EUROPEAN FOOD SAFETY AUTHORITY

Doc J removal - Instructions for applicants on data reporting in IUCLID v.3 (latest changes highlighted)

EFSA

CONTENTS

GENERAL INFORMATION

As of **IUCLID 6 Version 9**, the IUCLID document 'FLEXIBLE_RECORD.Manufacturer_EU_PPP' along with its field to provide the **Document J** attachment is no longer available for chemical active substance dossiers.

These instructions provide guidance to applicants on where in IUCLID to enter the data previously included in Document J.

All chemical active substance (a.s.) initial dossier submissions made after the release of IUCLID 6.9 must follow the updated data entry process in IUCLID, as outlined below. **Previously submitted dossiers will remain unchanged**, but any new submissions made after release of IUCLID 6.9, must comply with these updated requirements.

Important Note: Applicants must ensure that all information previously included in Document J is correctly reported in the designated IUCLID fields. Any attempt to attach Document J elsewhere should not be accepted by the RMS during the admissibility check. Also note that this change is only applicable to chemical active substance dossiers while for **microorganisms** this change will be implemented at a later stage.

Applicants should read these instructions in conjunction with the **Doc J - crosswalks.xlsx** mapping file, which provides additional guidance on where to enter specific data elements in IUCLID, and with the IUCLID Active Substance Applications Manual.

REQUIRED SECTIONS FOR DATA REPORTING

Applicants must enter data in the sections listed below. These instructions focus on describing the newly created fields and highlight some of the existing ones when particularly relevant in the context of removing Document J. Please note that the documents listed below should nonetheless be completed in full, as described in the IUCLID user manual.

Active substance dataset

- **Identity of the active substance and applicant**
- **Producer of the active substance**
- **Method of manufacture (synthesis pathway) of the active substance**
- **Specification of purity of the active substance (g/kg)**
- **Analytical profile of batches**
- **Analytical methods**
- **Impurities**
- **Batches and test material**

Product datasets

- **Identity of the plant protection product, trade name or proposed trade name, and applicant**

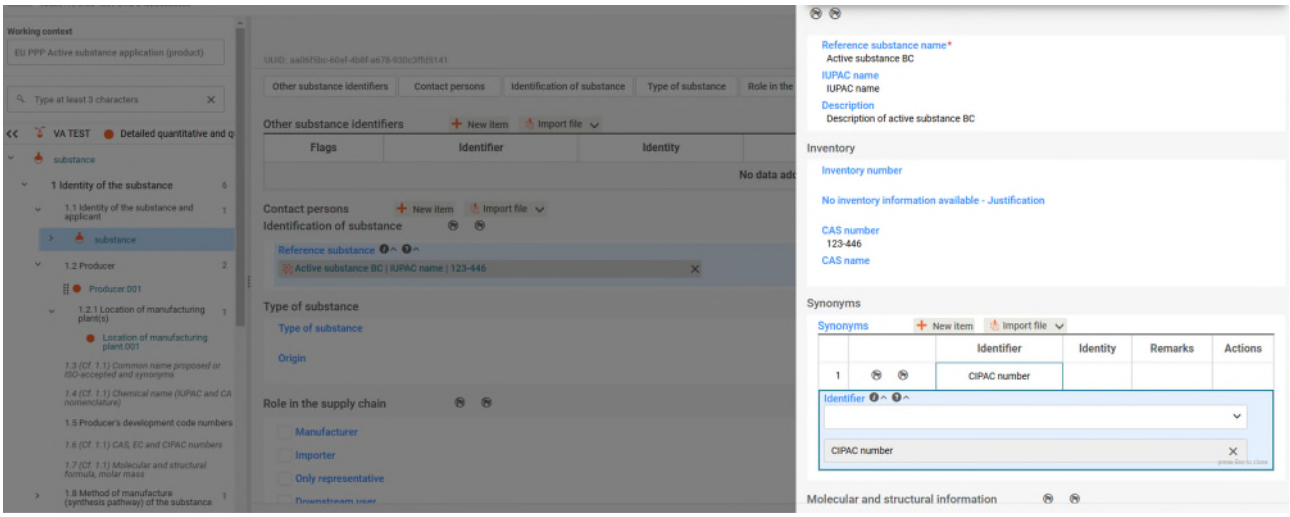
- **Producer of the plant protection product**
- **Detailed quantitative and qualitative information on the composition of the plant protection product**
- **Method of manufacture (synthesis pathway) of the plant protection product**

ACTIVE SUBSTANCE DATASET

IDENTITY OF THE ACTIVE SUBSTANCE AND APPLICANT

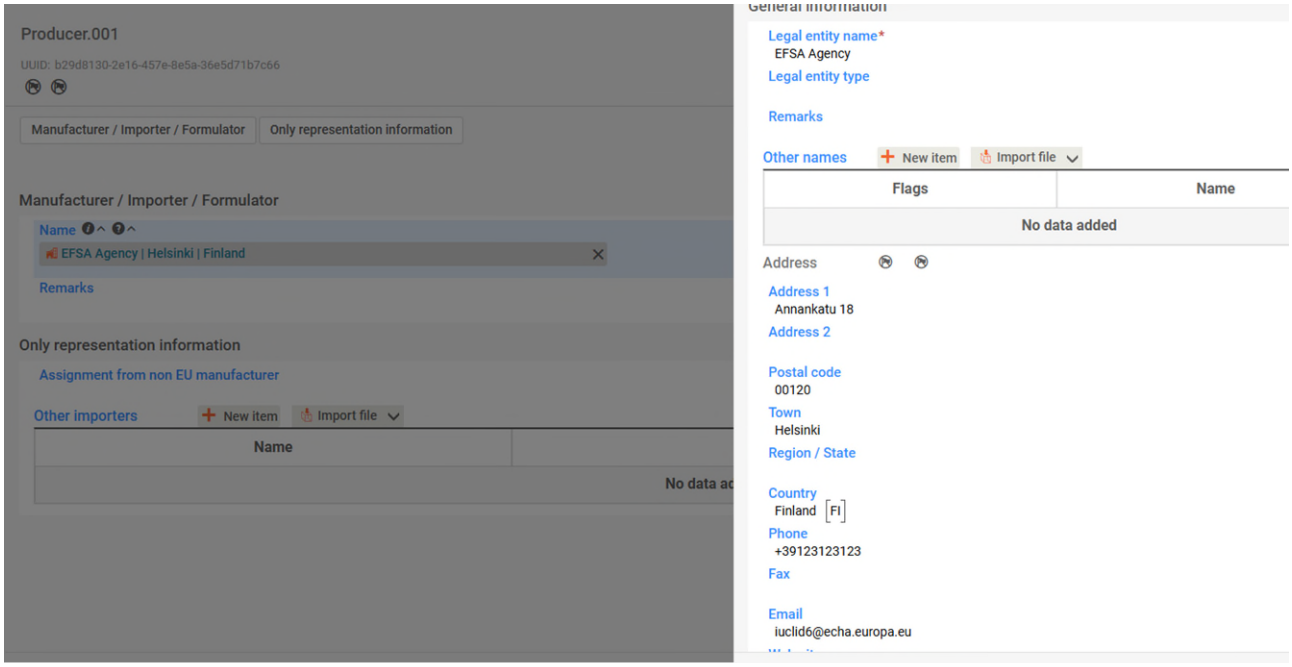
All relevant information on the identity of the active substance, such as chemical identifiers, and applicant (legal entity owner) must be provided in section *'1.1 Identity of the active substance and applicant'*.

All relevant chemical identifiers of the active substance such as the CAS number, EC number, IUPAC name, molecular and structural formula, SMILE, InChI, ISO common name, and CIPAC number must be provided in the REFERENCE_SUBSTANCE entity linked to the 'Reference substance' field.



