

07 April 2014

ANNEX to the information letter about Substance Identity issues found in your registration dossier

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Introduction

This Annex is sent to registrants receiving an information letter in the context of the Substance Identity screening campaign¹. This Annex provides you with more information on the different issues that may have been detected in your dossier, as well as the recommended next steps. Please note that all the issue types covered in this campaign are described here, so you may find sections that are not relevant for your dossier.

Steps to address potential substance identity shortcomings

- Identify the specific issue types in your information letter

¹ For more information about IT screening campaigns go to: <http://echa.europa.eu/support/how-to-improve-your-dossier/screening-activities>

- Read carefully the instructions related to the specific issue types indicated in point a) of this Annex
- Address specific issues in your dossier by providing missing information and/or revising the existing data in your IUCLID file as appropriate
- Use the Validation Assistant plug-in (former TCC plug-in) with the **Dossier Quality Assistant** tool to verify the information provided in your updated dossier, as explained under point b) of this Annex.
- Analyse any other issues that the Dossier Quality Assistant identifies and address them as appropriate. Please note that you may find issues that are not covered by this letter.
- Submit your updated dossier as explained in point c) of this Annex

If you have questions about the content of this letter and the information in the Annex, please contact ECHA via the ECHA Helpdesk at <http://echa.europa.eu/contact/helpdesk-contact-form> selecting 'I have a question related to a REACH/CLP submission'. Please indicate in the subject of your question: '**SID2014**' in order to facilitate the processing of your question.

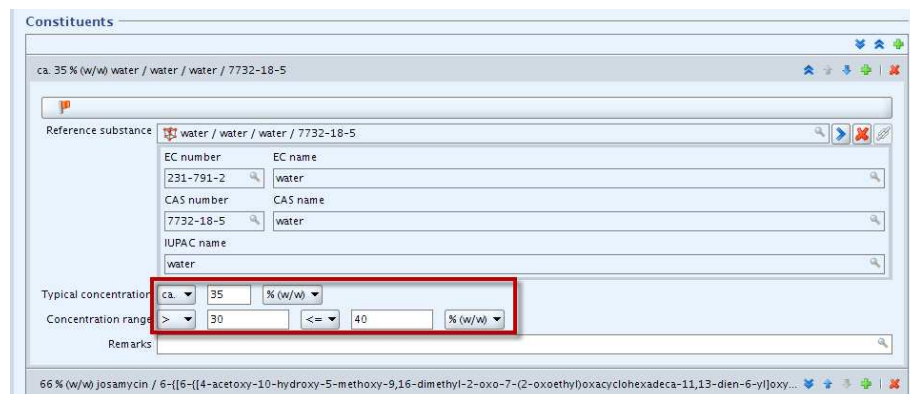
a) How to address specific issues listed in the information letter

Please check which of the following issues were detected in your dossier (see the information letter) and address them as appropriate:

Issue type 1: Missing concentration ranges

The information on the lower and upper limit of the concentration ranges for constituents, impurities and additives, as well as their typical concentrations, is necessary to understand the variability in the composition of the registered substance for the purpose of determining substance identity and substance sameness. This information is also essential to assess the validity of categories and read-across arguments.

Please provide for every constituent, additive and impurity, the typical concentration and the concentration range (minimum and maximum value) with consistent units (preferably % (w/w)) inside the block of the constituent, additive or impurity in IUCLID section 1.2 (see the screenshot below). Values must be representative for the substance as manufactured or imported by the registrant; theoretical values should not be reported.



The screenshot shows the 'Constituents' window in IUCLID. The top bar displays 'ca. 35 % (w/w) water / water / water / 7732-18-5'. Below this, the 'Reference substance' is identified as 'water / water / water / 7732-18-5'. A table of properties is shown:

EC number	231-791-2	EC name	water
CAS number	7732-18-5	CAS name	water
IUPAC name	water		

Below the table, the 'Typical concentration' is set to 'ca.' with a value of '35' and units of '% (w/w)'. The 'Concentration range' is set to '>' with a minimum value of '30' and a maximum value of '40', both with units of '% (w/w)'. A red box highlights these two rows.

Screenshot of IUCLID showing typical concentration and concentration range.

ECHA expects that all fields related to the concentration (typical, minimum and maximum) are provided. In some cases, the absence of concentration ranges is not highlighted in the letter because the typical concentration value is considered to provide sufficient characterisation of the constituent/impurity/additive.

Exceptional cases: Please note that in some exceptional cases you may have to report a theoretical first composition which does not correspond to the substance as manufactured/imported. Such cases are the registration of an individual constituent of a multi-constituent substance, the registration of an anhydrous form covering also hydrated forms of a substance, and the registration of an element in smelted alloys. In these cases, you are advised to provide the theoretical value 100% for the degree of purity of the composition and theoretical concentration values in the typical concentration and concentration ranges fields for the constituent(s). The reason for providing a theoretical composition must be clearly stated in the "Brief description" field of the reported composition.

Further information is available in chapters 4 and 8 of the Guidance for identification and naming of substances under REACH and CLP and in chapter 2 of the Data Submission Manual Part 18 - How to report the substance identity in IUCLID 5 for registration under REACH (links available under point d) of this Annex).

Dossier Quality Assistant: The Dossier Quality Assistant tool verifies that all concentration values have been provided.

Issue type 2: Typical concentration outside of concentration range

The typical concentration in IUCLID section 1.2 should be indicated for each constituent, impurity and additive, and should be within the specified concentration range. An inconsistent typical concentration casts doubt on the reliability of the composition information. Please ensure that for every constituent, additive and impurity the typical concentration falls inside the corresponding concentration range. Values must be representative for the substance as manufactured or imported; theoretical values should not be reported.

Dossier Quality Assistant: The Dossier Quality Assistant tool verifies that a typical concentration is given and is inside the corresponding concentration range.

Issue type 3: Composition reported with no constituents

Each composition in IUCLID section 1.2 must be described using at least one constituent. To this end, a block needs to be created under 'Constituents', the appropriate reference substance linked, and information on the concentration range and the typical concentration provided. Further constituents, impurities and additives should be specified as appropriate.

Validation Assistant plug-in: The Business rules and Technical Completeness Check modules of the Validation Assistant plug-in verify that each composition contains at least one constituent, and that each constituent is identified by a reference substance.

Issue type 4: Low or ambiguous degree of purity for well-defined substances

A low or very wide degree of purity range indicates great variability in the composition of the registered substance and it raises questions about whether the dossier covers a single substance. Please re-assess whether the purity accurately describes the substance as manufactured/imported, and perform the relevant adjustments of the purity information. If the degree of purity is indeed accurate you are requested to include a justification in the "Brief description" field of the composition to why such a low/wide purity occurs in the manufacture/import of this substance.

The degree of purity should correspond to the purity of the substance as manufactured or imported and should therefore not be theoretical. The degree of purity should be consistent with the concentration ranges.

Dossier Quality Assistant: The Dossier Quality Assistant tool does not verify low or ambiguous degree of purity information.

Issue type 5: Unidentified constituent or impurity present at significant concentration

Well-defined substances. For well-defined substances, the constituents are expected to be present at $\geq 80\%$ (mono-constituent) or $\geq 10 - < 80\%$ (multi-constituent) and should be identified completely by substance identifiers, including EC and CAS information (where applicable), a chemical name, and molecular and structural information. Impurities present at a concentration $\geq 1\%$ should be identified by at least one of the following identifiers: chemical name (IUPAC and/or CAS name), CAS-number and EC-number and/or molecular formula. Impurities that are relevant for the classification and/or PBT assessment shall always be specified, independently of their concentration.

UVCB substances. For UVCB substances, all known constituents and all constituents present at concentrations $\geq 10\%$ should be individually identified by substance identifiers, including available and appropriate EC and CAS information, a chemical name, and molecular and structural information. Constituents that are relevant for the classification and/or PBT assessment of the substance shall always be identified, independently of their concentration. Due to the lack of differentiation between constituents and impurities, the terms 'constituents' and 'impurities' are not regarded as relevant for UVCB substances. Instead, all constituents should be reported under the 'Constituents' heading in IUCLID section 1.2. Unknown constituents should be identified as far as possible by a generic description of their chemical nature. A reference substance should be created for each group of unknown constituents presenting a common chemical feature, as illustrated in chapter 2.1, figure 5 of the Data Submission Manual Part 18 - How to report the substance identity in IUCLID 5 for registration under REACH.

