Key substance identity concepts and dossier preparation

Andreas Uphoff

Alberto Martin Aparicio

Overview

- Introduction
- Required data for substance identity purposes
- Dossier preparation (introduction)
- Substance identity
  - Mono-constituent substances
  - Multi-constituent substances
  - … with additional identifiers
- Dossier preparation (mono & multi-constituent substances)

- BREAK

- Substance identity of UVCB substances
- Dossier preparation (UVCB substances)

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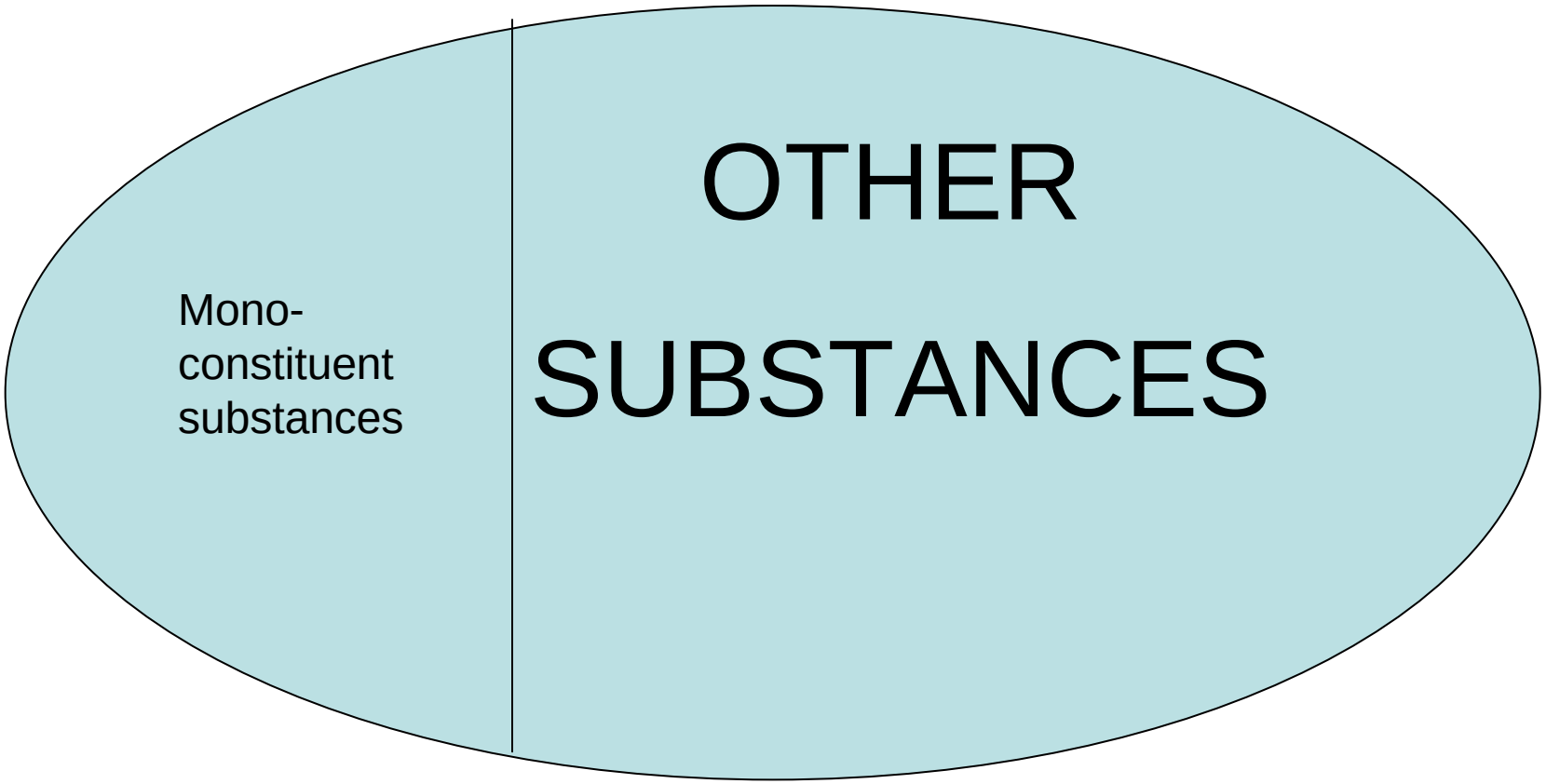
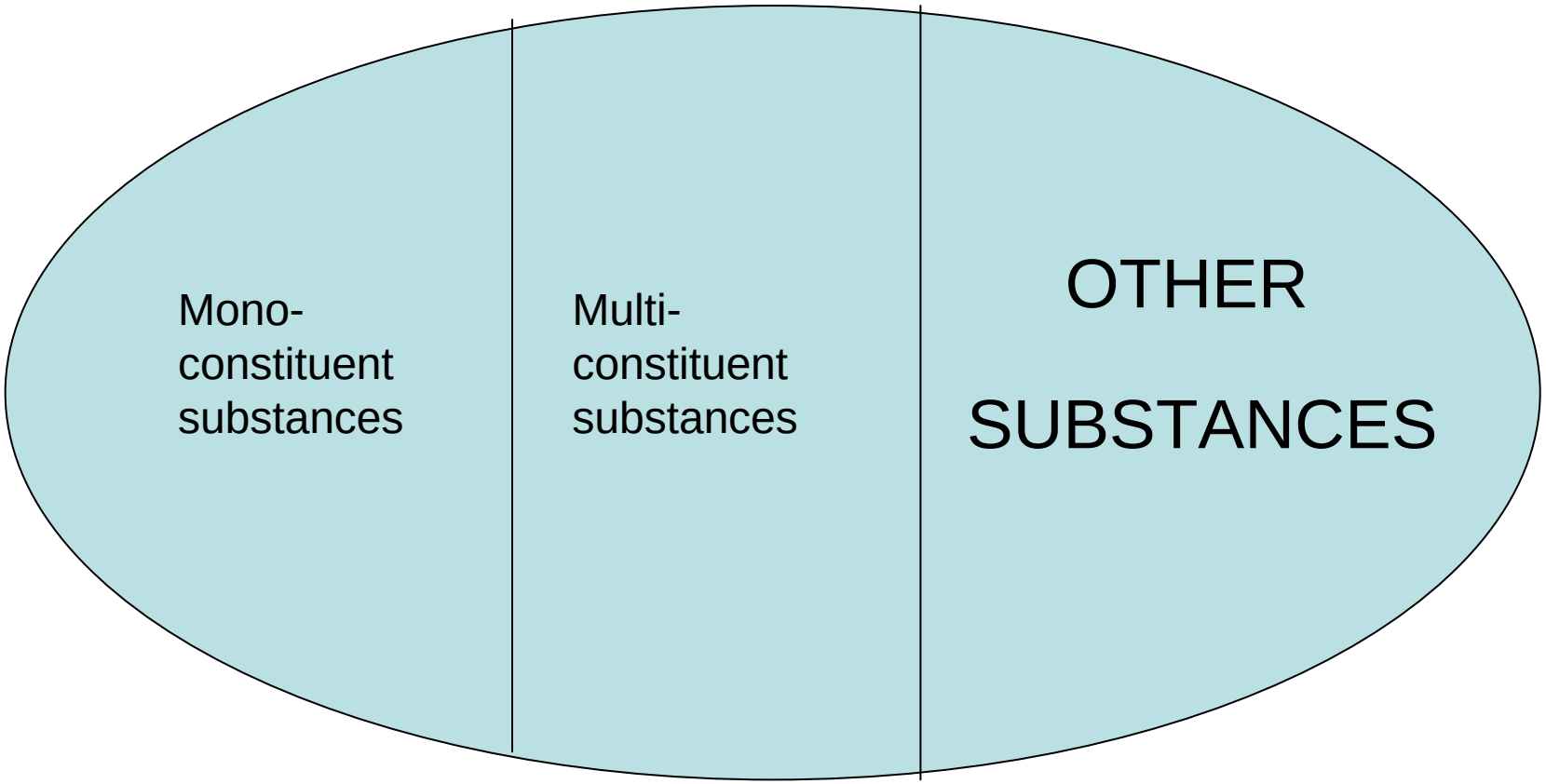
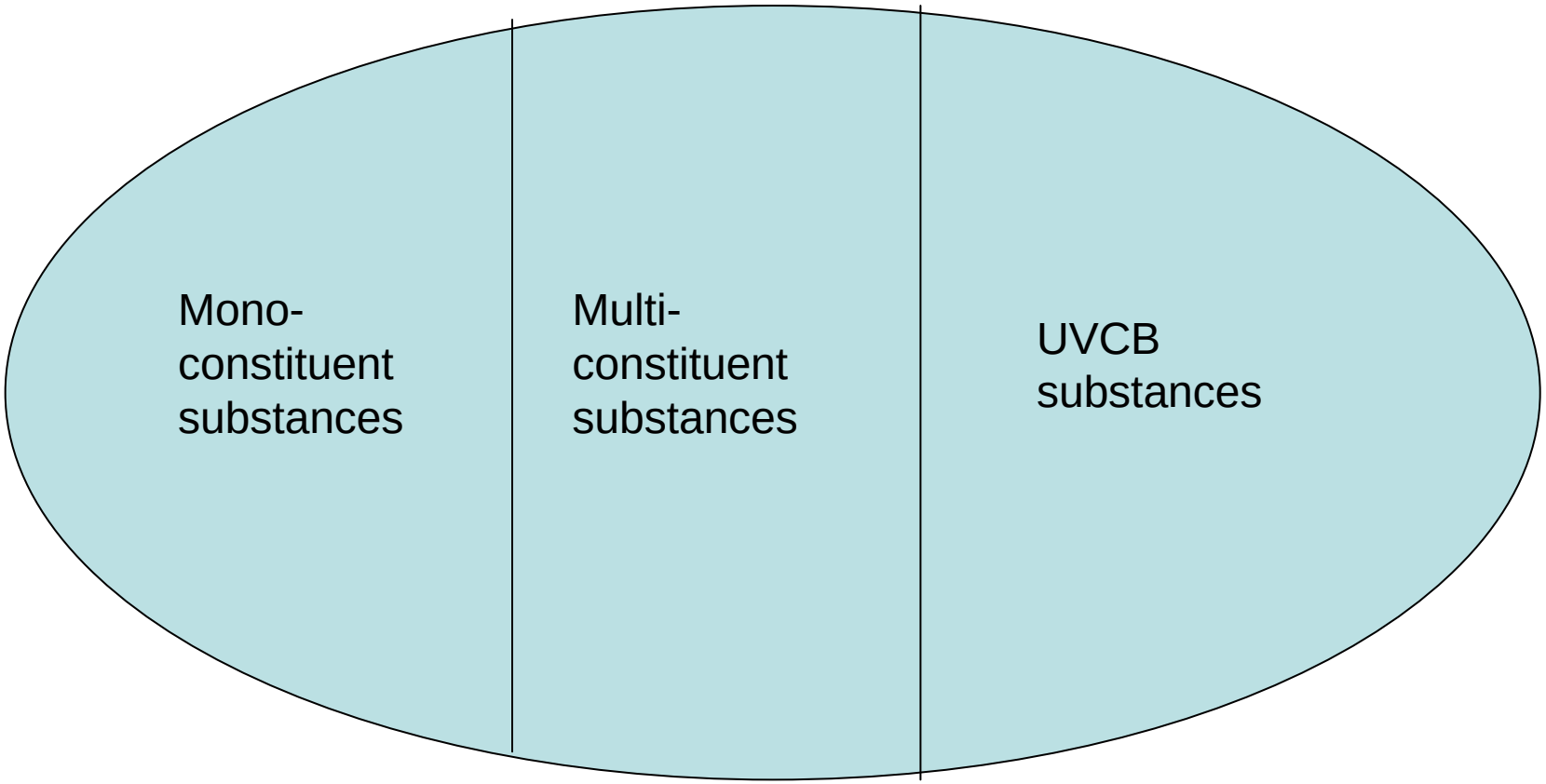
Introduction