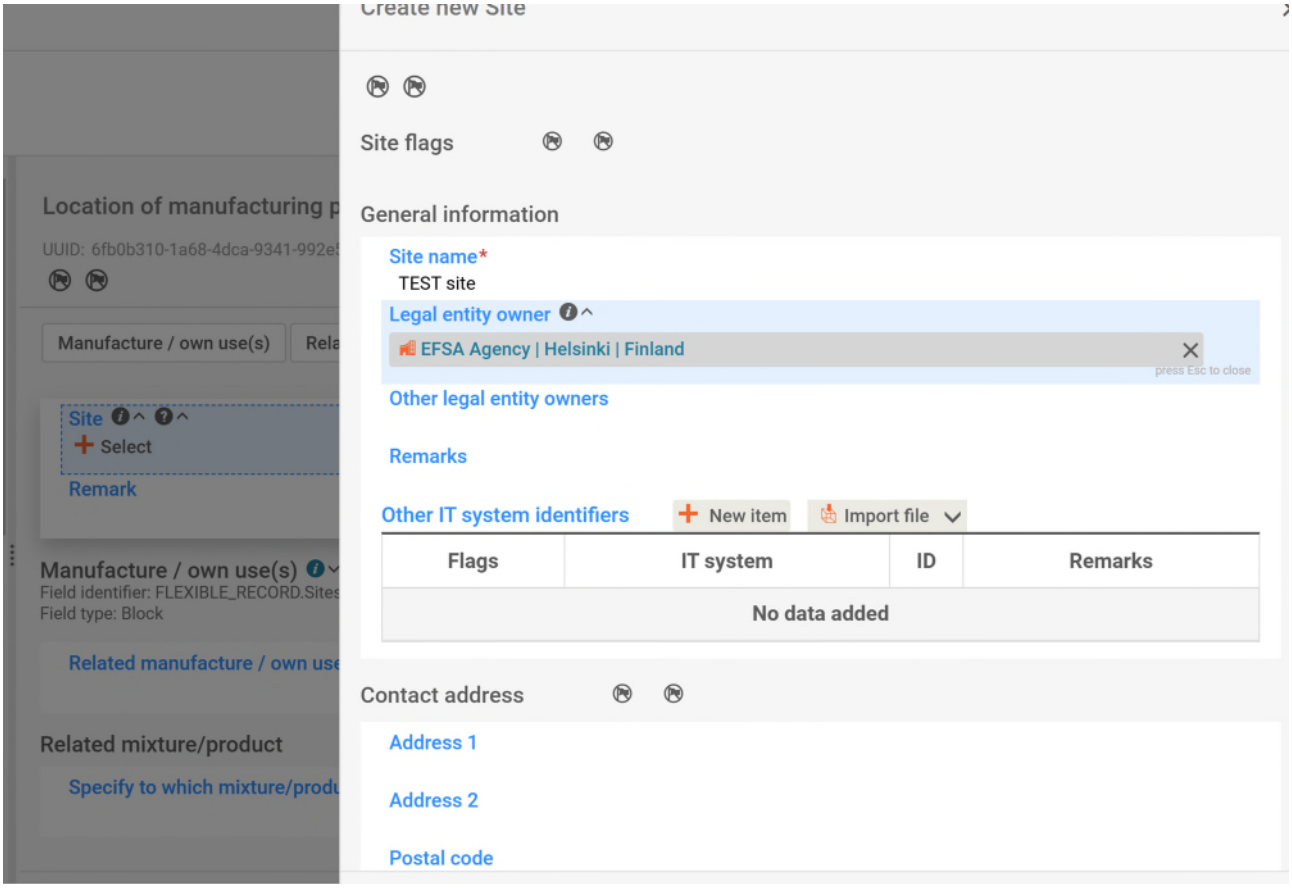
PRODUCER

The name, address and other contact information of the producer of the active substance must be provided in the FLEXIBLE_RECORD.Suppliers of section *'1.2 Producer'*, by referencing the LEGAL_ENTITY under the 'Name' field.



Detailed information on the location and contacts of each manufacturing plant (address, region, phone, email, etc) are to be provided in the FLEXIBLE_RECORD.Sites in section '1.2.1 Location of manufacturing plant(s)', by referencing a SITE entity in the 'Site' field. This SITE should be linked in the corresponding Manufacturer document.

Both for the active substance and plant protection product, the Remarks field of the SITE entity should be used in order to describe or clarify the history/status of the manufacturing plant (e.g. if it has changed since the previous approval).



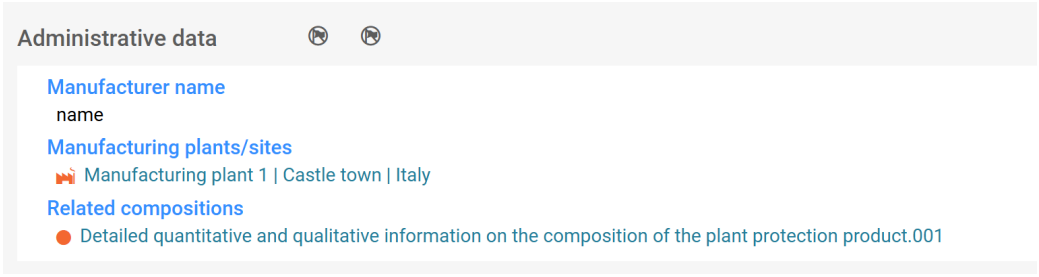
In case of more than one producer and/or manufacturing sites, a separate document for each of them must be created in these sections.

METHOD OF MANUFACTURE (SYNTHESIS PATHWAY) OF THE ACTIVE SUBSTANCE

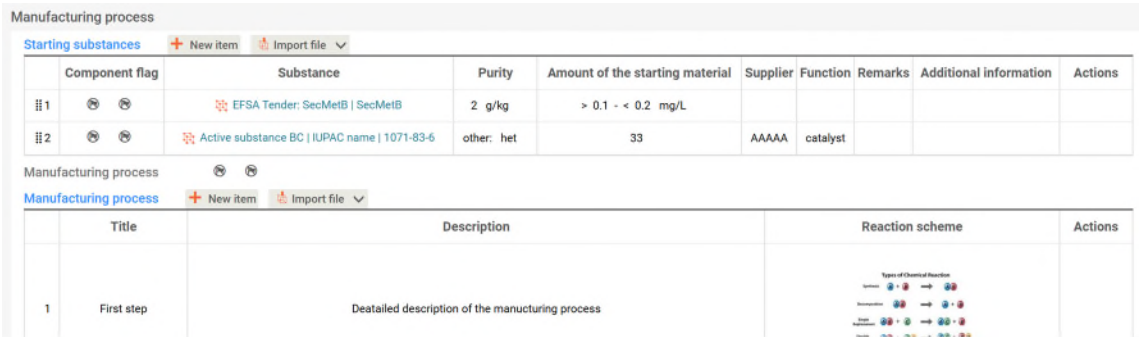
All information related with the manufacturing process must be reported in the document 'FLEXIBLE_RECORD.Manufacturer_EFSA' in section '1.8 Method of manufacture (synthesis pathway) of the active substance'. This document replaces the previous 'FLEXIBLE_RECORD.Manufacturer_EU_PPP' as of IUCLID 6.9.

This document includes three main blocks with structured fields that must be completed:

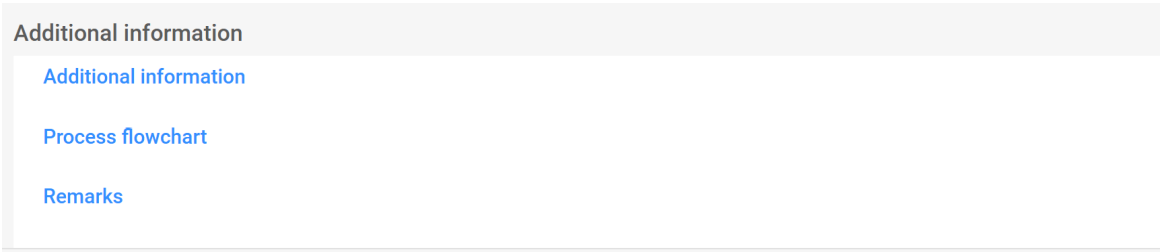
- **Administrative data** to report the manufacturer name and plants/sites. Multiple manufacturing plants/sites can be linked to the same manufacturing process. The related composition (result of the manufacturing process) should be linked here.



- **Manufacturing process:**
  - For each starting material a 'Reference substance' record should be created including all required identifiers (e.g. name, CAS number, structural formula). Purity and commercial availability of each starting material should be reported in the dedicated column of the 'starting substances' section.
  - A detailed description of the different steps of the production should be reported in the 'manufacturing process' section. The option to attach a reaction scheme (as an image) is available.



  - **Additional information** to provide any additional information related to the manufacturing process. The process flowchart can be attached in this section.