Further information is available in chapters 4 and 8 of the Guidance for identification and naming of substances under REACH and CLP and in chapter 2 of the Data Submission Manual Part 18 - How to report the substance identity in IUCLID 5 for registration under REACH (links available under point d) of this Annex).

Dossier Quality Assistant: The Dossier Quality Assistant tool does not verify the presence of insufficiently identified constituents or impurities.

Issue type 6: Well-defined substance with inconsistency between degree of purity and constituent concentrations²

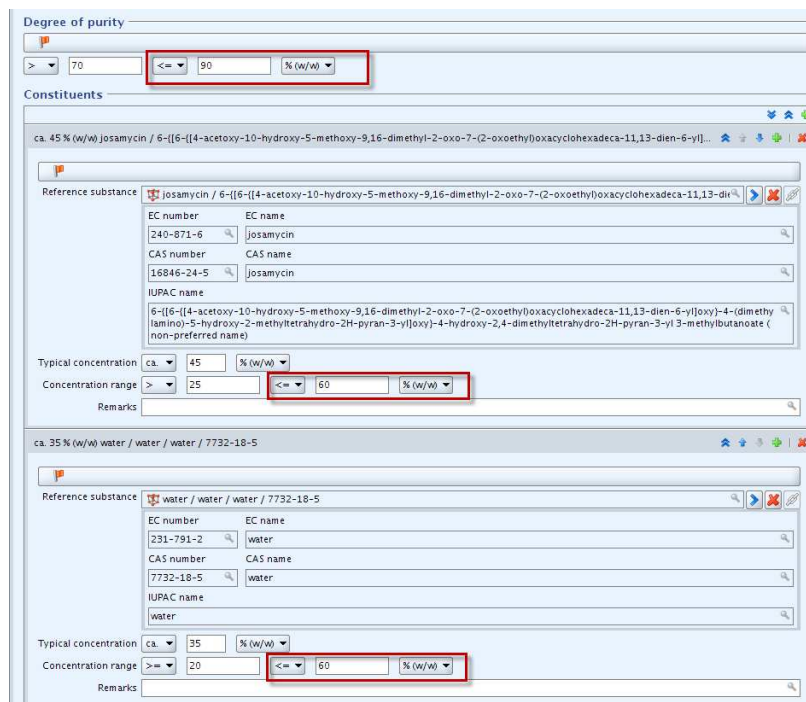
For well-defined substances, the degree of purity shall correspond to the overall concentration range of the constituents. Please note that in absence of lower or upper bounds in the purity/concentration ranges, some assumptions are made e.g. maximum purity/concentration assumed to be 100%, same figure for lower and upper bound, etc.

a) The sum of the maximum concentrations of all the constituents should never be below the maximum degree of purity. E.g. if the maximum concentrations of the constituents only add up to 90%, this is not compatible with a maximum purity of 95%.

Therefore, the following is expected:

$$\sum_{i=1}^n c_i^{max} \geq \text{purity}^{max} \quad (6-1)$$

(c_i^{max} = maximum concentration of constituent i ; n = number of constituents in a given composition)



The screenshot shows the IUCLID interface for defining a substance. At the top, the 'Degree of purity' is set to 90% (w/w). Below, two constituents are listed:

- Constituent 1:** Josamycin. Reference substance: 6-[[[4-acetoxy-10-hydroxy-5-methoxy-9,16-dimethyl-2-oxo-7-(2-oxoethyl)oxacyclohexadeca-11,13-dien-6-yl]]...]. Typical concentration: 45% (w/w). Concentration range: 25% to 60% (w/w).
- Constituent 2:** water. Reference substance: water / water / water / 7732-18-5. Typical concentration: 35% (w/w). Concentration range: 20% to 60% (w/w).

Screenshot of IUCLID showing that the sum of the maximum concentrations of all the constituents is above the maximum degree of purity (60% + 60% ≥ 90%).

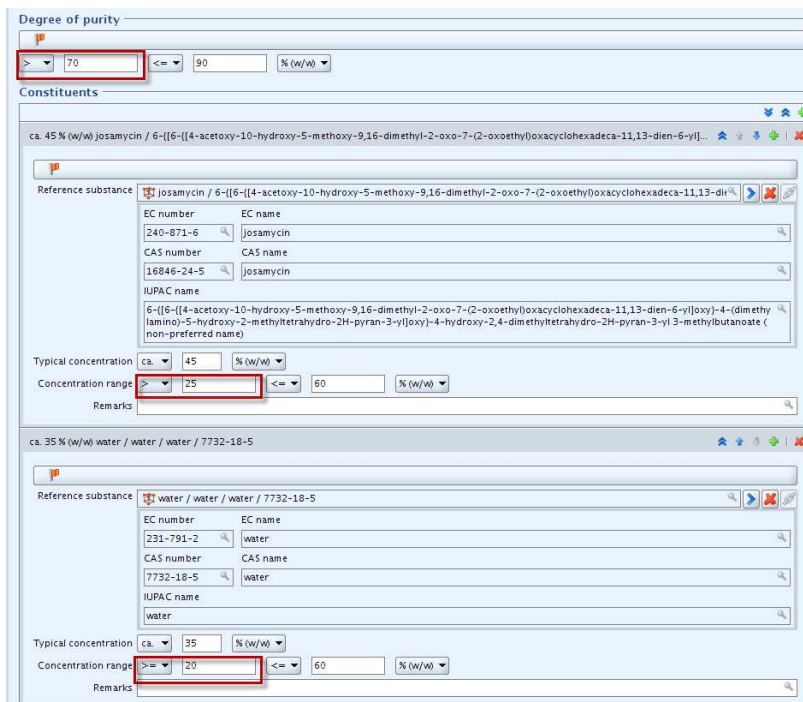
Similarly, the sum of the minimum concentrations of all the constituents should never be above the minimum degree of purity. E.g. if the minimum concentrations of the constituents add up to 90%, a minimum purity of 85% cannot be obtained.

² Please note that all the examples included in this issue type are fictional. Their purpose is only to illustrate the relevant fields that need verification and consistency.

Therefore, the following is expected:

$$\sum_{i=1}^n c_i^{min} \leq \text{purity}^{min} \quad (6-2)$$

(c_i^{min} = minimum concentration of constituent i ; n = number of constituents in a given composition)



The screenshot shows the IUCLID interface for setting constituent concentrations. At the top, the 'Degree of purity' is set to 70%. Below, two constituents are defined:

- Constituent 1:** josamycin / 6-[[[4-acetoxy-10-hydroxy-5-methoxy-9,16-dimethyl-2-oxo-7-(2-oxoethyl)oxacyclohexadeca-11,13-dien-6-yl]...]]
 - Reference substance: josamycin / 6-[[[4-acetoxy-10-hydroxy-5-methoxy-9,16-dimethyl-2-oxo-7-(2-oxoethyl)oxacyclohexadeca-11,13-dien-6-yl]...]]
 - EC number: 240-871-6
 - EC name: josamycin
 - CAS number: 16846-24-5
 - CAS name: josamycin
 - IUPAC name: 6-[[[4-acetoxy-10-hydroxy-5-methoxy-9,16-dimethyl-2-oxo-7-(2-oxoethyl)oxacyclohexadeca-11,13-dien-6-yl]oxy]-4-(dimethylamino)-5-hydroxy-2-methyltetrahydro-2H-pyran-3-yl]oxy]-4-hydroxy-2,4-dimethyltetrahydro-2H-pyran-3-yl 3-methylbutanoate (non-preferred name)
 - Typical concentration: ca. 45 % (w/w)
 - Concentration range: > 25 % (w/w) to <= 60 % (w/w)
- Constituent 2:** water / water / water / 7732-18-5
 - Reference substance: water / water / water / 7732-18-5
 - EC number: 231-791-2
 - EC name: water
 - CAS number: 7732-18-5
 - CAS name: water
 - IUPAC name: water
 - Typical concentration: ca. 35 % (w/w)
 - Concentration range: >= 20 % (w/w) to <= 60 % (w/w)