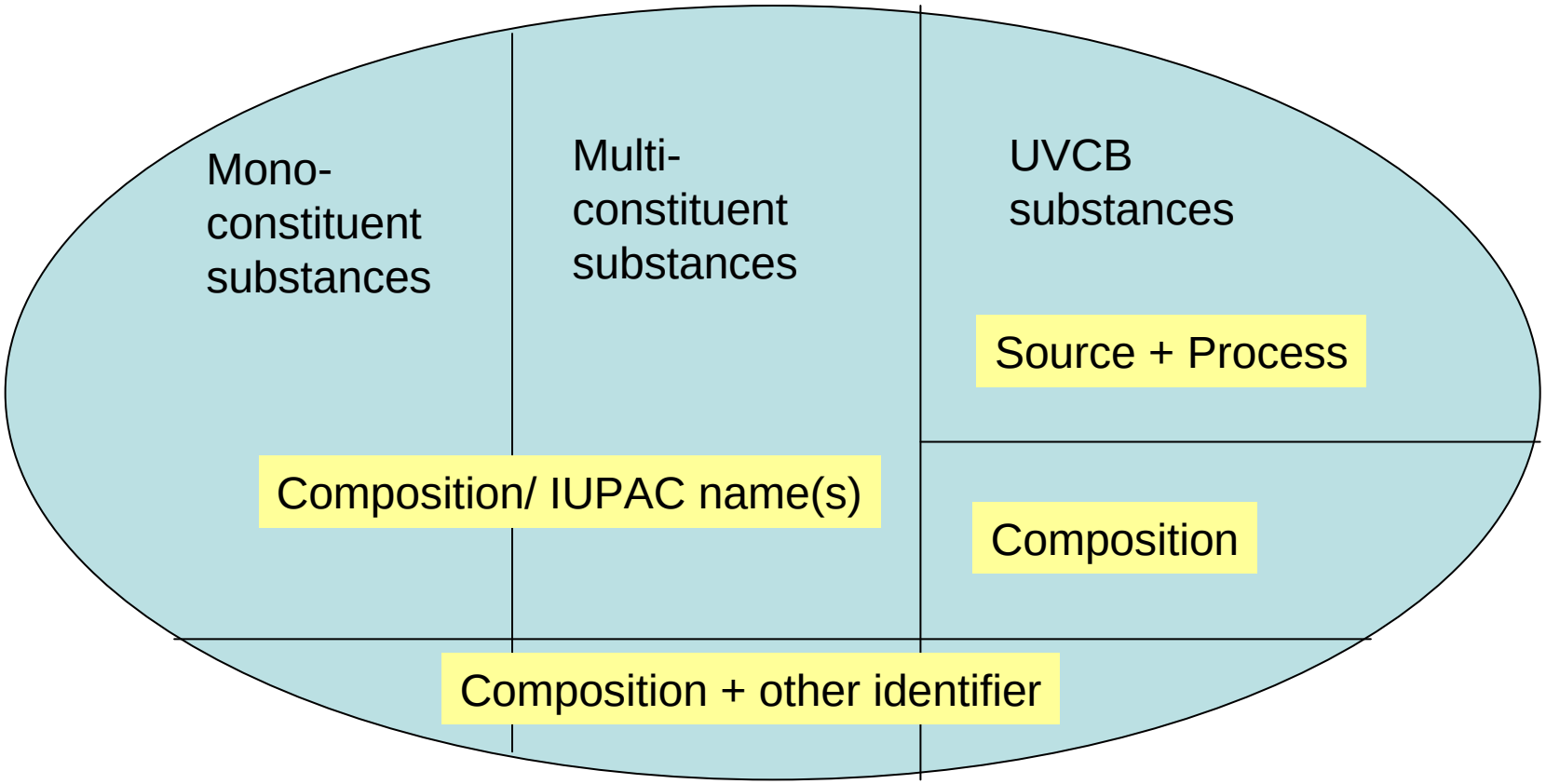
Introduction



Introduction



Introduction



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Required data

1. Substance identifiers
2. Composition
3. Qualitative analytical methods and results (identification)
4. Quantitative analytical methods and results (composition)

Required data

1. Substance identifiers
2. Composition
3. Qualitative analytical methods and results (identification)
4. Quantitative analytical methods and results (composition)

Required data

1. Substance identifiers
   - Name derived according to guidance on substance identity (often **IUPAC name**)
   - Numerical identifiers if available (**EC** number, **CAS** number, C.I. number, …)
   - Structure if appropriate (human readable structural formula & SMILES code)
   - If appropriate: molecular formula (Hill format), molecular weight range,

Required data

1. Substance identifiers
2. Composition
3. Qualitative analytical methods and results (identification)
4. Quantitative analytical methods and results (composition)

Required data

2. Composition

- Purity
- Concentration and identification of each constituent > 1%
  - The composition has to give the ratio of all isomers present
  - Solvents are not considered part of the substance
  - Additives in the sense of REACH need to have stabilising function

Required data

1. Substance identifiers
2. Composition
3. Qualitative analytical methods and results (identification)
4. Quantitative analytical methods and results (composition)

Required data

3. Qualitative analytical methods and results (identification)
   - "shall be sufficient to enable each substance to be identified"
     - UV/Vis, IR, ^{1}H NMR
       - If analysis technically impossible: justification needed
     - If necessary: 13C NMR, MS, XRD, …
     - All (ionic) parts of the substance need to be determined

Required data

1. Substance identifiers
2. Composition
3. Qualitative analytical methods and results (identification)
4. Quantitative analytical methods and results (composition)

Required data

4. Quantitative analytical methods and results (composition)
   - Quantitation of all constituents > 1%
     - For ionic constituents each ion should be quantified
   - Typical concentration and concentration ranges
   - GC or HPLC
     - If necessary other methods: AAS, titration, …
   - Provide a table of results with assignment to constituents mentioned in the composition
   - Explain method of quantitative evaluation (areas, standards, calibration curve)
   - Number and concentration range of unknown impurities have to be given
     - Justification needed if significant amount of constituents unknown