N.B. One document per manufacturing process must be created. **If multiple manufacturing processes need to be reported, a dedicated document must be created for each manufacturing process.**

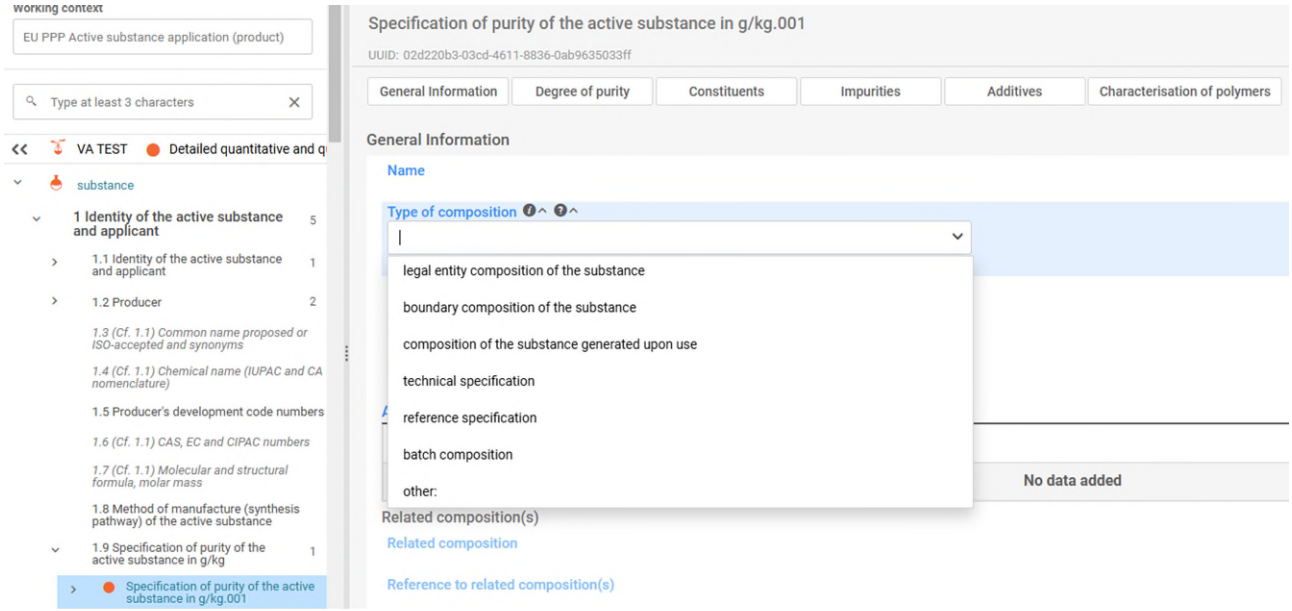
SPECIFICATION OF PURITY OF THE ACTIVE SUBSTANCE (G/KG)

The 'FLEXIBLE_RECORD.SubstanceComposition' document in section '1.9 Specification of purity of the active substance in g/kg' should be used to report the technical specification(s), the reference specification(s) and each batch composition used in the batch analysis (minimum 5 representative batches). As of IUCLID 6.9, the following three picklist values applicable to pesticides are available in the 'Type of composition' field:

- **Batch composition** to be used to report the composition of individual batches which are part of the analysis of the representative batches
- **Technical specification** to be used to report the proposed specification based on batch data and supporting data (if any) for a particular manufacturing site
- **Reference specification** to be used to report the (proposed) reference specification (e.g. agreed at the first Approval and to be maintained also for the renewal procedure or proposed reference specification in case of a new active substance)

Note: For active substances manufactured as technical concentrates, separate documents should be created with the relevant type of composition (e.g. "technical specification") to report the composition of the technical concentrate and composition in the theoretical dry weight material.

The Description and Justification of deviations fields can be used to provide additional information on the reference or technical specifications.



To provide the reference specification of the previous assessment, if available to the applicant, a document with the type of composition "Reference specification" should be created and should be linked in the Change Log (FLEXIBLE_RECORD.ChangeLog in 9.2 Change log). The right Status must then be selected:

- New: for the proposed reference specification (in all dossiers)
- Previously used: for the existing reference specifications (for renewals)

The Remarks field in the Change Log can be used to report additional information such as a reference to where the specifications had been used previously, e.g. "DAR 2014... / EFSA opinion XYZ".

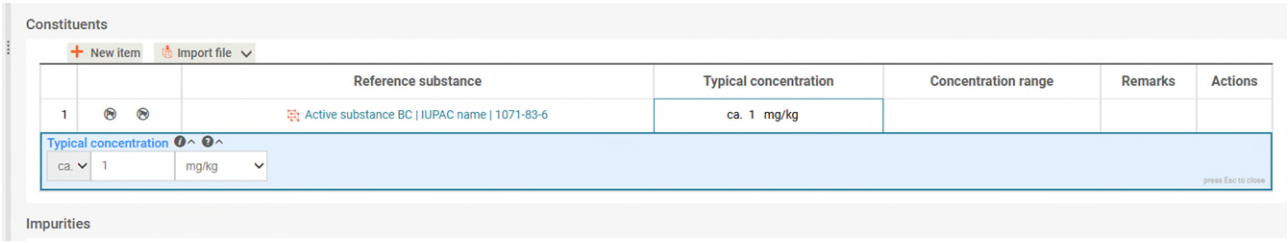
The minimum purity of the active substance is to be reported in the 'Degree of purity' field.

For each 'Type of composition' (i.e. batch composition, proposed (technical) specification and reference specification) the designated table sections 'constituents', 'impurities' and 'additives' must be completed:

Constituents: to report the identity and the content of the active substance in the composition. It is a repeatable block which allows the reporting of more than one constituent of the active substance if needed (e.g. in case the active substance is a defined mixture of two isomers).

Note: When the type of composition is 'Technical' or 'Reference specification', the (proposed) minimum content of the active substance in the technical material should be reported in the field 'Typical concentration'.

In case of technical concentrate, the minimum and maximum content of the active substance in the technical concentrate should be reported in the 'Concentration range' field. For 'Batch composition' in the field 'Typical concentration' the measured amount of the active substance in the relevant (individual) batches is to be reported.

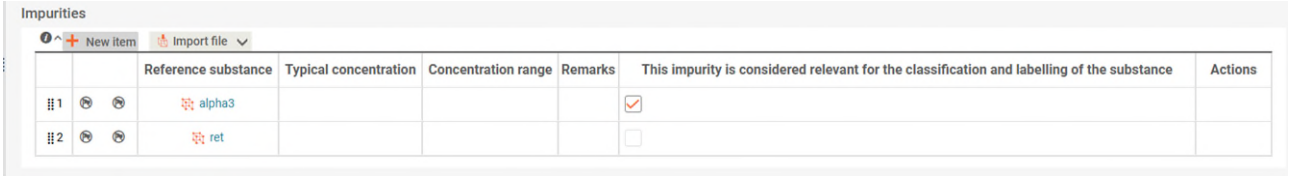


The 'Remarks' field should be used to report any additional information on the specification of purity of the active substance as manufactured.

Impurities: to report the identity and the content of each impurity in the composition.

Note: When the Type of composition is 'Technical' and 'Reference specification' the (proposed) maximum content of the impurities in the technical material or technical concentrate should be reported in the 'Typical concentration' field. For "batch composition" the measured amount of the impurities in the relevant (individual) batches should be reported in the 'Typical concentration' field.

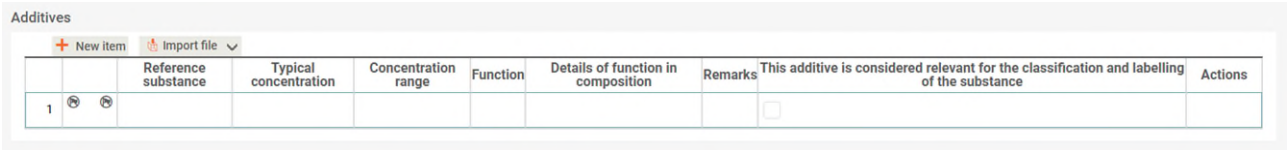
The checkbox 'This impurity is considered relevant for the classification and labelling of the substance' should be used to indicate that the impurity has an impact on the classification and labelling of the substance.



All impurities reported in this document should also be included in the 'Impurities' document in which more details on the impurities e.g. type of impurities (e.g. significant, relevant, etc), origin, etc can be provided (see dedicated paragraph below)**.**

Additives: to report the identity and the content of Additives in the composition. This is a repeatable block subsection which enables the applicant to provide details on all additives (if more than one) of the active substance as manufactured.

Use the 'Concentration range' field to report the minimum and maximum content of each additive in the technical and/or reference specification type of composition, and use "Typical concentration" to report the exact measured value for the "batch composition" if applicable.



ANALYTICAL PROFILE OF BATCHES

As of IUCLID 6.9, two types of documents should be created under section '1.11 Analytical profile of batches':

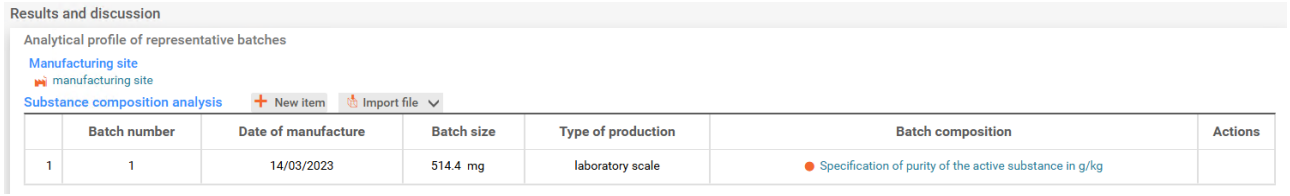
- **An endpoint study record ('ENDPOINT_STUDY_RECORD.AnalyticalProfileOfBatches') for each manufacturing plant and/or for each 5-batch analysis (5BA)**.