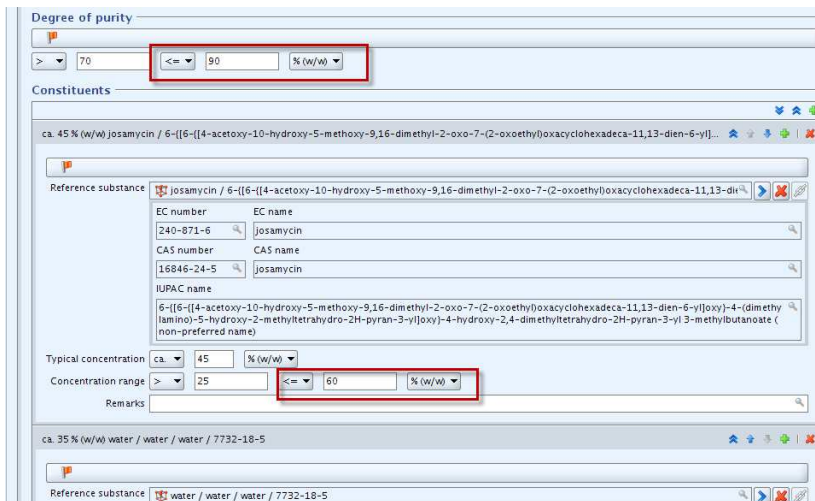
Screenshot of IUCLID showing that the sum of the minimum concentrations of all the constituents is below the minimum degree of purity (25% + 20% ≤ 70%).

b) A constituent should not be present at a concentration higher than the maximum degree of purity. E.g. the typical concentration of one constituent cannot be 97% if the maximum purity is 95%.

Therefore, the following is expected:

$$c_i \leq \text{purity}^{max} \quad (6-3)$$

(c_i = maximum, typical or minimum concentration of any constituent i in a given composition)



Degree of purity

> 70 <= 90 % (w/w)

Constituents

ca. 45 % (w/w) Josamycin / 6-[[[4-acetoxy-10-hydroxy-5-methoxy-9,16-dimethyl-2-oxo-7-(2-oxoethyl)oxacyclohexadeca-11,13-dien-6-yl]...

Reference substance: Josamycin / 6-[[[4-acetoxy-10-hydroxy-5-methoxy-9,16-dimethyl-2-oxo-7-(2-oxoethyl)oxacyclohexadeca-11,13-di...

EC number: 240-871-6 EC name: josamycin

CAS number: 16846-24-5 CAS name: josamycin

IUPAC name: 6-[[[4-acetoxy-10-hydroxy-5-methoxy-9,16-dimethyl-2-oxo-7-(2-oxoethyl)oxacyclohexadeca-11,13-dien-6-yl]oxy]-4-(dimethylamino)-5-hydroxy-2-methyltetrahydro-2H-pyran-3-yl]oxy]-4-hydroxy-2,4-dimethyltetrahydro-2H-pyran-3-yl 3-methylbutanoate (non-preferred name)

Typical concentration: ca. 45 % (w/w)

Concentration range: > 25 <= 60 % (w/w)

Remarks:

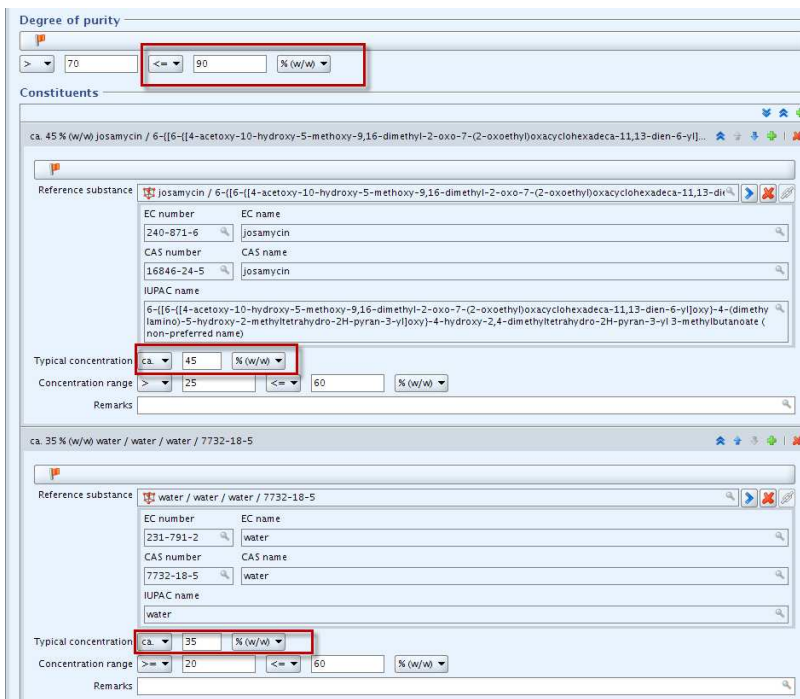
ca. 35 % (w/w) water / water / water / 7732-18-5

Reference substance: water / water / water / 7732-18-5

Screenshot of IUCLID showing that constituent 1 is present at a concentration which is consistent with the maximum degree of purity (60% ≤ 90%).

$$\sum_{i=1}^n c_i^{typ} \leq \text{purity}^{max} \quad (6-4)$$

(c_i^{typ} = typical concentration of constituent i ; n = number of constituents in a given composition)



Degree of purity

> 70 <= 90 % (w/w)

Constituents

ca. 45 % (w/w) Josamycin / 6-[[[4-acetoxy-10-hydroxy-5-methoxy-9,16-dimethyl-2-oxo-7-(2-oxoethyl)oxacyclohexadeca-11,13-dien-6-yl]...

Reference substance: Josamycin / 6-[[[4-acetoxy-10-hydroxy-5-methoxy-9,16-dimethyl-2-oxo-7-(2-oxoethyl)oxacyclohexadeca-11,13-di...

EC number: 240-871-6 EC name: josamycin

CAS number: 16846-24-5 CAS name: josamycin

IUPAC name: 6-[[[4-acetoxy-10-hydroxy-5-methoxy-9,16-dimethyl-2-oxo-7-(2-oxoethyl)oxacyclohexadeca-11,13-dien-6-yl]oxy]-4-(dimethylamino)-5-hydroxy-2-methyltetrahydro-2H-pyran-3-yl]oxy]-4-hydroxy-2,4-dimethyltetrahydro-2H-pyran-3-yl 3-methylbutanoate (non-preferred name)

Typical concentration: ca. 45 % (w/w)

Concentration range: > 25 <= 60 % (w/w)

Remarks:

ca. 35 % (w/w) water / water / water / 7732-18-5

Reference substance: water / water / water / 7732-18-5

EC number: 231-791-2 EC name: water

CAS number: 7732-18-5 CAS name: water

IUPAC name: water

Typical concentration: ca. 35 % (w/w)

Concentration range: > 20 <= 60 % (w/w)

Remarks:

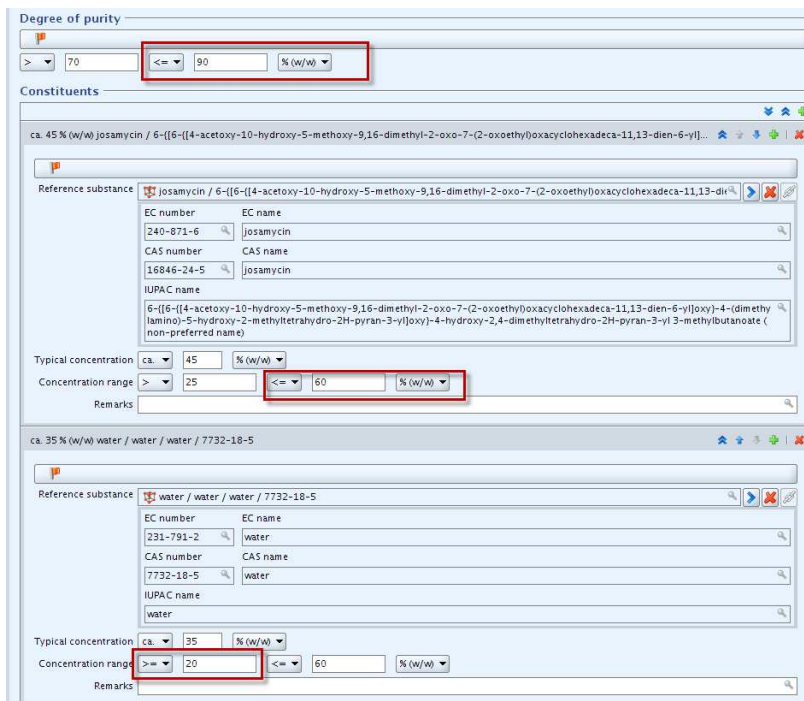
Screenshot of IUCLID showing that all constituents are present at a typical concentration consistent with the maximum degree of purity (45% + 35% ≤ 90%).

c) The maximum concentration of each constituent added to the minimum concentrations of the remaining constituents must not be higher than the maximum degree of purity of that composition.