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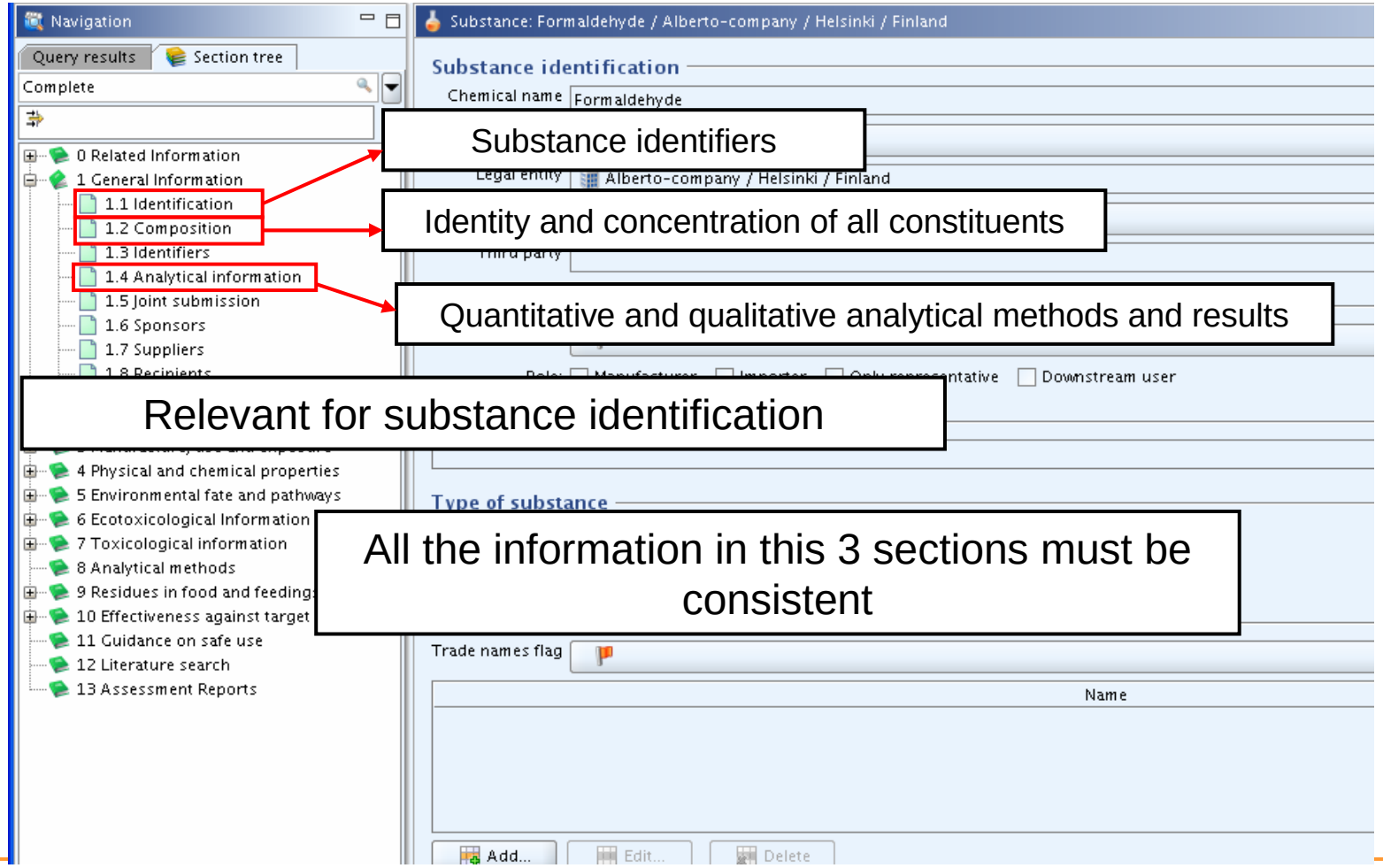
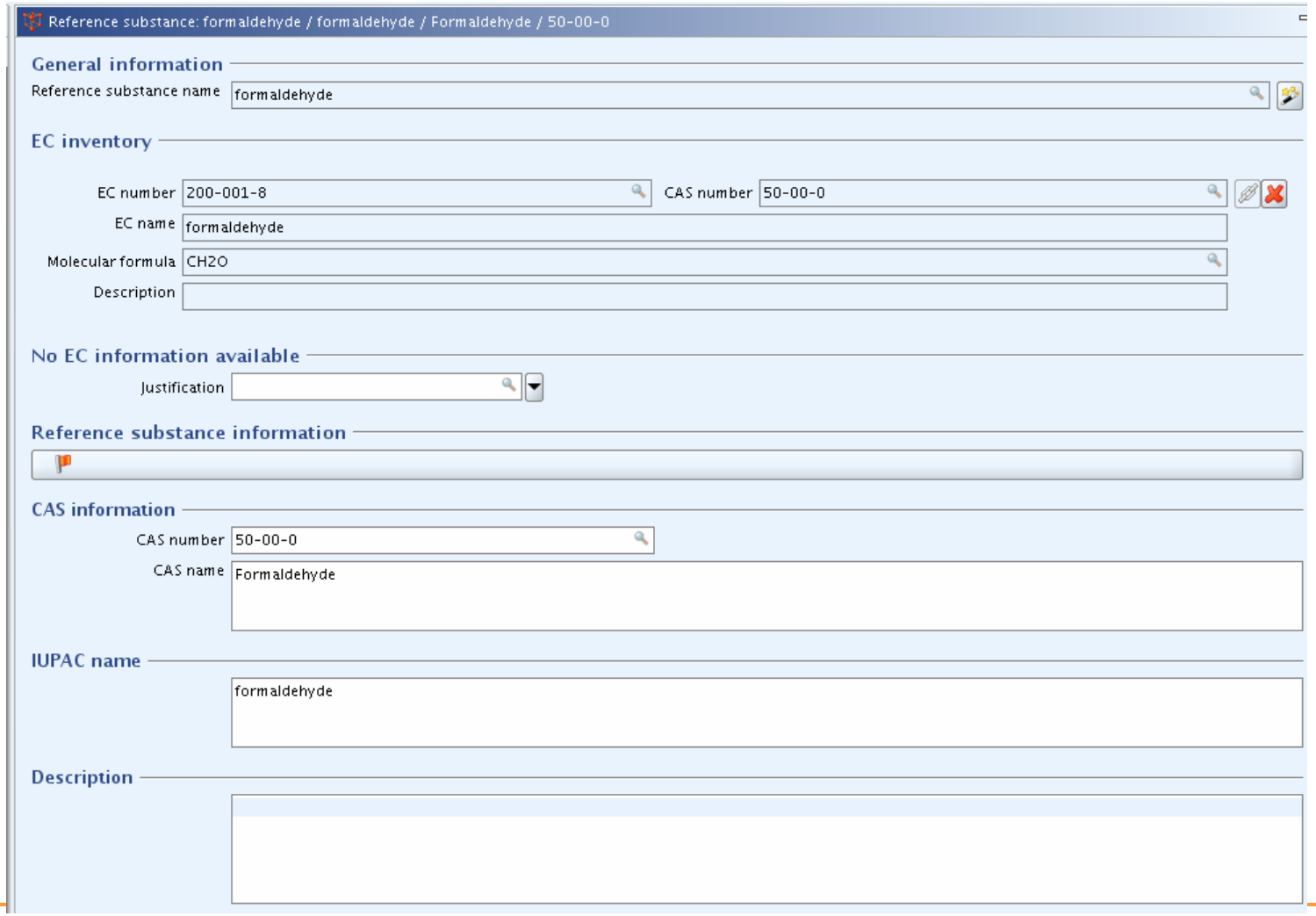
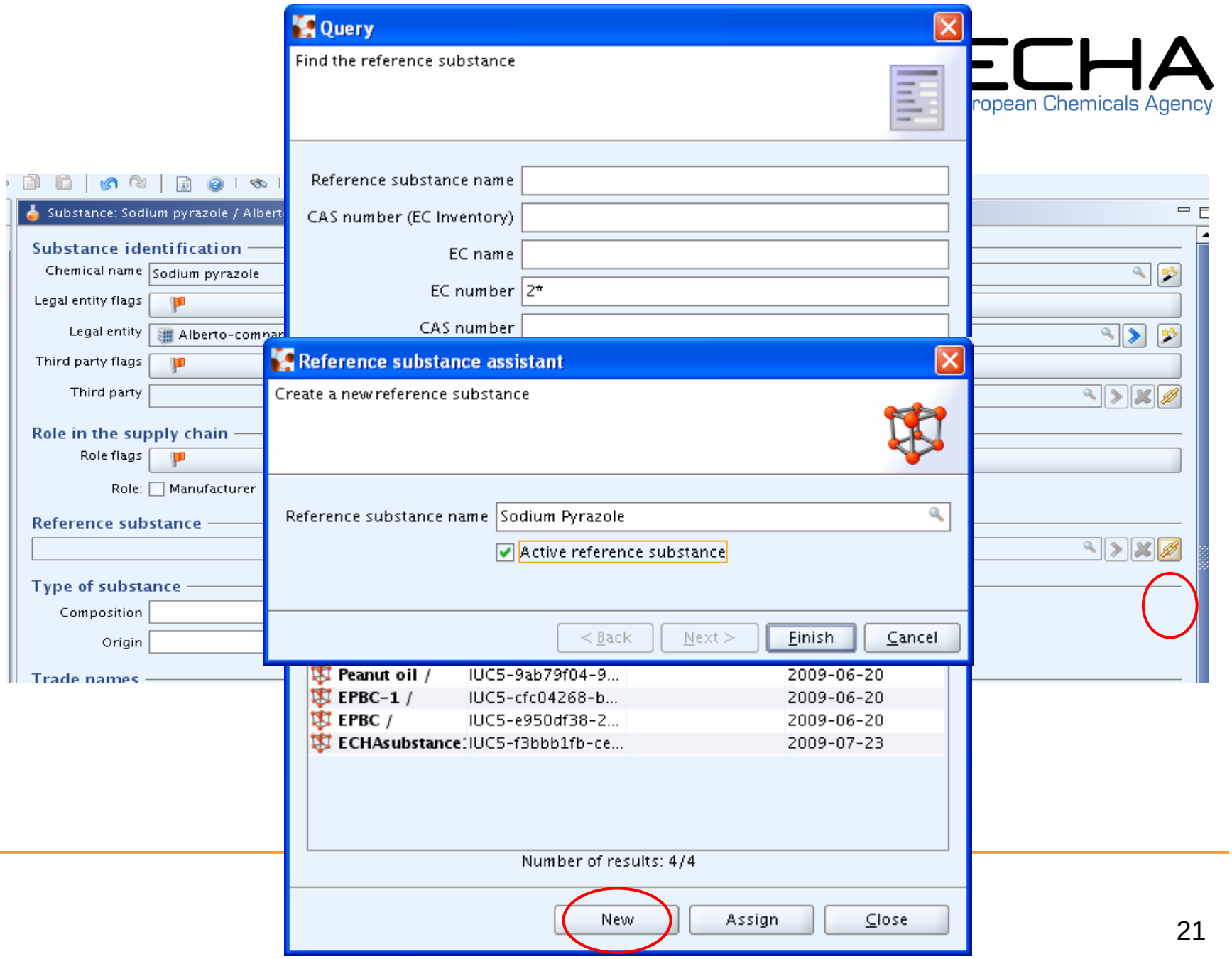
- Substance identity of UVCB substances
- Dossier preparation (UVCB substances)