  The endpoint "analytical profile of technical batches" should be used to report the information on the 5-batch analysis (the other available endpoints should only be used for the comparison of batches used in (eco)toxicity tests, see FAQ section).

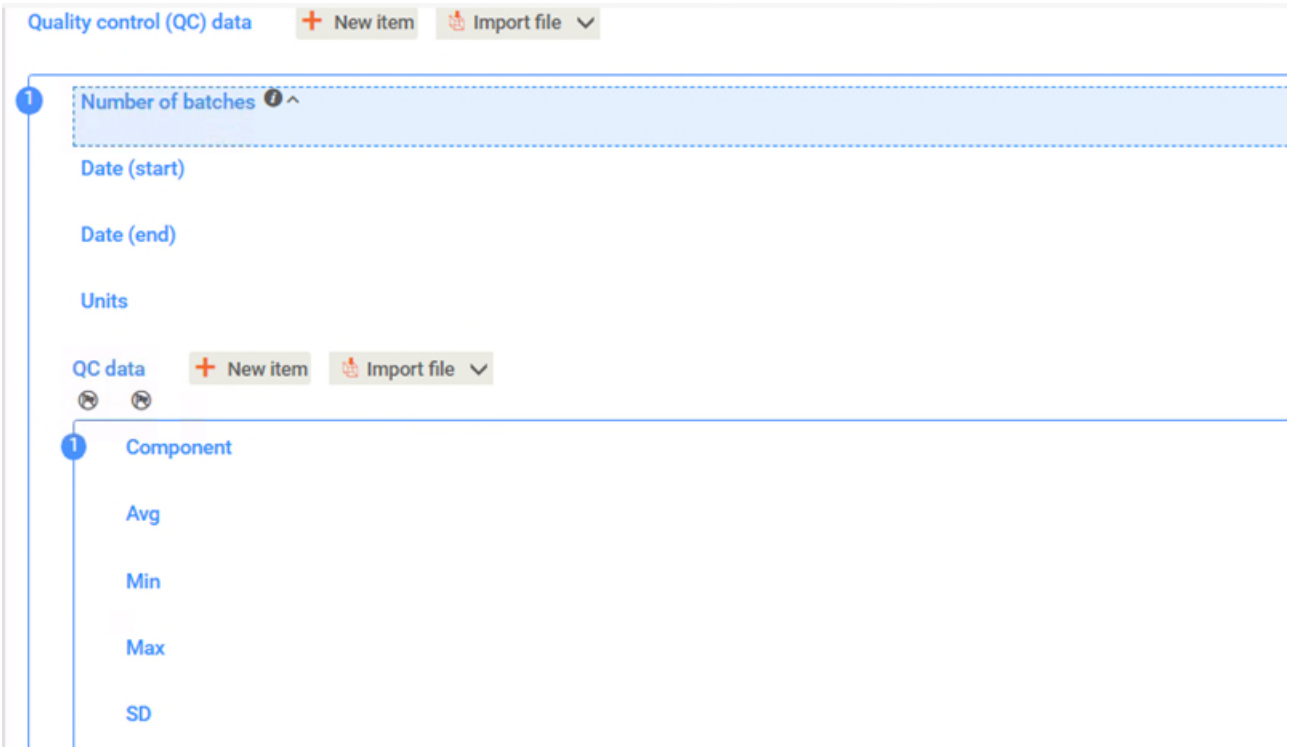
  All standard fields common to endpoint study records should be fully completed, including the data source linking the study report.

  Importantly, the 'Results and discussion' > 'Analytical profile of representative batches' section should be fully completed, including:

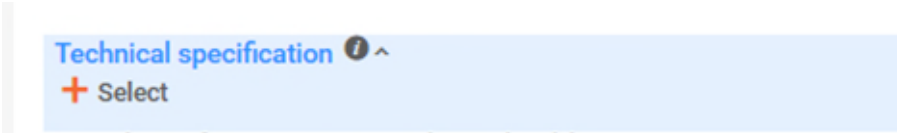
  - Link to the Manufacturing site entity, including address, contact details, etc.
  - One entry per batch within the repeatable table 'Substance composition analysis', providing all the batch-specific data and linking the corresponding 'Substance composition' document for the batch (type = 'batch composition') as described in section 1.9



  - Quality control (QC) data for the same manufacturing site, including quantitative information for each of the analysed substances (average, min, max, SD). More than one quality control dataset can be provided, if applicable.



- Link to the 'Substance composition' document for the proposed technical specification (type = "technical specification", see section 1.9) derived from the batch analysis and QC data reported in this document



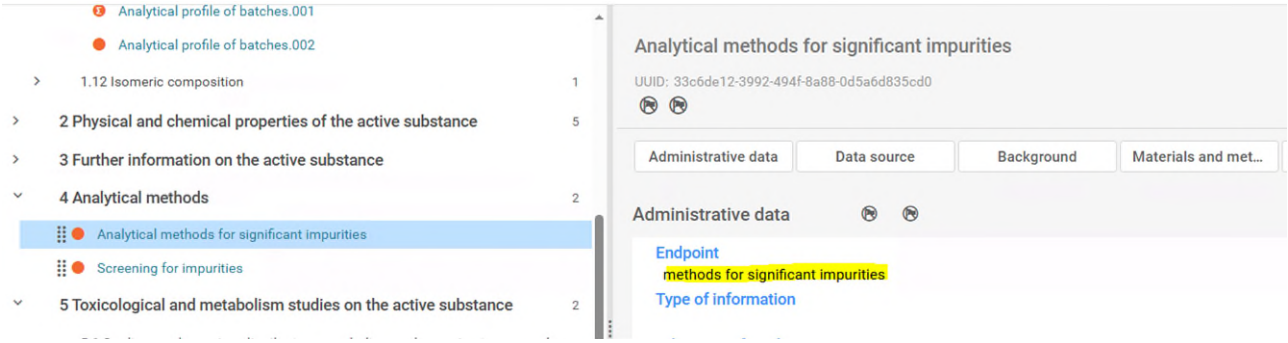
To provide study reports on the analysis of the composition of (eco)tox batches specific endpoints have been introduced as of IUCLID6 10.0.0 and should be used as appropriate:

- "analytical profile of batches used in mammalian toxicity tests"
- "analytical profile of batches used in ecotoxicity tests"
- "analytical profile of batches used in (eco)toxicity tests"

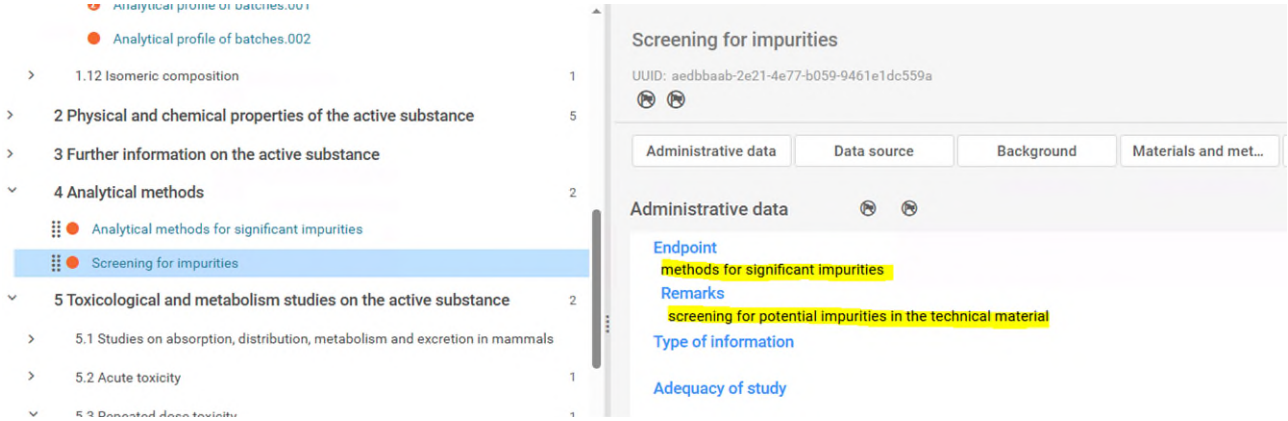
- **An endpoint summary (ENDPOINT_SUMMARY.AnalyticalProfileOfBatches) to collect the outcome of all the 5BAs submitted for the active substance**, to sum up all the technical aspects and lead to a conclusion on the specifications. All relevant endpoint study records detailing the 5-batch analysis must be linked in the dedicated field 'Link to relevant study record(s)' of the endpoint summary.