Therefore, the following is expected:

$$c_i^{max} + \sum_{j=1, j \neq i}^n c_j^{min} \leq purity^{max} \quad (6-5)$$

(c_i^{max} = maximum concentration of constituent i ; c_j^{min} = minimum concentration of constituent j ; n = number of constituents in a given composition)



Degree of purity

> 70 <= 90 % (w/w)

Constituents

ca. 45 % (w/w) josamycin / 6-[[[6-[[[4-acetoxy-10-hydroxy-5-methoxy-9,16-dimethyl-2-oxo-7-(2-oxoethyl)oxacyclohexadeca-11,13-dien-6-yl]...]]]]

Reference substance: josamycin / 6-[[[6-[[[4-acetoxy-10-hydroxy-5-methoxy-9,16-dimethyl-2-oxo-7-(2-oxoethyl)oxacyclohexadeca-11,13-dien-6-yl]...]]]]

EC number	EC name
240-871-6	josamycin
CAS number	CAS name
16846-24-5	josamycin
IUPAC name	
6-[[[6-[[[4-acetoxy-10-hydroxy-5-methoxy-9,16-dimethyl-2-oxo-7-(2-oxoethyl)oxacyclohexadeca-11,13-dien-6-yl]oxy]-4-(dimethylamino)-5-hydroxy-2-methyltetrahydro-2H-pyran-3-yl]oxy]-4-hydroxy-2,4-dimethyltetrahydro-2H-pyran-3-yl]3-methylbutanoate (non-preferred name)	

Typical concentration: ca. 45 % (w/w)

Concentration range: > 25 <= 60 % (w/w)

Remarks:

ca. 35 % (w/w) water / water / water / 7732-18-5

Reference substance: water / water / water / 7732-18-5

EC number	EC name
231-791-2	water
CAS number	CAS name
7732-18-5	water
IUPAC name	
water	

Typical concentration: ca. 35 % (w/w)

Concentration range: >= 20 <= 60 % (w/w)

Remarks:

Screenshot of IUCLID showing that the maximum concentration of constituent 1 added to the minimum concentrations of the remaining constituents (in this case, constituent 2) must not be higher than the maximum degree of purity (60% + 20% ≤ 90%).

Dossier Quality Assistant: The Dossier Quality Assistant tool verifies the consistency of the degree of purity and the constituents' concentration ranges, provided these have been properly indicated (complete ranges, same units).

Issue type 7: Well-defined substance with inconsistency between degree of purity and impurity concentrations³

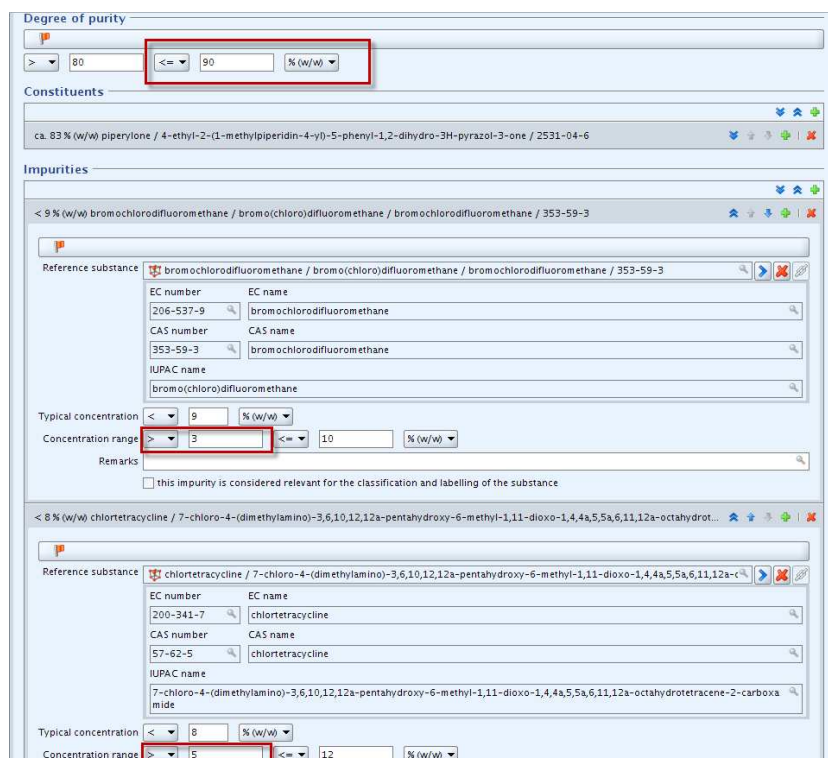
For well-defined substances, the impurities and the degree of purity shall together sum up to 100% of the composition. These scenarios are similar to the ones described under issue type 6. Please note that in absence of lower or upper bounds in the purity/concentration ranges, some assumptions are made e.g. maximum purity/concentration assumed to be 100%, same figure for lower and upper bound, etc.

a) As a consequence, it is expected that the sum of the minimum concentrations of the impurities is consistent with the maximum degree of purity; and the sum of the maximum concentrations of the impurities is consistent with the minimum degree of purity. These two values are consistent if their sum does not exceed 100%.

Therefore, the following is expected:

$$purity^{max} + \sum_{i=1}^n c_i^{min} \leq 100\% \quad (7-1)$$

(c_i^{min} = minimum concentration of impurity i ; n = number of impurities in a given composition)



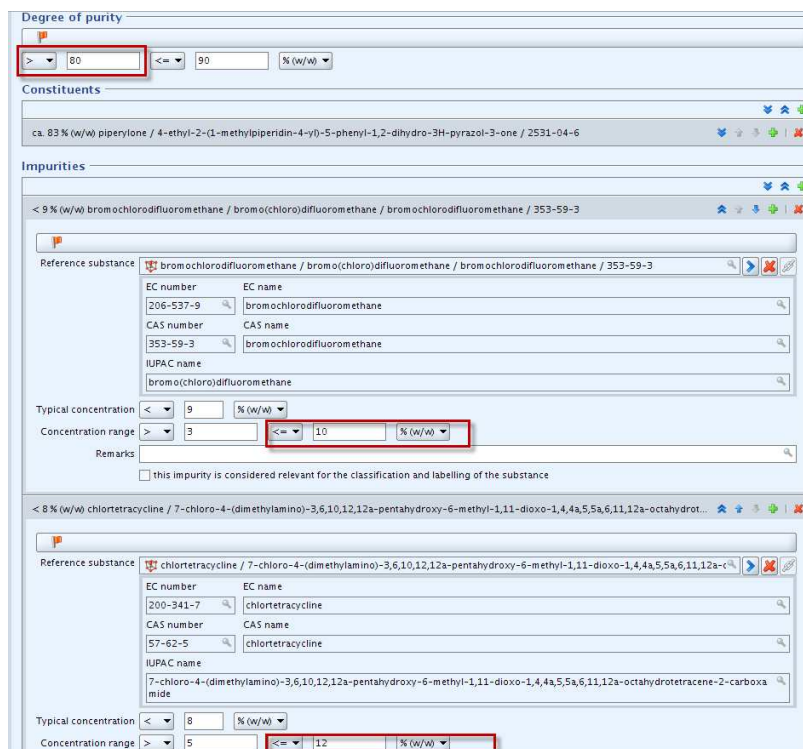
The screenshot shows the IUCLID interface for a substance. In the 'Degree of purity' section, the maximum value is set to 90% (w/w). In the 'Impurities' section, two impurities are listed: bromochlorodifluoromethane with a concentration of 3% (w/w) and chlortetracycline with a concentration of 5% (w/w). The sum of these minimum concentrations (3% + 5%) is consistent with the maximum degree of purity (90%) as per equation 7-1.