Navigation
Query results
Section tree
Complete
0 Related Information
1 General Information
1.1 Identification
1.2 Composition
1.3 Identifiers
1.4 Analytical information
1.5 Joint submission
1.6 Sponsors
1.7 Suppliers
4 Physical and chemical properties
5 Environmental fate and pathways
6 Ecotoxicological Information
7 Toxicological information
8 Analytical methods
9 Residues in food and feeding
10 Effectiveness against target
11 Guidance on safe use
12 Literature search
13 Assessment Reports
Substance: Formaldehyde / Alberto-company / Helsinki / Finland
Substance identification
Chemical name
Formaldehyde
Alberto-company / Helsinki / Finland
Downstream user
Type of substance
Trade names flag
Name
Add...
Edit...
Delete
Substance identifiers
Identity and concentration of all constituents
Quantitative and qualitative analytical methods and results
Relevant for substance identification
All the information in this 3 sections must be consistent


Reference substance: formaldehyde / formaldehyde / Formaldehyde / 50-00-0
General information
Reference substance name
formaldehyde
EC inventory
EC number
200-001-8
CAS number
50-00-0
EC name
formaldehyde
Molecular formula
CH2O
Description
No EC information available
Justification
Reference substance information
CAS information
CAS number
50-00-0
CAS name
Formaldehyde
IUPAC name
formaldehyde
Description


Query
Find the reference substance
Reference substance name
CAS number (EC Inventory)
EC name
EC number
2*
CAS number
Reference substance assistant
Create a new reference substance
Reference substance name
Sodium Pyrazole
Active reference substance
< Back
Next >
Finish
Cancel
Substance: Sodium pyrazole / Albert
Substance identification
Chemical name
Sodium pyrazole
Legal entity flags
Legal entity
Third party flags
Third party
Role in the supply chain
Role flags
Role:
Manufacturer
Reference substance
Type of substance
Composition
Origin
Trade names
Peanut oil / IUC5-9ab79f04-9... 2009-06-20
EPBC-1 / IUC5-cfc04268-b... 2009-06-20
EPBC / IUC5-e950df38-2... 2009-06-20
ECHAsubstance: IUC5-f3bbb1fb-ce... 2009-07-23
Number of results: 4/4
New
Assign
Close

Before you start

- Make sure that you have all the relevant identifiers for your substance and all its constituents (name according to guidance, EC#, CAS#, etc)
- If you are using IUCLID:
  - Create beforehand all the reference substances you are going to need
  - Fill them with all the necessary information (identifiers, structural formula, molecular weight, etc)
- Make sure that you have all the necessary electronic files (documents and/or image files) with the relevant analytical information.

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- Substance identity of UVCB substances
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Mono-constituent substance

- Composition known
- Concentration of main constituent ≥ 80%
- Main constituent completely identified by IUPAC name

Mono-constituent substance

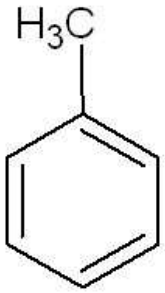
- Borderline cases
  - Typical concentration ≥ 80% but lower concentration limit < 80%

    → possibly mono-constituent, justification needed

    → possibly multi-constituent, justification needed
  - Considerable amounts of second constituent that is “important for the desired technical effect of the substance”

    → possibly multi-constituent substance (justification needed)

Mono-constituent substance

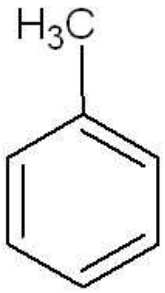


100%

toluene

0%

Mono-constituent substance

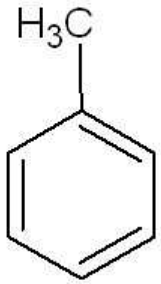


95 – 100%

toluene

0 - 5%

Mono-constituent substance

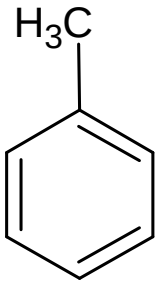


75 – 85 %

toluene

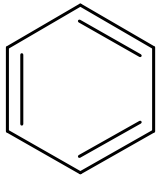
15 – 25 %

Mono-constituent substance



75 – 85 %

toluene



15 – 25 %

reaction mass of toluene and benzene

?

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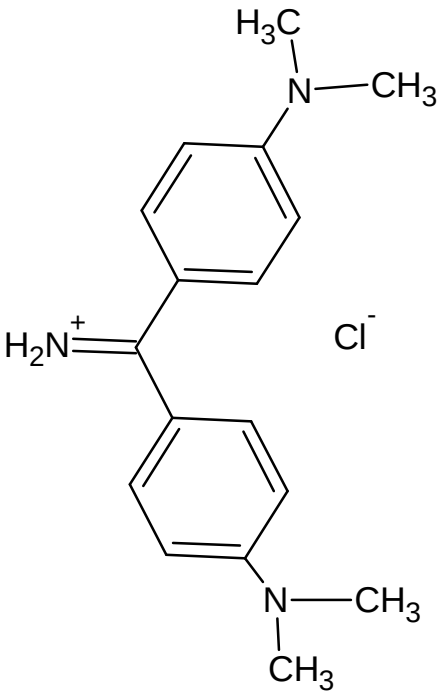
Multi-constituent substance

- Composition known and defined
- More than one constituent ≥ 10% and < 80%
- Each main constituents completely identified by IUPAC name
  - "Reaction mass of [IUPAC name] and [IUPAC name] and …"

Multi-constituent substance

- Borderline cases
  - Typical concentration < 80% but higher concentration limit ≥ 80%
    - → possibly multi-constituent, justification needed
    - → possibly mono-constituent, justification needed
  - Constituent ≥ 10% but clearly “impurity”
    - → possibly not included in name (justification needed)

Multi-constituent substance?



75 %

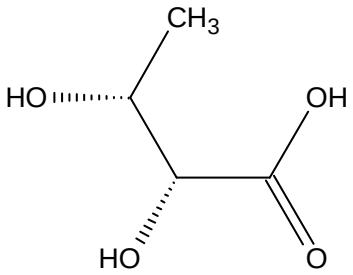
bis[4-(dimethylamino)phenyl] methaniminium chloride (C.I. Basic Yellow 2)

NaCl 25 %

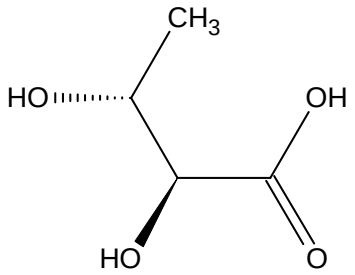
Multi-constituent substance

- Isomers
  - racemic mixture of enantiomers
  - two enantiomers
  - multiple structural isomers
- Unspecific IUPAC name acceptable
  - if all isomers present
- Specification of all isomers in composition
  - except racemic mixture w/o optical activity
- “Reaction mass of …”
  - if not all isomers present ≥ 10%

Multi-constituent substance

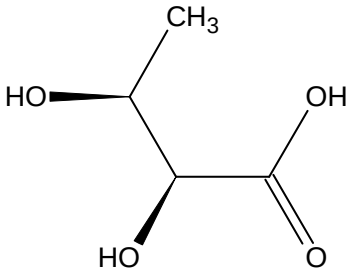


25%

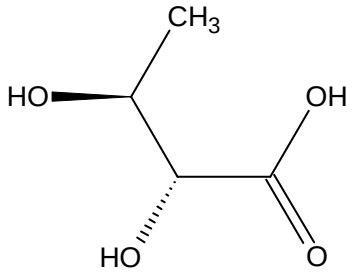


25%

2,3-dihydroxybutanoic acid

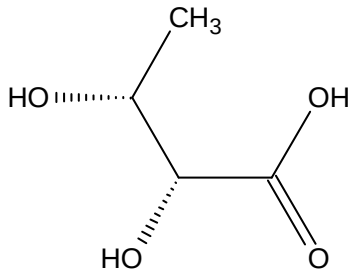


25%



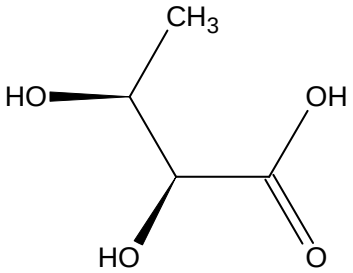
25%

Multi-constituent substance



25%

Reaction mass of
(2R,3R)-2,3-dihydroxybutanoic acid and
(2S,3S)-2,3-dihydroxybutanoic acid