ANALYTICAL METHODS

In order to facilitate further extraction of the analytical method(s) related to analysis of the impurities (other than relevant impurities) in a Confidential report[1] all analytical methods for significant impurities must have 'Methods for significant impurities' in the 'Endpoint' field as shown below.



To report studies on the screening for impurities, applicants should also use Section 4 Analytical methods, with the same Endpoint = 'Methods for significant impurities', clarifying in the Remarks that the study is a screening.



The documents should be duly filled in, including all the dedicated structured fields for the Materials and methods and Results sections, as described in the IUCLID manual.

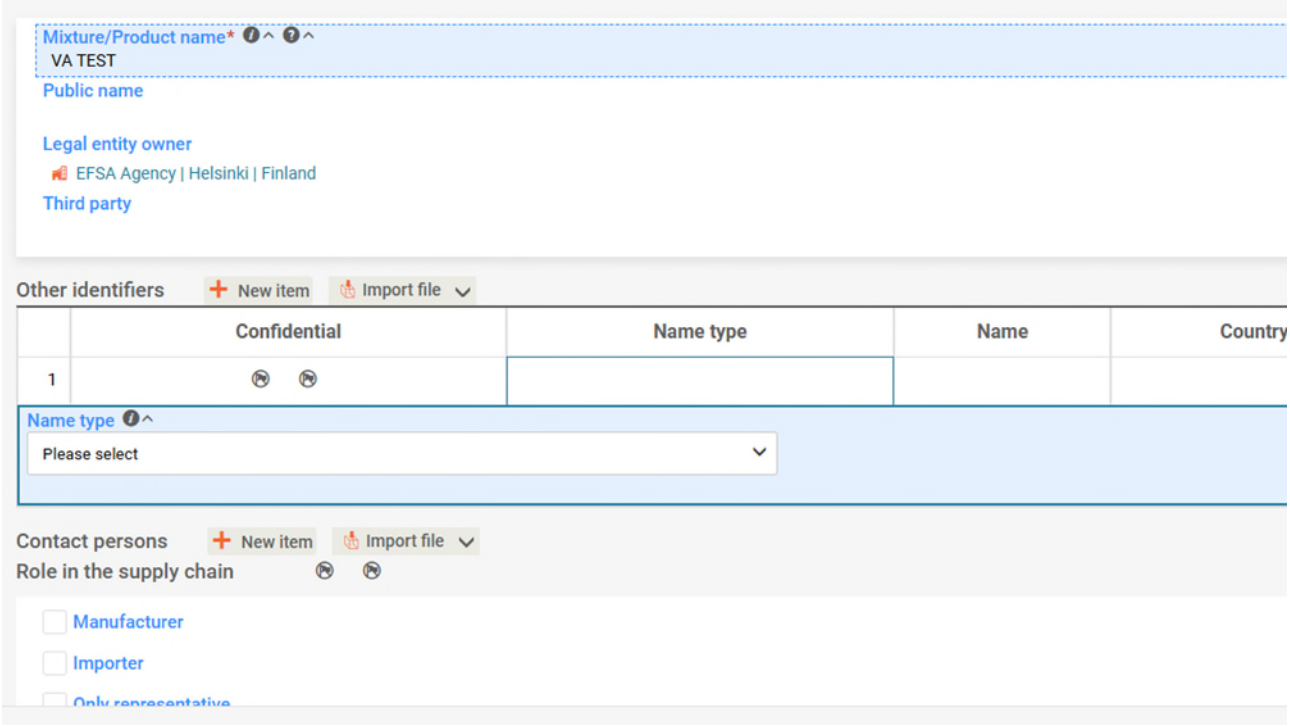
[1] To replace Document J

PRODUCT DATASET

This section refers both to the main/representative product and to any other representative product(s) that the applicant may have included in the dossier (Section 1.4.5 "Other Representative Products").

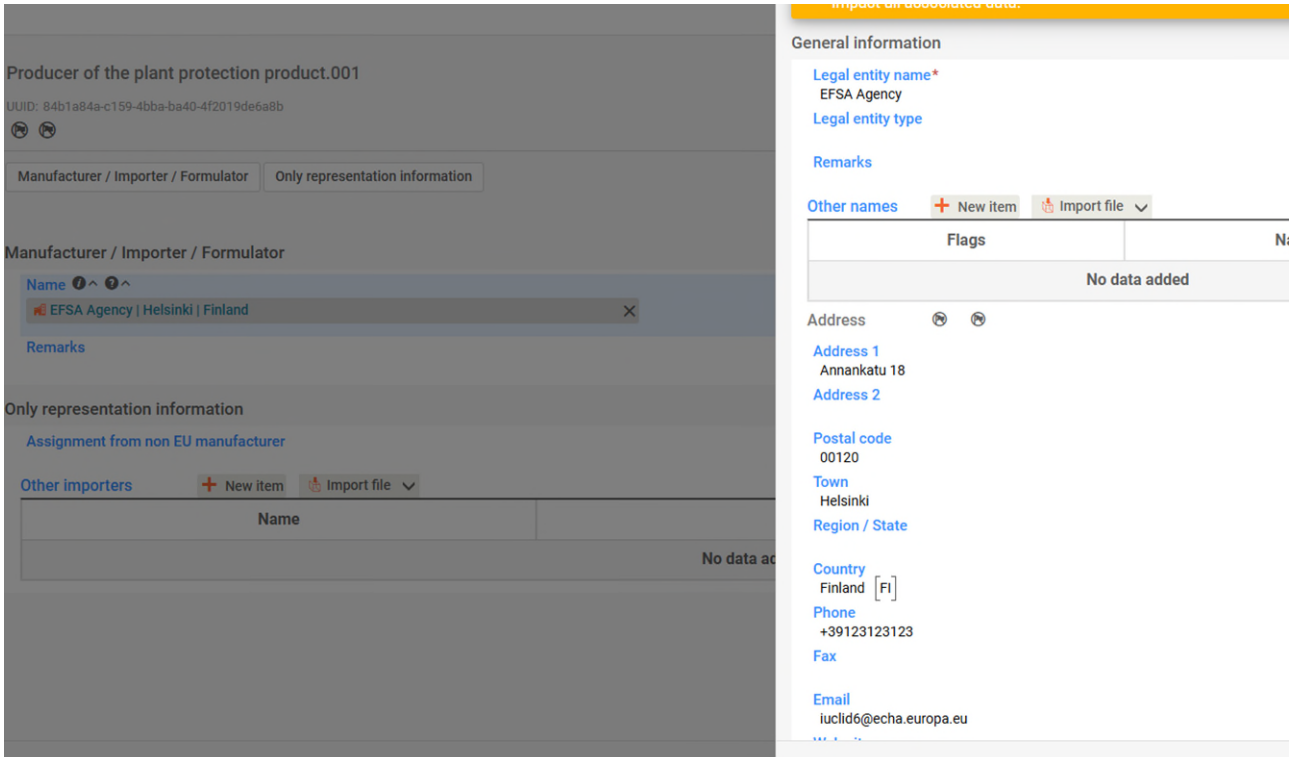
IDENTITY OF THE PLANT PROTECTION PRODUCT, TRADE NAME OR PROPOSED TRADE NAME, AND APPLICANT

This document must be completed to report information on the Legal Entity owner and contact person for the plant protection product. The trade name or proposed trade name and producer's development code number of the plant protection product can also be provided.