Screenshot of IUCLID showing that the sum of the minimum concentrations of the impurities is consistent with the maximum degree of purity (90% + (3% + 5%) ≤ 100%).

³ Please note that all the examples included in this issue type are fictional. Their purpose is only to illustrate the relevant fields that need verification and consistency

$$purity^{min} + \sum_{i=1}^n c_i^{max} \geq 100\% \quad (7-2)$$

(c_i^{max} = maximum concentration of impurity i ; n = number of impurities in a given composition)



The screenshot shows the IUCALID software interface. At the top, the 'Degree of purity' is set to 80% (w/w). Below this, two impurities are listed:

- Impurity 1:** bromochlorodifluoromethane / bromo(chloro)difluoromethane / bromochlorodifluoromethane / 353-59-3. Its typical concentration is 9% (w/w) and its concentration range is 3% to 10% (w/w).
- Impurity 2:** chlortetracycline / 7-chloro-4-(dimethylamino)-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydro-2-carboxamide. Its typical concentration is 8% (w/w) and its concentration range is 5% to 12% (w/w).

Red boxes highlight the 80% minimum purity, the 10% maximum concentration for the first impurity, and the 12% maximum concentration for the second impurity.

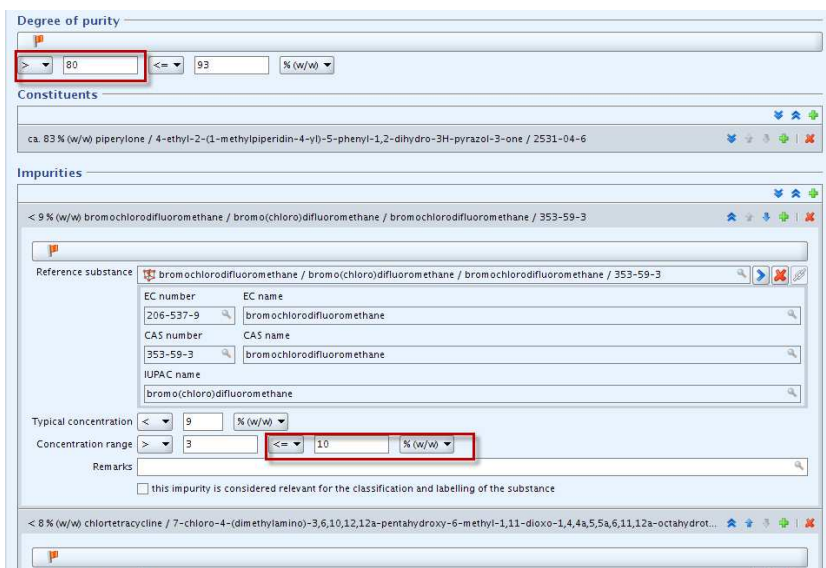
Screenshot of IUCALID showing that the sum of the maximum concentrations of the impurities is consistent with the minimum degree of purity ($80\% + (10\% + 12\%) \geq 100\%$).

b) An impurity should not be present at a concentration which is not consistent with the minimum degree of purity. E.g. the typical concentration level of an impurity cannot be 15% if the minimum purity is 88%.

Therefore, the following is expected:

$$purity^{min} + c_i \leq 100\% \quad (7-3)$$

(c_i = maximum, typical or minimum concentration of any impurity in a given composition)



Degree of purity

> 80 <= 93 % (w/w)

Constituents

ca. 83 % (w/w) piperitone / 4-ethyl-2-(1-methylpiperidin-4-yl)-5-phenyl-1,2-dihydro-3H-pyrazol-3-one / 2531-04-6

Impurities

< 9 % (w/w) bromochlorodifluoromethane / bromo(chloro)difluoromethane / bromochlorodifluoromethane / 353-59-3

Reference substance: bromochlorodifluoromethane / bromo(chloro)difluoromethane / bromochlorodifluoromethane / 353-59-3

EC number	EC name
206-537-9	bromochlorodifluoromethane
CAS number	CAS name
353-59-3	bromochlorodifluoromethane
IUPAC name	
bromo(chloro)difluoromethane	

Typical concentration < 9 % (w/w)

Concentration range > 3 <= 10 % (w/w)

Remarks

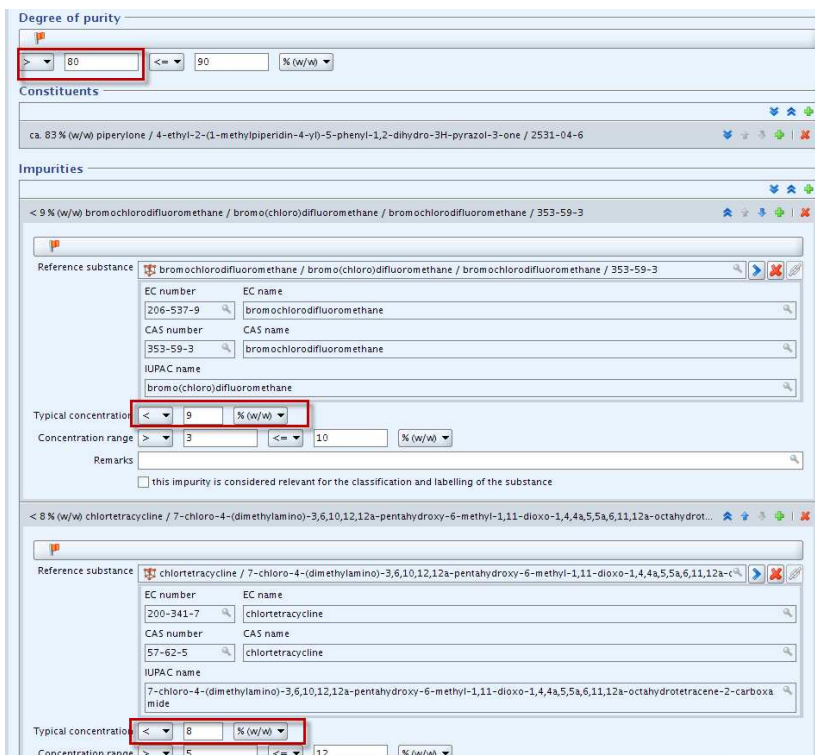
this impurity is considered relevant for the classification and labelling of the substance

< 8 % (w/w) chlortetracycline / 7-chloro-4-(dimethylamino)-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydrodrot... / 57-62-5

Screenshot of IUCLID showing that impurity 1 is present at a concentration which is consistent with the minimum degree of purity (80% +10% ≤ 100%).

$$\text{purity}^{\text{min}} + \sum_{i=1}^n c_i^{\text{typ}} \leq 100\% \quad (7-4)$$

(c_i^{typ} = typical concentration of impurity i ; n = number of impurities in a given composition)



Degree of purity

> 80 <= 90 % (w/w)

Constituents

ca. 83 % (w/w) piperitone / 4-ethyl-2-(1-methylpiperidin-4-yl)-5-phenyl-1,2-dihydro-3H-pyrazol-3-one / 2531-04-6

Impurities

< 9 % (w/w) bromochlorodifluoromethane / bromo(chloro)difluoromethane / bromochlorodifluoromethane / 353-59-3

Reference substance: bromochlorodifluoromethane / bromo(chloro)difluoromethane / bromochlorodifluoromethane / 353-59-3

EC number	EC name
206-537-9	bromochlorodifluoromethane
CAS number	CAS name
353-59-3	bromochlorodifluoromethane
IUPAC name	
bromo(chloro)difluoromethane	

Typical concentration < 9 % (w/w)

Concentration range > 3 <= 10 % (w/w)

Remarks

this impurity is considered relevant for the classification and labelling of the substance

< 8 % (w/w) chlortetracycline / 7-chloro-4-(dimethylamino)-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydrodrot... / 57-62-5

Reference substance: chlortetracycline / 7-chloro-4-(dimethylamino)-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-1,4,4a,5,5a,6,11,12a-c... / 57-62-5