75%

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Additional identifiers

- Composition known
- Otherwise mono- or multi-constituent as before
- BUT: IUPAC name not enough to identify the substance
  - E.g. inorganic, crystalline material

- If possible structure as additional identifier
  - If not: hardness, swelling capacity, density, surface area,…

Additional identifiers

- Examples:
  - Rutile (TiO2)
    (**EC# :** 215-282-2, **CAS# :** 1317-80-2)
  - Anatase (TiO2)
    (**EC# :** 215-280-1, **CAS# :** 1317-70-0)
  - Spinel (Mg(AlO2)2)
    (**EC# :** 215-105-9, **CAS# :** 1302-67-6)

Additional identifiers

- Note:
  - Data requirements remain the same:
    "shall be sufficient to enable each substance to be identified"
  - Structural information is required even if the IUPAC name is sufficient for identification
  - Applies also to UVCB substances:
    - **EC# :** 310-193-6
    - **CAS# :** 1345-16-0
    - **Substance Name:** Cobalt aluminate blue spinel
    - **Description:** An inorganic pigment that is the reaction product of high temperature calcination in which cobalt (II) oxide and aluminum oxide in varying amounts are homogeneously and ionically interdiffused to form a crystalline matrix of spinel. Its composition may include any one or a combination of the modifiers MgO, ZnO, Li2O, or TiO2.

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- Substance identity of UVCB substances
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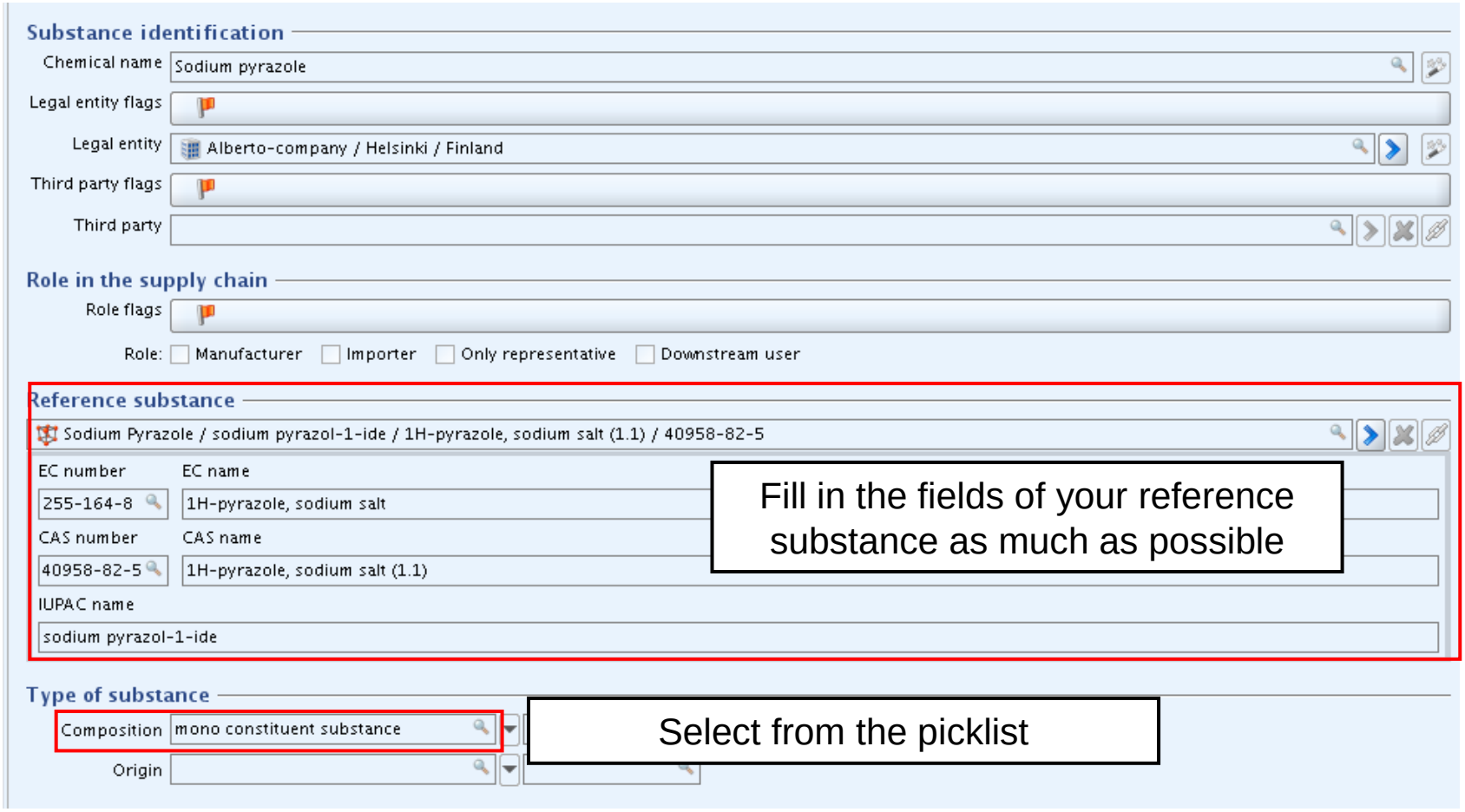
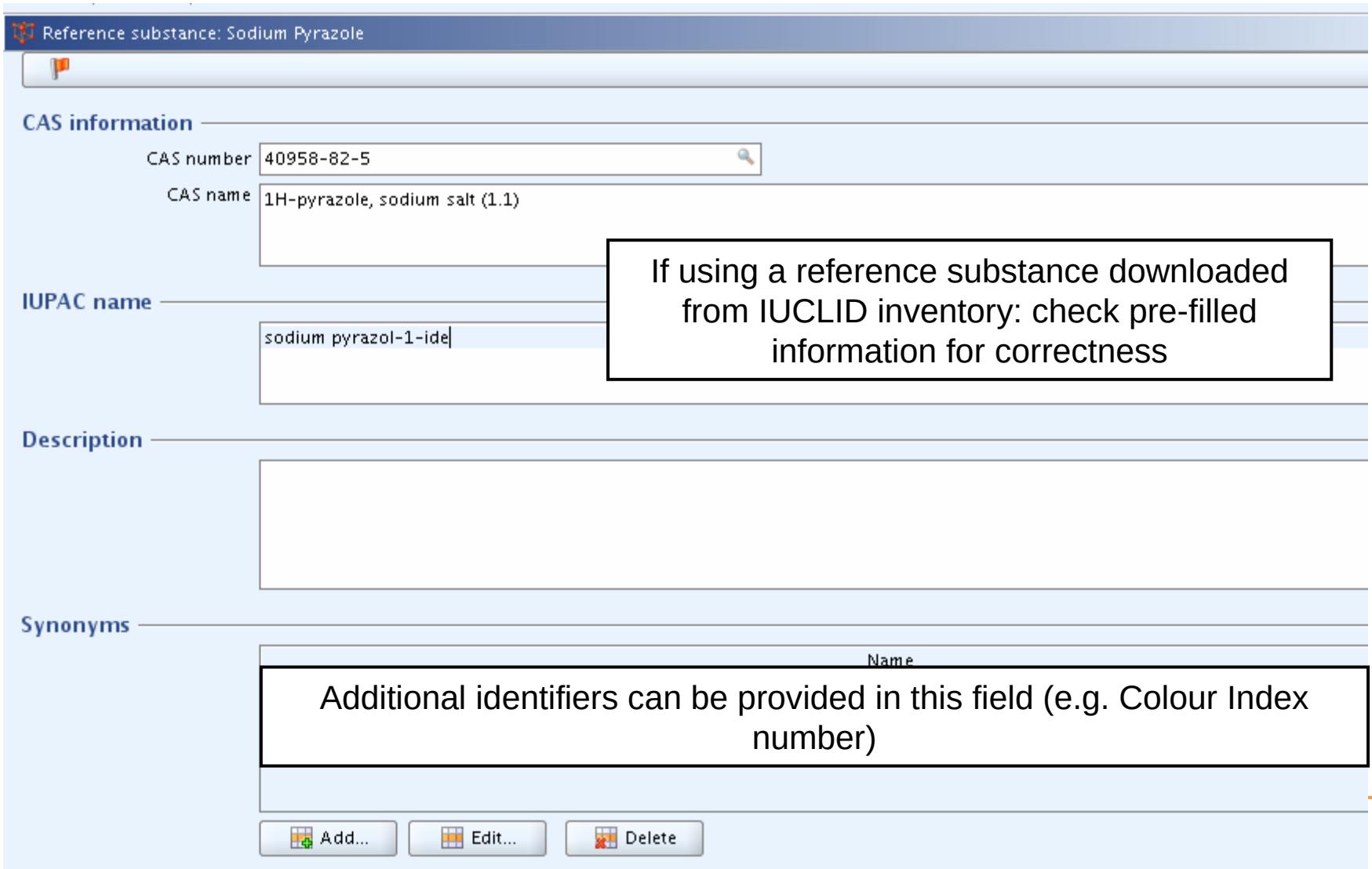
IUCLID 5 Dossiers