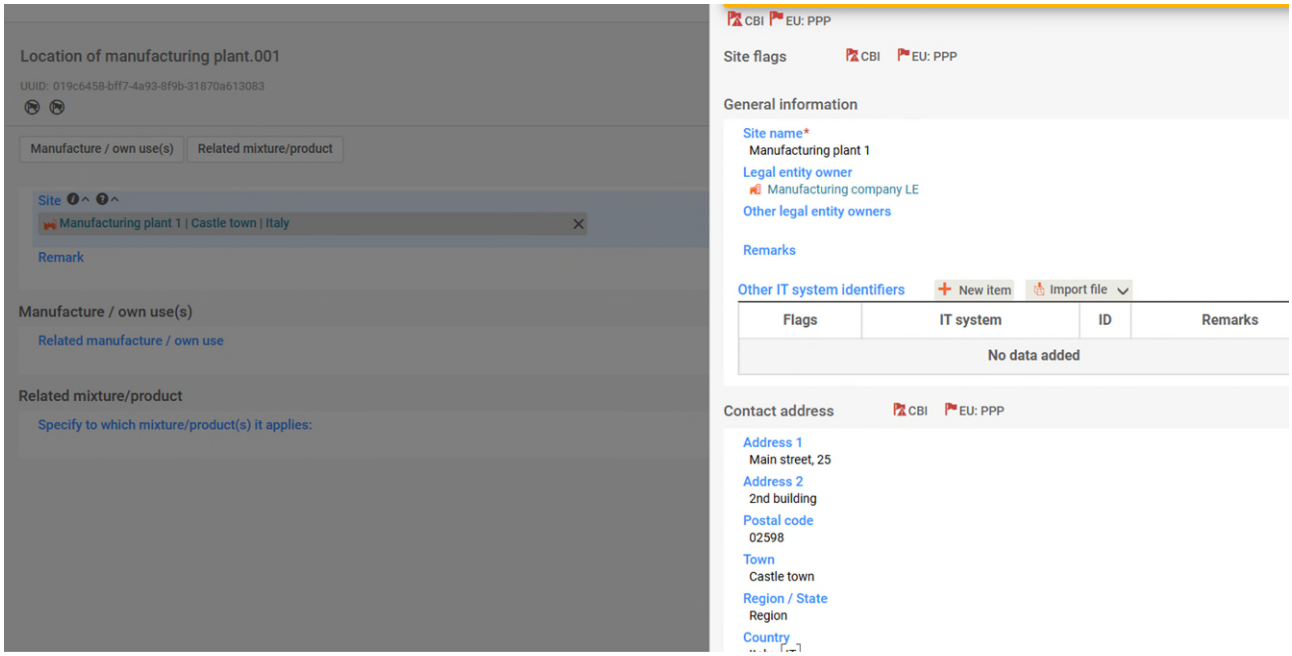


PRODUCER OF THE PLANT PROTECTION PRODUCT

Information on the producer of the plant protection product, including contact details of the supplier must be provided in this document.



Whereas information on the manufacturing plant of the plant protection product must be provided in the 'Location of manufacturing plant' document.



DETAILED QUANTITATIVE AND QUALITATIVE INFORMATION ON THE COMPOSITION OF THE PLANT PROTECTION PRODUCT

The full composition of the plant protection product as laid down in the applicable data requirements must be provided in this document, including information on co-formulants and relevant impurities.

For each component of the plant protection product, its concentration needs to be reported in the Typical concentration field within the Components repeatable block, using the most appropriate units (e.g. g/L). As of IUCLID6 10.0.0, an additional field called "Typical concentration (additional unit) is available and should be used to report the concentration selecting the units %w/w

Components

New item | Import file

	Component flag	Name	Function	Typical concentration	Typical concentration (additional unit)	Concentration range	Remarks	Substance of concern	Generic component identifier (GCI)	Interchangeable component group (ICG)	Stand (SF)
1		example 3	antioxidant	34.5 mg/L	<= 15 mg/L						
2		example 2	surfactant	41.32 mg/L	>= 20 mg/L						
3		example	active substance	567 mg/L	ca. 23 mg/L						

A general description of the composition (including some high-level summary on the co-formulants, safeners or synergists present) can be provided in the "Brief description" field.

For safeners and synergists a REFERENCE_SUBSTANCE must be provided, including the relevant chemical identifiers such as the CAS and EC number.

For co-formulants, the following should be provided depending on the data available:

- REFERENCE_SUBSTANCE: the relevant chemical identifiers should be provided. Trade name(s) can be provided in the "Synonyms" block, by selecting the Identifier "other" and indicating "Trade name" and providing the trade name in the Identity field
- SUBSTANCE: the relevant chemical identifiers should be provided in the REFERENCE_SUBSTANCE linked in the Reference substance field. Trade name(s) can be provided in the "Other substance identifiers" block of the SUBSTANCE document in section 1.1 Identity of the substance and applicant, by selecting the identifier "Trade name" from the picklist and providing the trade name in the Identity field
- MIXTURE: if applicable the Trade name of the co-formulant can be reported:
  - in the "Other identifiers" block of the MIXTURE document in Section 1.1. "Identity of the mixture", by selecting the Name type "Trade name" from the picklist. The available chemical identifiers of each component can be provided in the corresponding SUBSTANCE/REFERENCE_SUBSTANCE entities linked in the composition of the mixture.
  - in the "Trade names" block of the FLEXIBLE_RECORD.MixtureComposition document in Section 1.4 "Detailed quantitative and qualitative information on the composition of the mixture"

Any Safety Data Sheets (SDS) related to co-formulants should be provided and included in the FLEXIBLE_SUMMARY.SummaryEvaluation_EU_PPP Document (section 13)

METHOD OF MANUFACTURE (SYNTHESIS PATHWAY) OF THE PLANT PROTECTION PRODUCT

The FLEXIBLE_RECORD.Manufacturer_EFSA (introduced in IUCLID 6.9) must be used for providing detailed information on each step in the manufacturing process of the plant protection product, including the reaction schema. The related composition of the plant protection product must be provided in section 1.4 (as described in the above paragraph) and referenced in the 'Related compositions' field of this document.

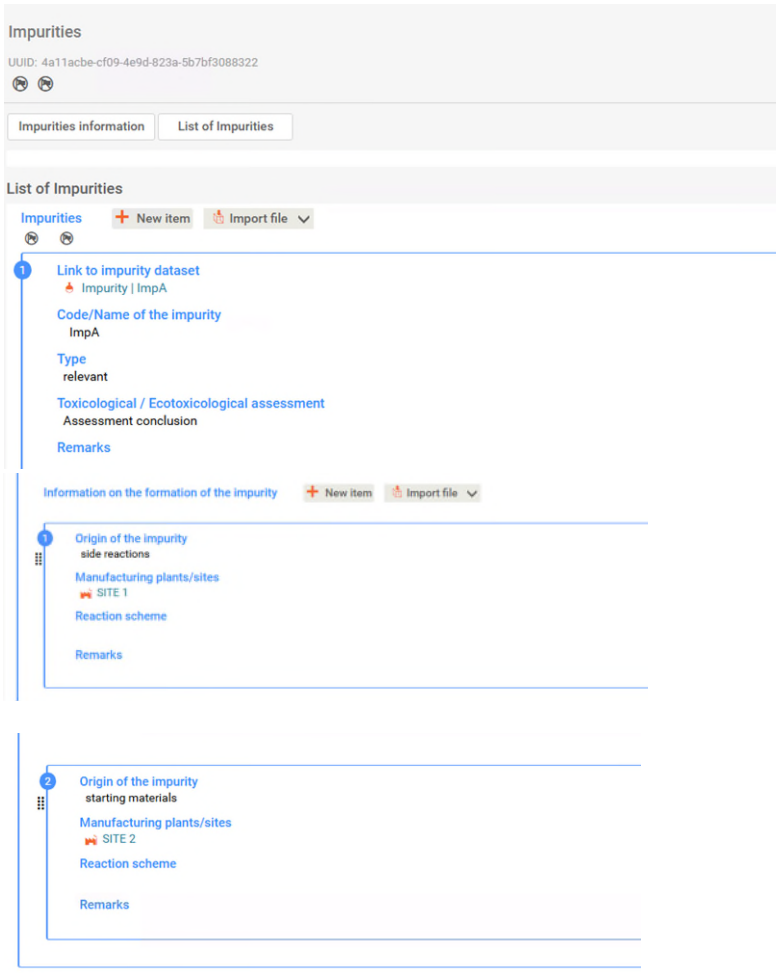
IMPURITIES

Relevant information on all impurities of the active substance must be included in the document FLEXIBLE_SUMMARY.Impurities of section 1.4.6 Impurities in the product dataset.

The block **List of impurities / Impurities** must be duly completed for each impurity of the active substance, including:

- A link to the impurity data:
  - If no studies for the impurity are to be reported, a Reference substance entity must be created including all required chemical identifiers (e.g. name, CAS number, molecular and structural formula, SMILES, etc)
  - If studies for the impurity are to be reported, a substance dataset must be created, including i) the Reference substance entity with all required chemical identifiers (e.g. name, CAS number, molecular and structural formula, SMILES, etc), and ii) all relevant studies performed with the impurity
  - Relevant information about the Tier I assessment in (eco)toxicity batches as well as other additional information or Tier II assessment (as of IUCLID6 10.0.0, see FAQ section)
- The type of the impurity, i.e. significant, relevant, non-significant or theoretical
- A high-level toxicological and ecotoxicological assessment and conclusion for the impurity (introduced in IUCLID 6.9)
- Details on the origin of the impurity, including the link to the Manufacturing plant and an image of the chemical reaction, if available. The link to the Manufacturing plant is key to connecting the impurity to the corresponding manufacturing process and batch analysis information. If the impurity has different origins at different manufacturing processes, more than one entry should be created in the repeatable block.

If needed, a general discussion on the impurities can be also provided in the field 'Impurities information overview'. However, this field should NEVER be used instead of the of the repeatable block mentioned above ("List of impurities") and should NOT duplicate the information provided there.