EC number	EC name
200-341-7	chlortetracycline
CAS number	CAS name
57-62-5	chlortetracycline
IUPAC name	
7-chloro-4-(dimethylamino)-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydrodrotrecene-2-carboxamide	

Typical concentration < 8 % (w/w)

Concentration range > 5 <= 12 % (w/w)

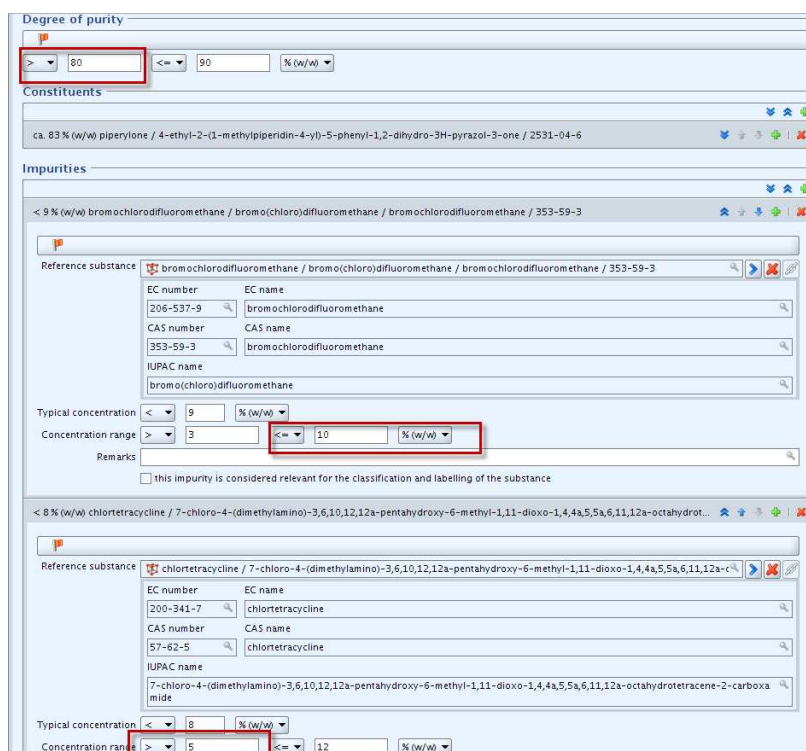
Screenshot of IUCLID showing that the sum of the typical concentrations of the impurities are consistent with the minimum degree of purity (80% +(9% +8%) ≤ 100%).

c) The maximum concentration of each impurity added to the minimum concentrations of the remaining impurities, should be consistent with the indicated minimum degree of purity. The maximum concentration level of an impurity added to the minimum concentrations of the remaining impurities and to the minimum purity level of the substance cannot exceed 100%.

Therefore, the following is expected:

$$purity^{min} + c_i^{max} + \sum_{j=1, j \neq i}^n c_j^{min} \leq 100\% \quad (7-5)$$

(c_i^{max} = maximum concentration of impurity i ; c_j^{min} = minimum concentration of impurity j ; n = number of impurities in a given composition)



The screenshot shows the IUCALID software interface with the following settings:

- Degree of purity:** Minimum: 80, Maximum: 90, Unit: % (w/w)
- Constituents:** ca. 83 % (w/w) piperlyone / 4-ethyl-2-(1-methylpiperidin-4-yl)-5-phenyl-1,2-dihydro-3H-pyrazol-3-one / 2531-04-6
- Impurities:**
 - Impurity 1:** bromochlorodifluoromethane / bromo(chloro)difluoromethane / bromochlorodifluoromethane / 353-59-3
 - Typical concentration: 9 % (w/w)
 - Concentration range: Minimum 3, Maximum 10, Unit: % (w/w)
 - Impurity 2:** chlortetracycline / 7-chloro-4-(dimethylamino)-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydro-2-carboxamide
 - Typical concentration: 8 % (w/w)
 - Concentration range: Minimum 5, Maximum 12, Unit: % (w/w)

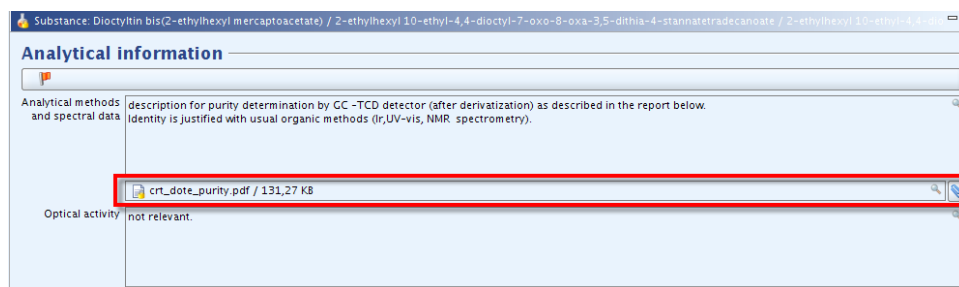
Screenshot of IUCALID showing that the maximum concentration of impurity 1 added to the minimum concentrations of the remaining impurities (in this case, impurity 2), should be consistent with the indicated minimum degree of purity (80% +10% +5% ≤ 100%).

Dossier Quality Assistant: The Dossier Quality Assistant tool verifies the consistency of the degree of purity and the impurity concentration ranges, provided that these have been properly indicated (complete ranges, same units).

Issue type 8: No spectral and analytical information provided

Sections 2.3.5, 2.3.6 and 2.3.7 in Annex VI of the REACH Regulation require registrations submitted according to Article 10 to include specific spectral and analytical information in section 1.4 of the technical dossier. The analytical data is a crucial part of the registration dossier in order to verify the information on the composition and therefore the identity of the registered substance. The analytical data including the description of the analytical methods and the actual results of analysis shall be reported in IUCLID section 1.4. This section consists of two parts:

- Analytical information: The description of analytical methods used for the identification and quantification of your substance including all constituents, impurities and additives, and/or corresponding references should be given in this section. The description must enable the analysis to be reproduced by an analytical expert. You are expected to attach a document by clicking the paperclip button (📎). (Please refer to the screenshot below).



Screenshot of IUCLID showing the attached document in Analytical information in Section 1.4.

Please note that you can only attach one file in this section. In case more than one file with description of the analytical methods needs to be attached, you may attach these additional files in the section "Results of analysis" by creating repeatable blocks.

- Results of analysis: The result of analysis block is intended to give you the possibility to provide information on the results of analysis and attach items like chromatograms and spectral data by clicking the paperclip button (📎). (Please see the screenshot below; note that you can only attach one file in each field).
- In terms of spectral data, you must provide, as a minimum, UV/Vis, IR and either NMR or mass spectra. In addition, HPLC or GC (as appropriate) chromatograms must be attached. For inorganic solid substances the XRD diffractogram and results of an elemental analysis (e.g. ICP or AAS) must be provided (when applicable). If it is not technically possible or if it does not appear scientifically necessary to provide such spectral data, a valid scientifically based justification must be given in this section of your dossier (see screenshot below). In case when other alternative or complementary analytical methods were used for identification and quantification of your substance, please provide respective results in this section.

Results of analysis

Spectrophotometry

Analysis type: Spectrophotometry

Tested substance: calcium dichloride

Method used: AAS

AAS.pdf / 24.63 KB

Remarks:

Chromatography

Analysis type: Chromatography

Tested substance:

Method used: GC

Remarks: Gas Chromatography is not applicable method for the analysis of the registered substance as it is an inorganic solid

Screenshot of IUCLID showing the recommended way to report the analytical results and the justification why some of the required results were not provided.

Please note that the analytical data must be generated on the substance as manufactured/imported. Data copied from other EU manufacturers/importers, generated on a sample provided from a different manufacturer/importer, or generated on a different substance is not acceptable. Please note that even if you are registering a substance being imported into a mixture, you still need to provide analytical information on the substance as such.

Please note that this issue may be triggered by the fact that the attachment is corrupted and it cannot be open.

Further information on the required spectral and analytical data, including the description of the analytical methods, is available in Appendix II chapters 10-12 of the Guidance for identification and naming of substances under REACH and CLP (links available under point d) of this Annex).