Dossier preparation for mono-constituent substances


Substance identification
Chemical name
Sodium pyrazole
Legal entity flags
Legal entity
Alberto-company / Helsinki / Finland
Third party flags
Third party
Role in the supply chain
Role flags
Role:
Manufacturer
Importer
Only representative
Downstream user
Reference substance
Sodium Pyrazole / sodium pyrazol-1-ide / 1H-pyrazole, sodium salt (1.1) / 40958-82-5
EC number
EC name
255-164-8
1H-pyrazole, sodium salt
CAS number
CAS name
40958-82-5
1H-pyrazole, sodium salt (1.1)
IUPAC name
sodium pyrazol-1-ide
Fill in the fields of your reference substance as much as possible
Type of substance
Composition
mono constituent substance
Origin
Select from the picklist

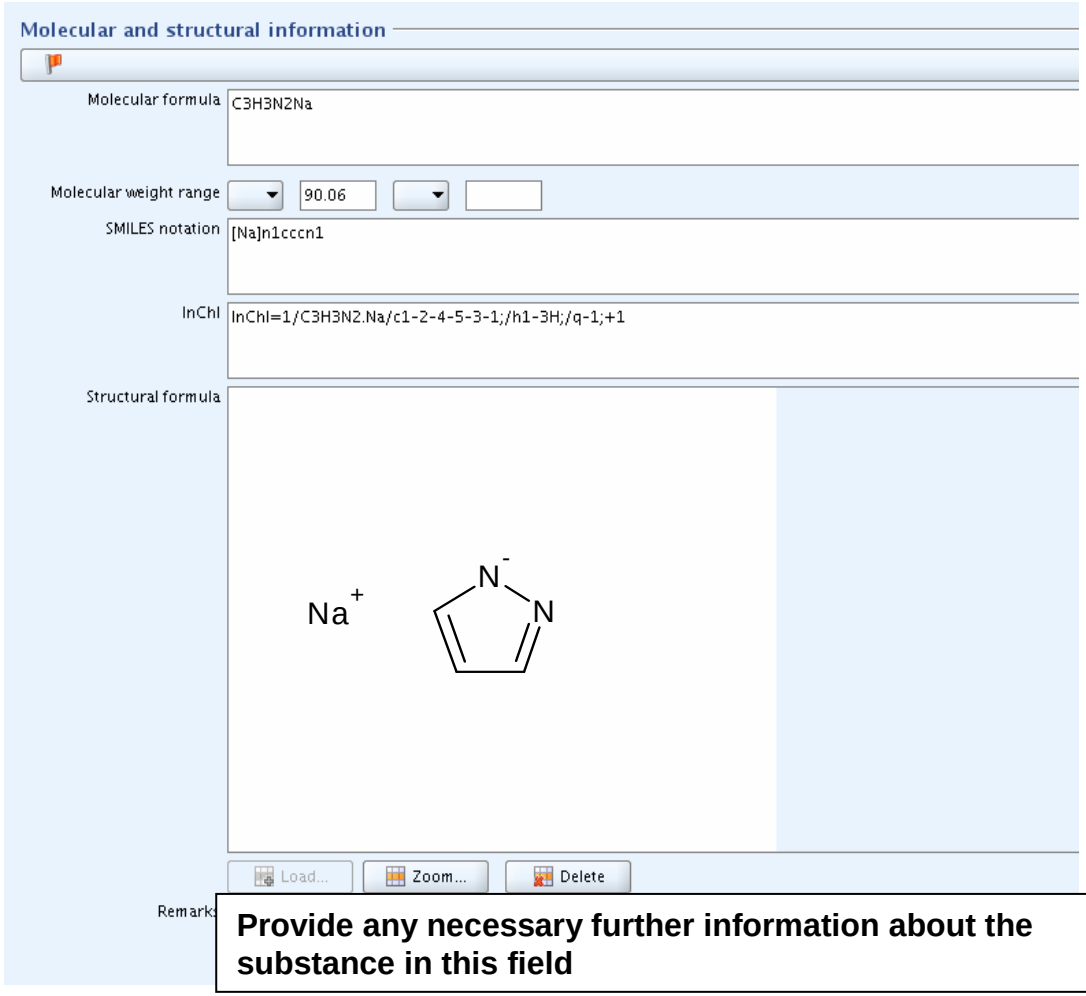
1.1 Identity (reference substance)



If using a reference substance downloaded from IUCLID inventory: check pre-filled information for correctness

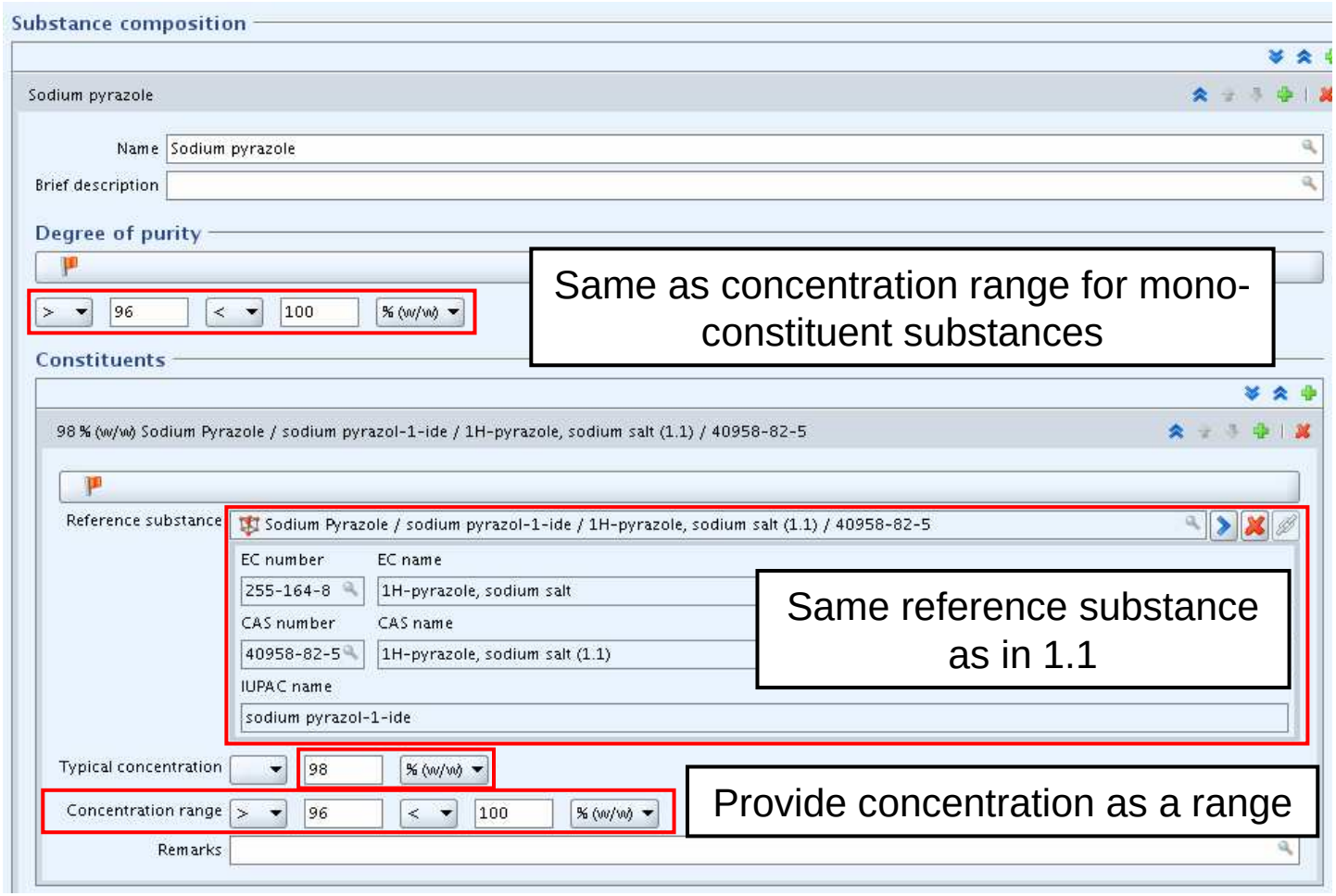
Additional identifiers can be provided in this field (e.g. Colour Index number)