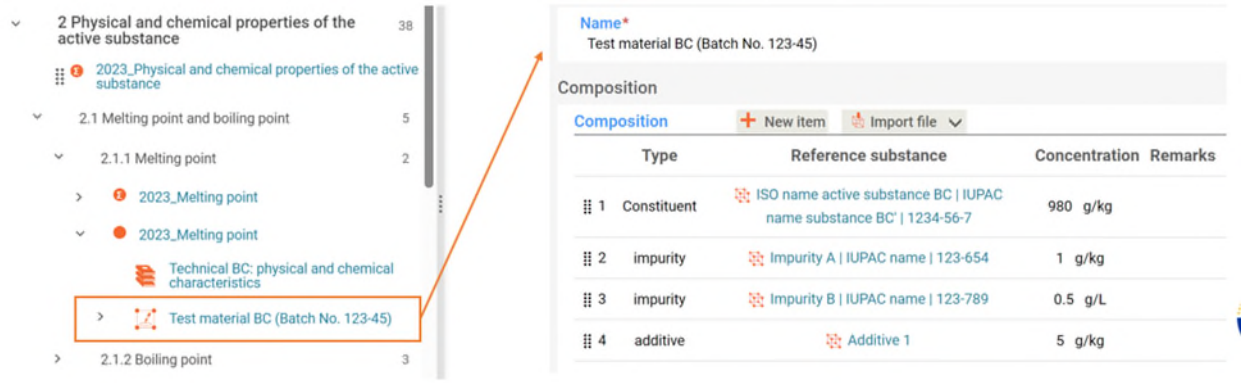


Relevant, significant, and non-significant impurities (if applicable) reported within this document should correspond to the impurities listed in the 1.9 Specification of purity of the active substance.

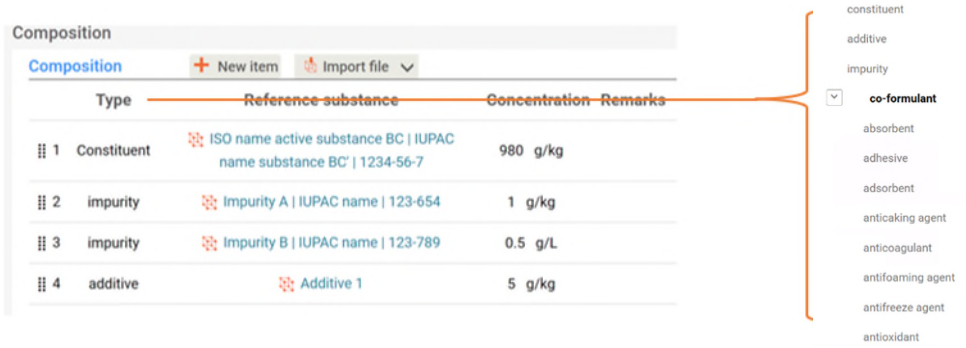
Relevant impurities should also be part of the product composition in section 1.4

TEST MATERIALS

Each study submitted for the active substance and the formulation must include a reference to a duly completed **TEST_MATERIAL_INFORMATION** document, including the identity and content of all components of the test material. These can be constituents (e.g. the active substance, a metabolite), impurities, additives, and co-formulants (for the formulation).



In the case of co-formulants, safeners and synergists, from IUCLID 6.9 the specific function must be selected from the 'Type' picklist, as shown below.



Duly completing the TEST_MATERIAL_INFORMATION documents will be key in order to aggregate and compare the compositions of i) the batches used in toxicological and ecotoxicological studies and the proposed technical / reference specification of the active substance, and ii) the formulations used in studies and the formulation for representative uses.

FREQUENTLY ASKED QUESTIONS (FAQ)

CO-FORMULANTS

HOW TO REPORT INFORMATION ON CO-FORMULANTS?

Depending on the nature of the information which needs to be reported for the co-formulants, different sections of IUCLID should be used. For example:

- The REACH registration number or any other Regulatory programme numbers can be reported under the "*Synonyms*" block of the co-formulant (REFERENCE_SUBSTANCE, SUBSTANCE or MIXTURE) with an explanation of the origin of this number under "Remarks".
- If studies performed with co-formulants are to be submitted, a SUBSTANCE or MIXTURE dataset for the relevant co-formulant needs to be created and the studies need to be reported under the relevant section / endpoint.
- Unacceptable co-formulants must be flagged by using the corresponding checkbox "Unacceptable co-formulant" in the FLEXIBLE_RECORD.MixtureComposition of section 1.4 in the PRODUCT dataset
- Classification & Labelling information in the document FLEXIBLE_RECORD.Ghs in section 10 Classification and labelling (for mixtures) or 10.1 GHS (for substances)
- SDS linked in the Other references (including SDS) block in document FLEXIBLE_SUMMARY.SummaryEvaluation_EU_PPP of section 11 Summary and evaluation (for mixtures) or 11.2 Other reports (for substances)
- Any relevant information on their registration, status and use in other legislations in section 11.1 Assessment from other authorities or alternatively in the FLEXIBLE_SUMMARY.SummaryEvaluation_EU_PPP document mentioned above

HOW TO REPORT CO-FORMULANTS THAT ARE MIXTURES?

In the mixture composition document of section 1.4 of the PRODUCT dataset, (FLEXIBLE_RECORD.MixtureComposition) a co-formulant that is a mixture must be listed by linking a **MIXTURE entity dataset**. Within this dataset, a mixture composition document must be created (FLEXIBLE_RECORD.MixtureComposition) indicating the full composition of the co-formulant, including REFERENCE_SUBSTANCE entities for each component duly completed with all relevant chemical information and identifiers (e.g. CAS number, molecular formula, molecular weight).

In the test materials linked to studies (TEST_MATERIAL_INFORMATION entity) a co-formulant that is a mixture must be indicated by creating a REFERENCE_SUBSTANCE, indicating that the substance is a mixture and providing a list of its components in the "*Remarks*" field. Importantly, the "*Reference substance name*" must be the same as the name used for the same co-formulant in the representative formulation document (section 1.4 of the PRODUCT dataset, FLEXIBLE_RECORD.MixtureComposition), even if in that case such co-formulant is defined by a MIXTURE entity (i.e. the "Mixture/Product name" field).

MANUFACTURING PROCESS

HOW TO REPORT STARTING MATERIALS THAT ARE MIXTURES?

In the manufacturing process of the active substance (see section 1.8 of ACTIVE SUBSTANCE dataset – FLEXIBLE_RECORD.Manufacturer_EFSA document) any starting material that is a mixture must be listed as a REFERENCE_SUBSTANCE in the '*Starting substances*' table. Applicants should clearly indicate that the reference substance is a mixture and provide a list of its components in the "*Remarks*" field.

In the manufacturing process of the product (see section 1.7 of the PRODUCT dataset – FLEXIBLE_RECORD.Manufacturer_EFSA document) applicants should cross-reference the relevant mixture composition document (FLEXIBLE_RECORD.MixtureComposition) in the "*Related composition*" field. In the mixture composition document applicants must list all components of the formulation used in the manufacturing process, including any co-formulants that can be created as mixture entities.

COMPARISON OF THE COMPOSITION OF THE FORMULATIONS USED IN STUDIES AND THE REPRESENTATIVE FORMULATION

HOW TO REPORT THE TABLE COMPARING THE COMPOSITION OF THE FORMULATIONS?

A table comparing the composition of the formulations used in studies and the representative formulation does not need to be reported as such in the dossier. Instead, all test materials (TEST_MATERIAL_INFORMATION entity) linked in the studies of each representative product dataset need to be duly completed, indicating all components with a link to a REFERENCE_SUBSTANCE, their function (i.e. active substance, co-formulant, safener, synergist) and their concentration.

A table will be generated automatically comparing the test materials in a report using Report Generator.

IF ONLY REFERENCE_SUBSTANCE ENTITIES ARE ALLOWED IN THE TEST MATERIAL, HOW CAN MIXTURES (E.G. A CO-FORMULANT) BE REPORTED?

Indeed, only REFERENCE_SUBSTANCES are allowed in a TEST_MATERIAL_INFORMATION entity. If the component to be reported is:

- **a substance**: the same REFERENCE_SUBSTANCE linked in the SUBSTANCE entity used in the representative formulation document (section 1.4 of the PRODUCT dataset, FLEXIBLE_RECORD.MixtureComposition) should be used.
- **a mixture**: a REFERENCE_SUBSTANCE entity should be created, indicating that the substance is a mixture and providing a list of its components in the "*Remarks*" field. Importantly, the *"Reference substance name"* must be the same as the name used for the same component in the representative formulation document (section 1.4 of the PRODUCT dataset, FLEXIBLE_RECORD.MixtureComposition), even if in that case such co-formulant is defined by a MIXTURE entity (i.e. the *"Mixture/Product name"* field). In case the composition of a mixture co-formulant please refer to the explanation provided above

HOW CAN THE DISCUSSION / JUSTIFICATION ON THE SIMILARITY OF THESE TEST MATERIALS WITH THE REPRESENTATIVE FORMULATION BE PROVIDED?

