulation endpoint)
Exposure type (static, flow-through etc)
Open/closed
Route of exposure
Test media type and source (e.g freshwater, marine water etc
Exposure duration
Depuration duration
Temperature, pH (including time of measurements)
Hardness, alkalinity, conductivity, DO
Light source, intensity, and cycle
Nominal and measured concentration
Any vehicle used
Pre-treatment details (if any): e.g. radioactive labelling, digestion, extraction
Analytical methods (incl. LOD and LOQ)
Feed composition and schedule
Stock solution information (clearly state concentration of substance and solvent)
Are results based on nominal or measured concentrations

Statistics
Number of replicates
Unit of measurement
Number of animals/replicate (if unit of measurement is not individual animal)
Statistical method used

Results
Results for each concentration
Statistically significant result clearly distinguished than others
Significance value (i.e. 0.05 or less)
Mean +- SEM/SD values
Raw data tables

CRED checklist reference:
http://www.scirap.org/Page/Index/9ced3317-ab2b-4617-86f4-f2d3b86a419f/reporting-checklist

Disclaimer

Reasonable efforts have been made throughout the review process to reach the conclusions and recommendations provided. The conclusions and recommendations given in this report are based upon and therefore limited to the information available and provided by the client at the time of writing. As such, Yordas Group accepts no liability if any regulating or enforcement bodies do not reach the same conclusions or recommendations.