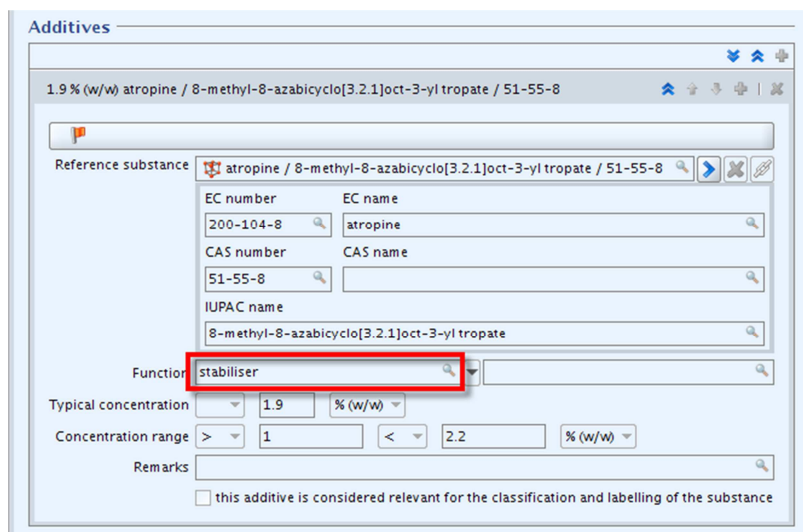
Dossier Quality Assistant: The Dossier Quality Assistant tool can verify whether an attachment is present in section 1.4 of the dossier, but not whether the adequate analytical information has been provided.

Issue type 9: Additives without stabilising function

Pursuant to article 3(1) of the REACH Regulation and as explained in chapters 2.2 and 4.2 of the Guidance for identification and naming of substances under REACH and CLP, substances intentionally added to provide a technical function other than stabilisation of the registered substance, are not part of the substance composition and shall not be reported in section 1.2 of the technical dossier. Additives under REACH are only substances that have been intentionally added to chemically stabilise the substance, and

are therefore considered as intrinsic part of the substance. Such additives should be taken into account when calculating the mass balance.

If an additive is necessary to stabilise your substance, you must include it in the composition and select the function "stabiliser" from the dropdown list (please see the screenshot below). It is also possible to select a stabilising function which is more specific than "stabiliser" from the dropdown list (i.e. inhibitor, antioxidant, UV absorber). In special cases where you wish to indicate an additive used as a stabiliser with a function not available in the dropdown list, you may also select the function "other" and specify in details the function (compatible with stabilisation) in the free text field.



The screenshot shows the 'Additives' window in IUCILID. The title bar indicates '1.9 % (w/w) atropine / 8-methyl-8-azabicyclo[3.2.1]oct-3-yl tropate / 51-55-8'. The 'Reference substance' field contains the same text. Below this, there are fields for 'EC number' (200-104-8), 'EC name' (atropine), 'CAS number' (51-55-8), and 'IUPAC name' (8-methyl-8-azabicyclo[3.2.1]oct-3-yl tropate). The 'Function' dropdown menu is highlighted with a red box and shows 'stabiliser' selected. Below the function field, there are fields for 'Typical concentration' (1.9 % (w/w)), 'Concentration range' (1 to 2.2 % (w/w)), and a 'Remarks' field. At the bottom, there is a checkbox labeled 'this additive is considered relevant for the classification and labelling of the substance'.

Screenshot of IUCILID showing the function "stabiliser" in an additive.

If your additive does not meet the definition of a stabiliser under REACH, it shall be removed from the composition, and you should consider whether it needs a separate registration. In this case the concentration of the remaining constituents must also be re-calculated to sum up to 100%.

Further information: Solvents, which are intentionally added after the manufacture of the substance to provide a technical function other than stabilisation of the substance, shall not be reported in section 1.2 of the technical dossier.

In the specific case of a solvent added during the manufacturing process of the substance, only the quantity of the solvent, which cannot be removed without affecting the chemical stability of the substance or changing its chemical composition, shall be reported in section 1.2 of the technical dossier as part of the substance composition. For UVCB substances, the quantity of solvent which cannot be removed shall be reported as a constituent. For well-defined substances, the quantity of solvent which cannot be removed shall be reported as a constituent, or an impurity depending on its concentration level.

If the residual solvent has a dual role (solvent and stabiliser) only the quantity of solvent necessary to preserve the chemical stability of the substance should be reported as an additive with the function "stabiliser".

Dossier Quality Assistant: The Dossier Quality Assistant tool verifies whether the function of the additive was reported as other than "stabiliser".

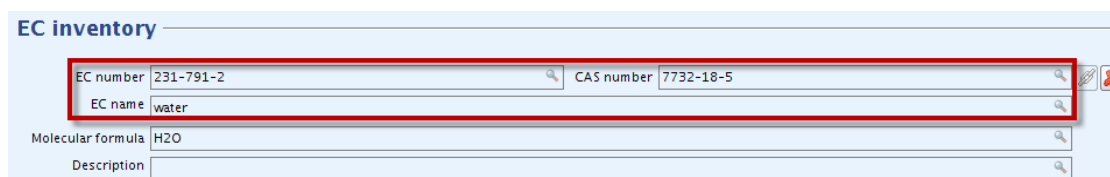
Issue type 10: Inconsistent identifiers of constituents, impurities and additives

In order to unambiguously identify the registered substance, a set of identifiers needs to be provided in the registration dossier. These identifiers may originate from the EC inventory (EC number and name, description and other associated information), from external databases like Chemical Abstracts (CAS number and name) and/or can be generated by the registrant on the basis of chemical structure and following established conventions (e.g. IUPAC /chemical name, SMILES notation and InChI code). In each case, all identifiers provided for a reference substance in your dossier shall be consistent and lead to the same molecular structure.

Please note that the information retrieved from your dossier is processed automatically and also compared with data available in external databases. This issue is flagged when at least one inconsistency is identified. Taking into account the complexity of the information related to the substance identity and the inherent technical limitations of automated IT-based tools, you may be in a situation when this issue is flagged even though all of the information in the reference substance is consistent. Furthermore, please note that in some cases information present in the pre-filled reference substances may not be necessarily comprehensive, complete, accurate or up to date. In this case, please correct the information in the pre-filled reference substance as appropriate.

Please ensure that for every constituent, additive and impurity, the identifiers (e.g. IUPAC name, EC, CAS, SMILES notation, InChI code) refer to the same chemical structure. These identifiers are to be provided in section 1.2 of the IUCLID dossier under the following headers inside the reference substance:

- EC inventory. You need to link here the appropriate EC inventory entry for the reference substance. Alternatively, you need to import into IUCLID and link here the list number entry provided to you by ECHA through the inquiry process or generated by REACH-IT during the registration process. The EC/list number entry normally contains the following information: EC number and EC name, CAS number (see screenshot below).



EC inventory	
EC number	231-791-2
CAS number	7732-18-5
EC name	water
Molecular formula	H2O
Description	

Screenshot of IUCLID showing the EC number, EC name and CAS number of an EC inventory entry.

In very exceptional cases you may consider that information in the EC inventory is not fully appropriate, e.g. if the CAS number linked to an EC entry has been deleted from the CAS registry. In this case, please provide the correct CAS number and CAS name in the "CAS information" section (please see screenshot) and indicate the reason for this discrepancy in the "Remarks" field of the reference substance.

General information

Reference substance name

EC inventory

EC number CAS number

EC name

Molecular formula

Description

No EC information available

Justification

Reference substance information

CAS information

CAS number

Remarks The CAS number linked to the EC inventory entry 247-005-6 is 25456-75-1. This CAS entry has however been deleted. The Correct CAS information for this constituent is the CAS entry with CAS number 45120-30-7"

Screenshot of IUCLID showing where to provide the correct CAS information and explanations for any discrepancy with the CAS information linked to an EC inventory entry.

- **Reference substance information.** You need to provide here the CAS number and name (if appropriate) and the IUPAC name.

Please note that the CAS information provided in this section is used by the automated screening tool to check consistency within identifiers.

- **Molecular and structural information.** You are advised to provide here the SMILES notation and InChI code. Please include the whole InChI that starts with InChI=1 or InChI=1S (see screenshot below).

Molecular and structural information

Molecular formula

Molecular weight range

SMILES notation

InChI

Structural formula

Screenshot of IUCLID showing where to provide the SMILES notation and InChI.