1.1 Identity (reference substance)

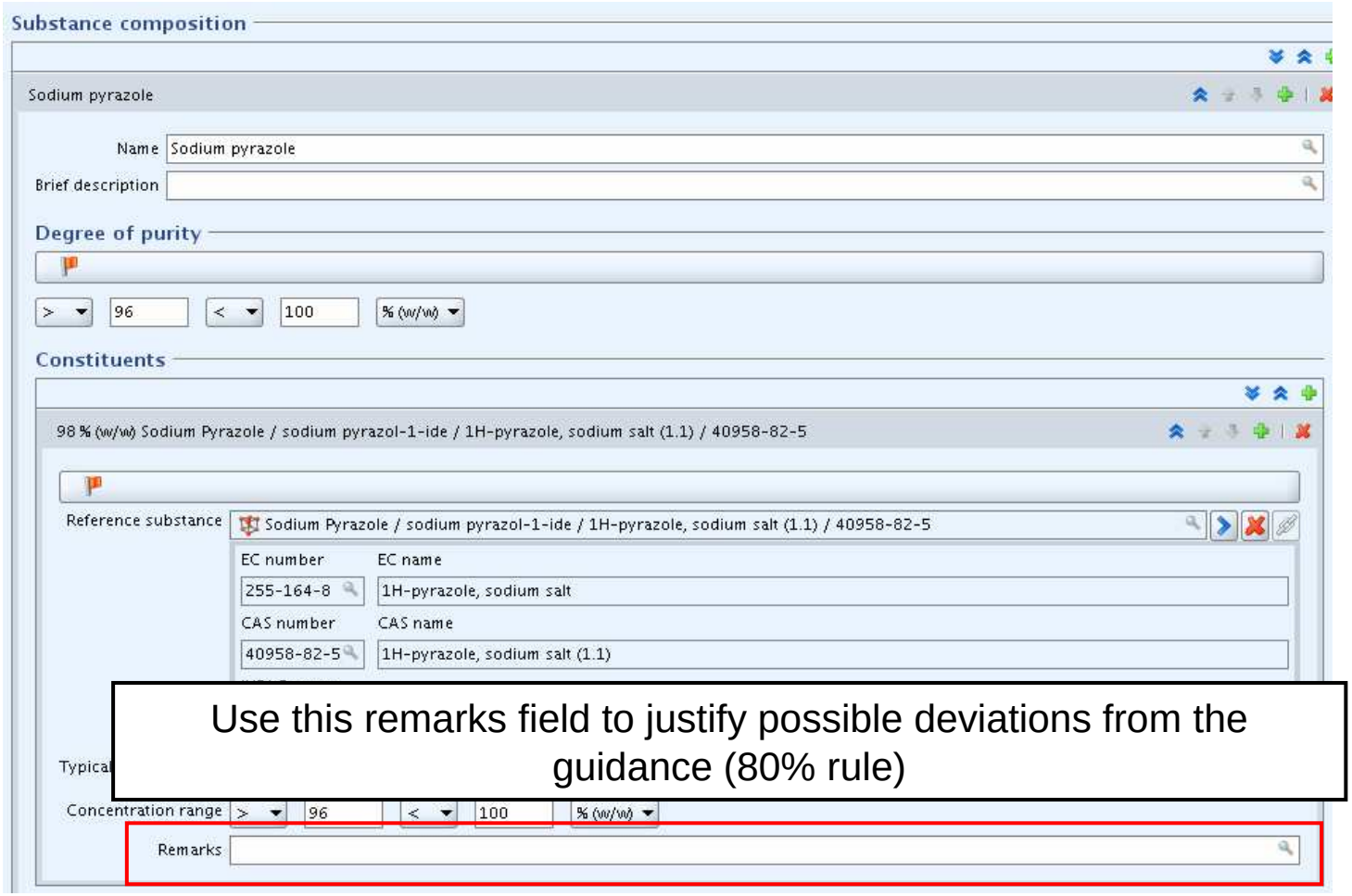


Provide any necessary further information about the substance in this field

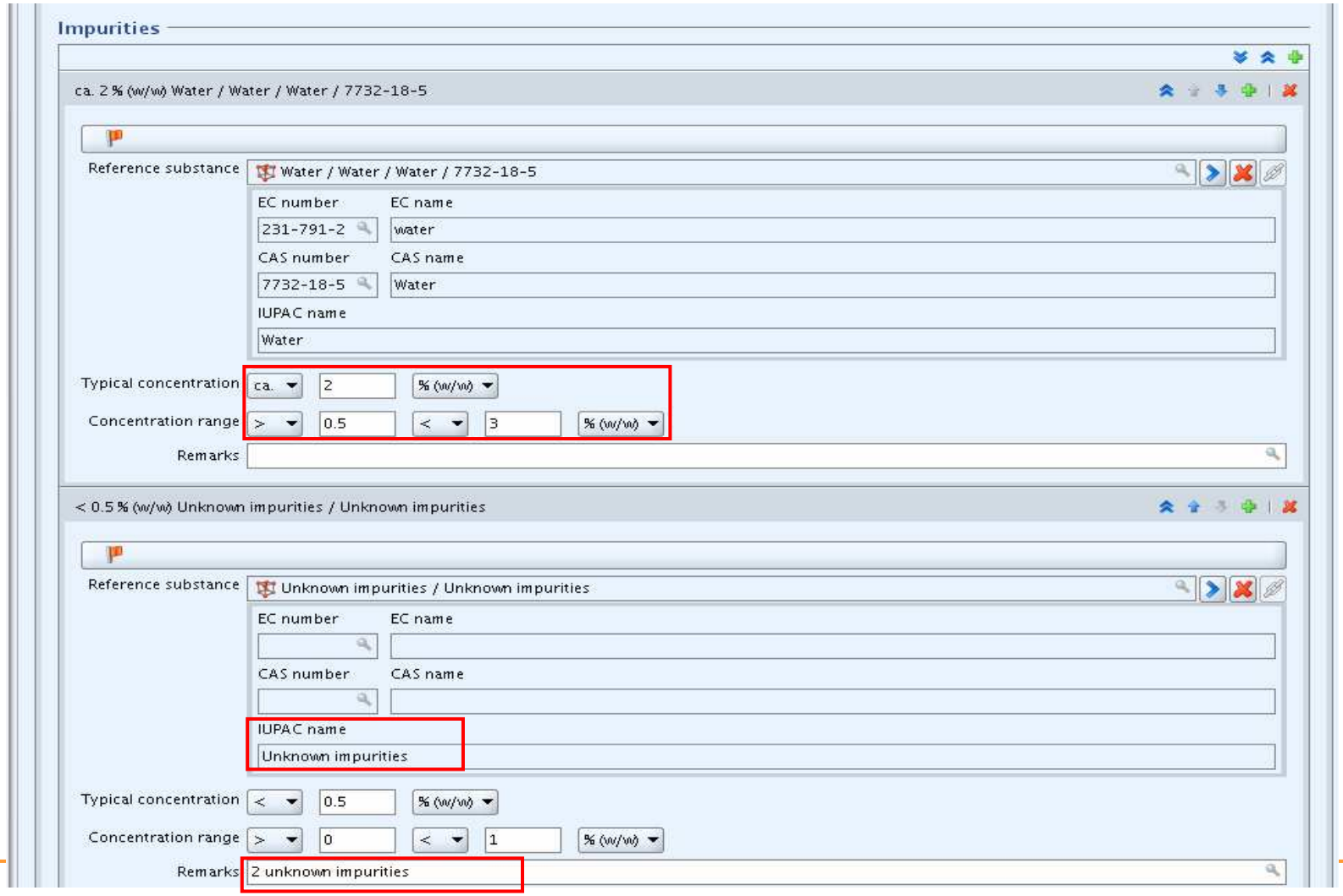
1.2 Composition (I)



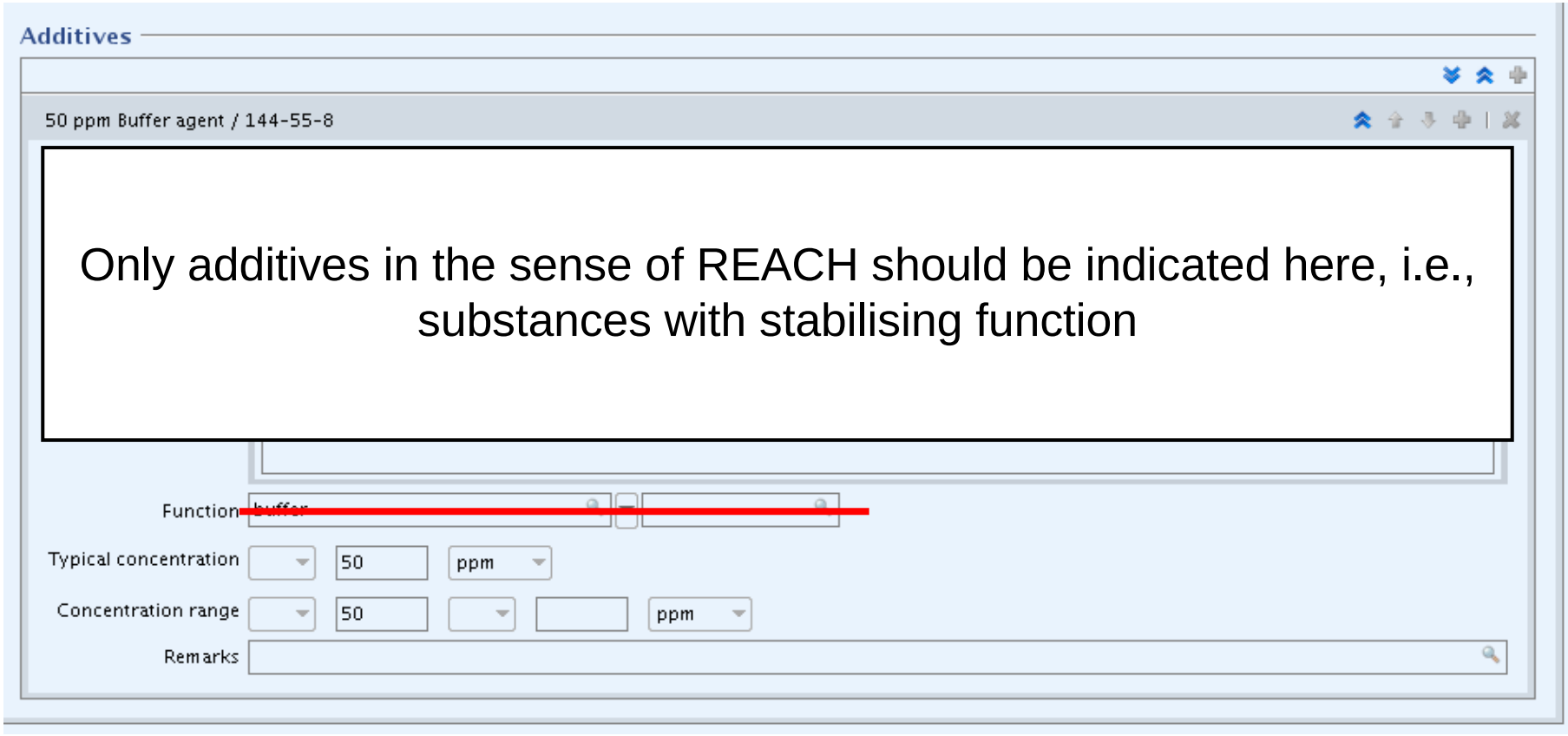
1.2 Composition (II)