The justification on the similarity of the test materials to the representative formulation must be provided for each test material under the field *"Confidential details on test material"* (path: TEST_MATERIAL_INFORMATION.Composition.OtherCharacteristics.ConfidentialDetailsOnTestMaterial).

This information will be automatically extracted using Report generator and shown below the table in the future report.

REPRESENTATIVENESS OF BATCHES USED IN (ECO)TOX STUDIES TO THE TECHNICAL SPECIFICATION OF THE ACTIVE SUBSTANCE

HOW TO REPORT THE TABLE COMPARING THE COMPOSITION OF BATCHES USED IN (ECO)TOX STUDIES?

The approach for comparing the composition of batches in (eco)tox studies is the same as described for the comparison of formulations in the section above.

IF NEEDED, HOW TO PROVIDE TIER I AND TIER II ASSESSMENT FOR THE IMPURITIES IDENTIFIED IN (ECO)TOX BATCHES?

New fields were introduced as of IUCLID6 10.0.0 in the FLEXIBLE_SUMMARY.Impurities document of section 1.4.6 Impurities in the product dataset. The information should be provided separately for batches used in Toxicity studies and for batches used in Ecotoxicity studies. The fields "Tier I assessment in toxicity batches" / "Tier I assessment in ecotoxicity batches" should be used to provide any relevant Tier I assessment, while the fields "Additional information on the assessment in toxicity batches" / "Additional information on the assessment in ecotoxicity batches" should be used to provide any other remarks, relevant information or Tier II assessment, if applicable.

HOW CAN THE DISCUSSION / JUSTIFICATION ON THE SIMILARITY OF THESE BATCHES TO THE PROPOSED TECHNICAL SPECIFICATION OF THE ACTIVE SUBSTANCE BE PROVIDED?

The approach for providing the justification on the similarity of batches is the same as described for the comparison of formulations in the section above.

In addition, a general conclusion should be provided in the summary document of section 1.11 Analytical profile of batches (ENDPOINT_SUMMARY.AnalyticalProfileOfBatches, "*Description of key information (confidential)*" field).

BOTANICALS

HOW SHOULD THE COMPOSITION OF BOTANICALS BE REPORTED?

For botanical active substances, **all components** which are considered as **part of the active substance composition** should be reported as "**constituents**" in FLEXIBLE_RECORD.SubstanceComposition of section 1.9 of the active substance dataset, and **only the components of concern** (as defined in SANCO/11470/2012– rev. 8) need to be reported as relevant "**impurities**". If one of the constituents is considered as **"active" component or "leading component"** such information can be indicated in the **"Remarks" field**.

IMPURITIES

HOW CAN CONFIDENTIAL DATA ON IMPURITIES (E.G. TOX, ECOTOX, QSAR) BE REPORTED?

All data on impurities (experimental or predicted e.g. QSARs, read-across) should be reported under the relevant sections (toxicological, ecotoxicological, etc) of the corresponding **impurity SUBSTANCE dataset**. This dataset should be linked in the FLEXIBLE_SUMMARY.Impurities document of section **1.4.6 Impurities** of the product, and the appropriate impurity type should be selected. Only impurities flagged with type "relevant" are published, while all other types can be claimed confidential.

HOW TO REPORT THE TOXICOLOGICAL AND ECOTOXICOLOGICAL ASSESSMENT FOR IMPURITIES?

A high-level toxicological and ecotoxicological assessment and conclusion should be provided in the "Toxicological assessment" / "Ecotoxicological assessment" fields of each impurity entry in the FLEXIBLE_SUMMARY.Impurities document of section 1.4.6 Impurities.

NOTE: before IUCLID6 10.0.0 there was only a single field called "Toxicological / Ecotoxicological assessment" which is now split into two allowing to differentiate the assessment for toxicology and ecotoxicology if needed. If additional information is needed, the corresponding documents (e.g. summaries, studies) should be created in the relevant sections of the impurity dataset, as explained above.

HOW SHOULD METHODS ON IMPURITIES BE REPORTED?

Methods for significant impurities in the active substance and for screening of potential impurities can be reported in the Active Substance dataset by selecting the **endpoint**

"Methods for significant impurities" in ENDPOINT_STUDY_RECORD.AnalyticalMethods in section 4 Analytical methods. A clarification can be provided in the Remarks to indicate that the study is a screening. Methods on any impurities can also be provided within the corresponding impurity dataset, as described for other types of studies in the question above.

HOW SHOULD THE TOXICOLOGICAL AND ECOTOXICOLOGICAL ASSESSMENT FOR IMPURITIES BE REPORTED?

A high-level toxicological and ecotoxicological assessment and conclusion should be provided in the **"Toxicological / Ecotoxicological assessment" field** of each impurity entry in the FLEXIBLE_SUMMARY.Impurities document of section **1.4.6 Impurities.** If additional information is to be provided, the corresponding documents (e.g. summaries, studies) should be created in the relevant sections of the impurity dataset, as explained above.

HOW TO REPORT THE HARMONISED CLASSIFICATION OF AN IMPURITY?

The harmonised classification of an impurity can be reported under the fields "Toxicological assessment" and "Ecotoxicological assessment" of the impurity entry in the document FLEXIBLE_SUMMARY.Impurities of section 1.4.6 Impurities. Detailed classification can be provided by using the document FLEXIBLE_RECORD.Ghs of section 10.1 GHS for each impurity dataset.

HOW TO REPORT AN IMPURITY THAT IS ALSO A METABOLITE?

Separate datasets are needed for such an impurity: one as a metabolite linked in the FLEXIBLE_SUMMARY.Metabolites in section 1.4.4 Information on metabolites, containing non-confidential information, and another one as an impurity in FLEXIBLE_SUMMARY.Impurities in section 1.4.6 Impurities, containing the confidential information.

MULTIPLE ACTIVE SUBSTANCE SOURCES

HOW SHOULD INFORMATION BE REPORTED WHEN THERE IS MORE THAN ONE ACTIVE SUBSTANCE SOURCE, BUT NOT ALL SOURCES ARE USED FOR FORMULATING THE REPRESENTATIVE PRODUCT? IS IT MANDATORY TO LINK ALL SOURCES OF THE ACTIVE SUBSTANCE TO THE PRODUCT COMPOSITION?

When **an applicant** has an active substance from different sources (i.e., active substance produced in different manufacturing sites) but supports one representative formulation, **separate manufacturing process and batch analysis documents** (FLEXIBLE_RECORD.Manufacturer_EFSA in section 1.8 and ENDPOINT_STUDY_RECORD.

AnalyticalProfileOfBatches in section 1.11 in the active substance dataset, respectively) should be provided within the Active Substance dataset, **one per manufacturing site**. Similarly, **separate batch compositions and technical specifications** (FLEXIBLE_RECORD.SubstanceComposition in section 1.9 of type "batch composition" and "technical specification", respectively) should be created and linked within each of the batch analysis documents. The full Active Substance dataset should be then linked within the representative formulation in the FLEXIBLE_RECORD.MixtureComposition of section 1.4 of the product dataset.

When **more than one applicant within a task force** is requesting the approval or renewal of an active substance, applicants are required to prepare a **joint submission**, which includes a **LEAD dossier** and **at least one MEMBER dossier**. The **LEAD dossier** contains the **joint information** submitted by the lead on behalf of all members, including all studies to be evaluated and presented in (robust) study summaries. It must also include at least one manufacturing process for the active substance and formulation, along with the full composition of the main representative formulation. The **MEMBER dossier**, on the other hand, contains only **limited confidential information** that is not shared with the lead. Consequently, the **MEMBER dossier** may include, for example, data on the manufacturing process of the active substance (FLEXIBLE_RECORD.Manufacturer_EFSA in section 1.8 of the active substance dataset) or on impurities related with the relevant source (i.e. manufacturing site) (FLEXIBLE_SUMMARY.Impurities in section 1.4.6 of the product dataset), but not on the product composition.

ISOMERS

HOW TO REPORT ACTIVE SUBSTANCES THAT ARE ISOMERS?

If the active substance is:

- **A pure isomer:**

The other isomer should be considered an impurity. It should therefore be created within the *FLEXIBLE_SUMMARY.Impurities* document (e.g. origin: "other: isomer of active substance") and will appear in section **C.1.2.2.1 – Impurities**.

- **A mixture of isomers:**

Each individual isomer, together with its concentration, should be reported in the *Constituents* section of the *FLEXIBLE_RECORD.SubstanceComposition*. In this case, the reference substance for the active substance corresponds to the mixture of all isomers. This information will be printed in **Volume 3 B1**, as the identity of the active substance is not confidential.

In this scenario, the *Constituents* section should not include the overall mixture of isomers as a separate entry. Only the individual isomers should be listed, ensuring that their sum corresponds to the total concentration of the active substance.