Please check the consistency within identifiers provided under the above-mentioned headers.

In case a constituent, impurity or additive of your substance shows stereoisomerism (e.g. enantiomerism, diastereoisomerism, *cis-trans* isomerism), please ensure that all identifiers (including SMILES and InChI) are consistent with the stereochemistry of this constituent, impurity or additive and that they are consistent with each other.

Further information is available in Appendix II chapters 1-6 of the Guidance for identification and naming of substances under REACH and CLP (links available under point d) of this Annex).

Dossier Quality Assistant: The Dossier Quality Assistant tool does not verify consistency between identifiers.

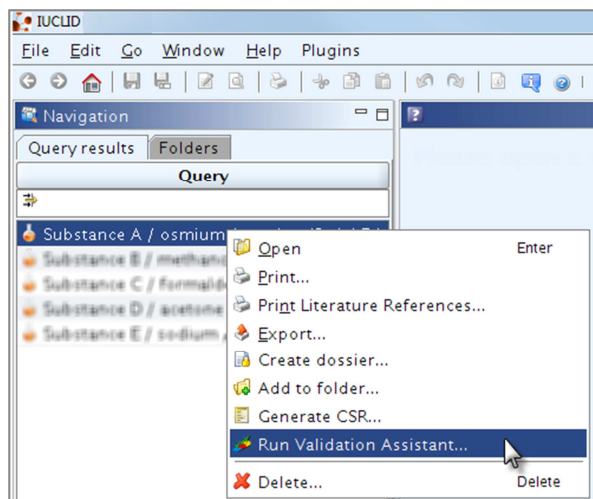
b) Use the Validation assistant plug-in and Dossier Quality Assistant

ECHA strongly advises that you use the Validation Assistant plug-in (former TCC plug-in) to check your registration dossier with updated substance identity information. Using the Validation assistant plug-in will help you to detect and correct Technical completeness check failures and most of the Business rule failures before submitting your dossier to ECHA.

This plug-in also includes the **Dossier Quality Assistant** tool which detects common inconsistencies found in registration dossiers. This tool runs automatically when you launch the Validation Assistant plug-in on your dossier or substance dataset in IUCLID 5. The results are shown in a new separate screen, where you can see the potential deficiencies detected by the tool, including some of the issues explained above.

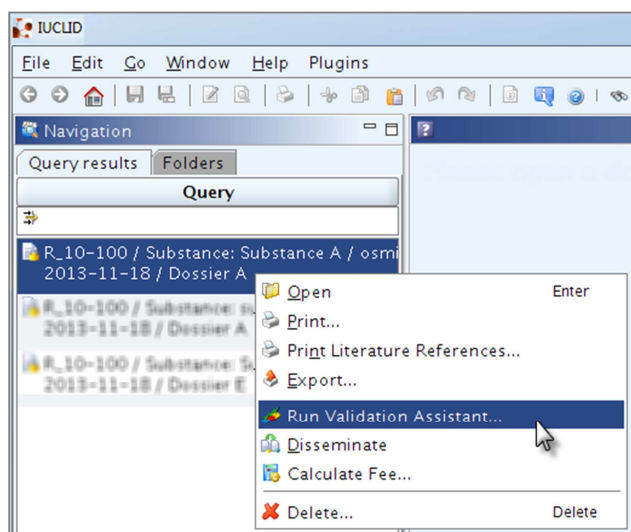
Before you submit your dossier to ECHA, please check the information provided by using the Validation assistant plug-in on both the substance dataset and the final dossier (see steps below). The latest version of the plug-in can be downloaded via your IUCLID 5 website account at <http://iuclid.eu/>.

Step 1) Run the plug-in first on your substance dataset (🧪).



Screenshot of IUCLID showing how to run the Validation assistant plug-in on a substance dataset.

Step 2) Run the plug-in again on the final dossier (📁)



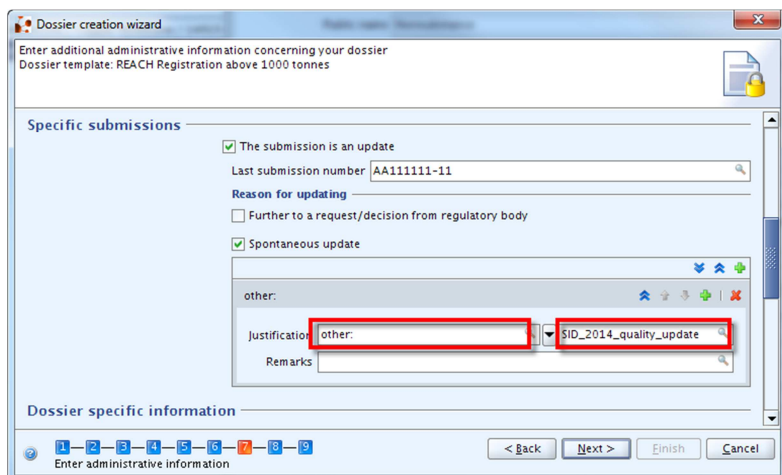
Screenshot of IUCLID showing how to run the Validation assistant plug-in on a dossier.

Please note that the **Dossier Quality Assistant** tool may also display warning messages for issues which are not specified in this information letter. You are strongly advised to carefully review and, when appropriate, address all warning messages displayed by the Dossier Quality Assistant tool, in order to further improve the consistency of your dossier.

c) How to update your dossier

After updating/correcting the information indicated in the letter, you should submit it to ECHA as a new IUCLID 5 dossier. This dossier should be indicated as a spontaneous update, making reference to the latest accepted dossier you have submitted for this substance.

To do so, when filling in the administrative information during dossier creation you need to indicate in the dossier header "The submission is an update" and enter the last submission number in the corresponding field. The "Last submission number" is the one linked to the latest accepted dossier for this substance, which is also quoted in the header of the letter. In the same step, you must then indicate that the dossier is a "Spontaneous update" and provide a "Justification" for updating. Please select "other:" from the drop-down list as (one of) the reason(s) for updating and make sure you include "**SID_2014_quality_update**" in the unlabelled field right next to the drop-down list (please see the screenshot).



Screenshot of IUCLID showing how to indicate the reason for updating in the dossier creation wizard.

Please note that when logging into REACH-IT to access the letter or submit the updated dossier, users will be asked to accept the new Terms and Conditions before the company account can be accessed. A factsheet is now available to explain these changes: http://echa.europa.eu/documents/10162/13652/reachit_2-7_factsheet_en.pdf

If your company does not currently import or manufacture the substance, you can reflect this situation by making use of the opportunity provided by Article 50(2) of the REACH Regulation. REACH-IT provides a functionality to inform ECHA of cease and restart manufacture. For detailed step-by-step instructions on how to inform ECHA of cease and restart manufacture, please see REACH-IT Industry User Manual Part 6 – Dossier submission available at: <http://echa.europa.eu/web/guest/support/dossier-submission-tools/reach-it>.

In case you need to contact ECHA regarding this particular information letter, please contact ECHA via the ECHA Helpdesk at <http://echa.europa.eu/contact/helpdesk-contact-form> selecting 'I have a question related to a REACH/CLP submission'. Please indicate in the subject of your question: '**SID2014**' in order to facilitate the processing of your question.

d) References

For further information please see:

Guidance for identification and naming of substances under REACH and CLP:
http://echa.europa.eu/documents/10162/13643/substance_id_en.pdf

Data Submission Manual Part 18 - How to report the substance identity in IUCLID 5 for registration under REACH:
http://echa.europa.eu/documents/10162/13653/substance_id_report_iuclid_en.pdf

Questions and Answers on Substance Identification:
http://echa.europa.eu/documents/10162/13648/qa_substance_id_en.pdf

Validation Assistant plug-in (requires sign-up):
http://iuclid.eu/index.php?fuseaction=home.download55&area_id=55010

In the case that you are in doubt about how to present the information in an updated dossier, how to run the Validation assistant plug-in with the Dossier Quality Assistant tool, or you need any additional assistance, please contact the ECHA Helpdesk at <http://echa.europa.eu/web/guest/contact>.

You may also wish to contact your national Helpdesk:
<http://echa.europa.eu/web/guest/support/helpdesks/national-helpdesks>