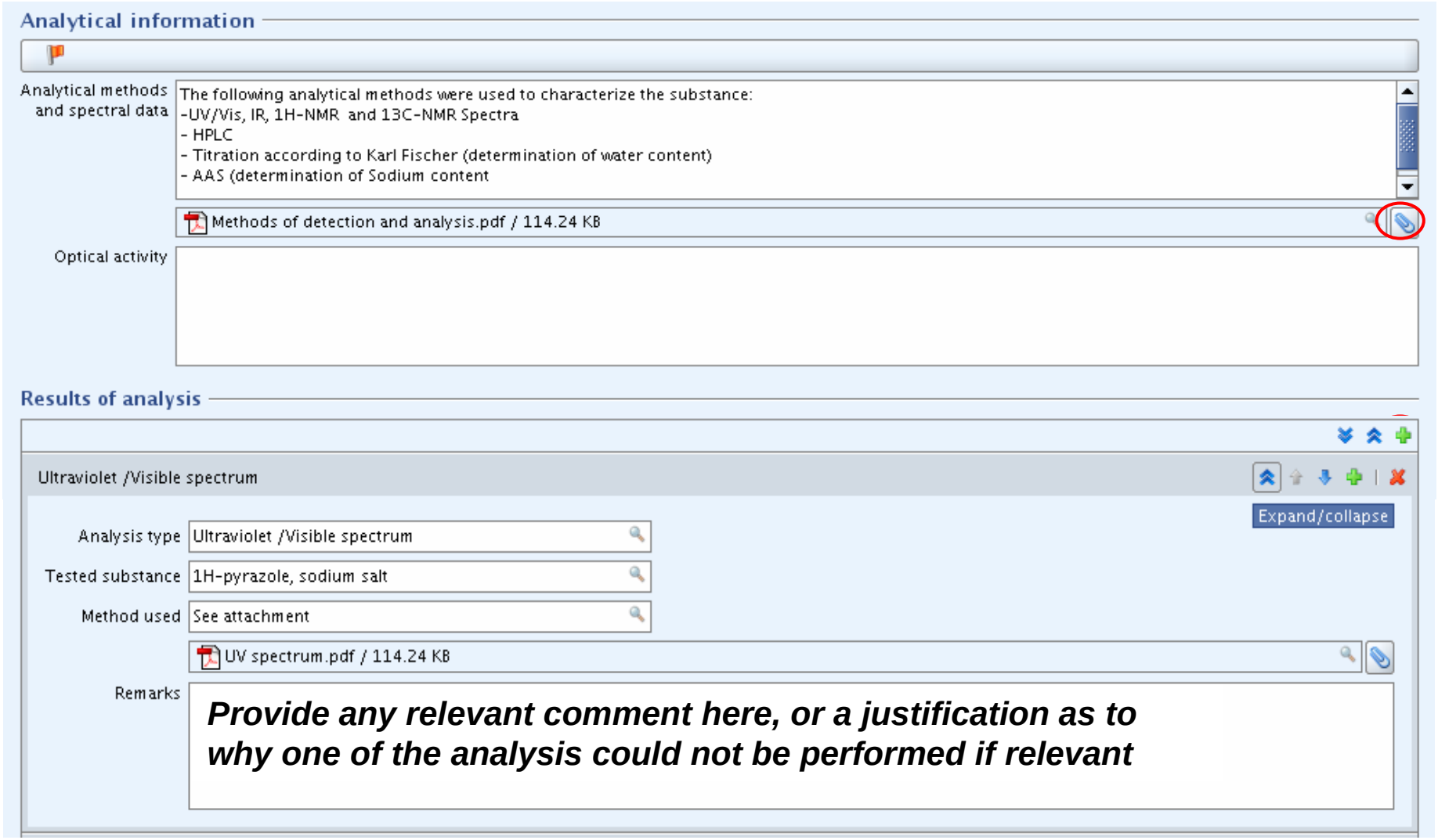
1.2 Composition (III)



1.2 Composition



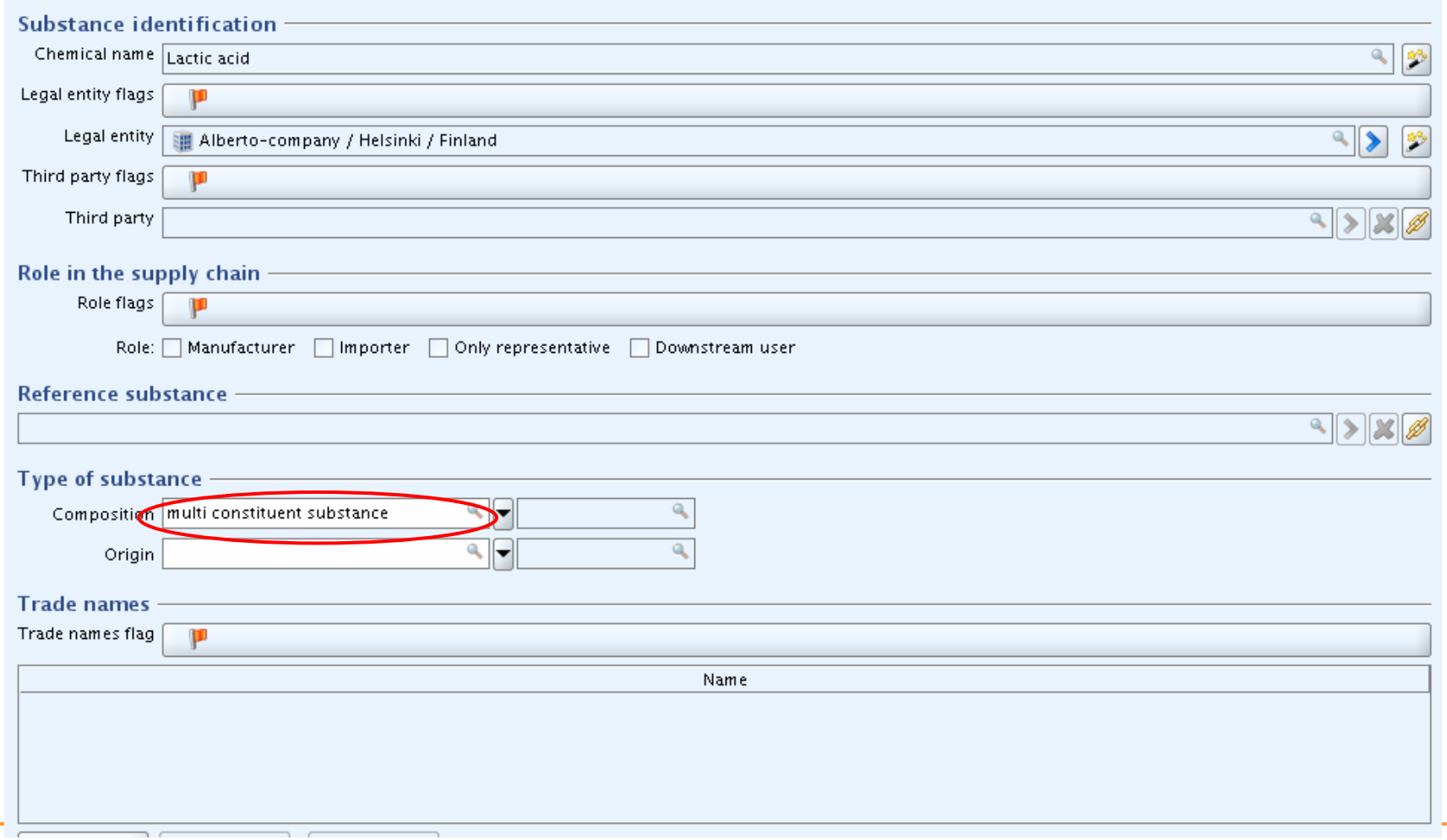
1.4 Analytical information



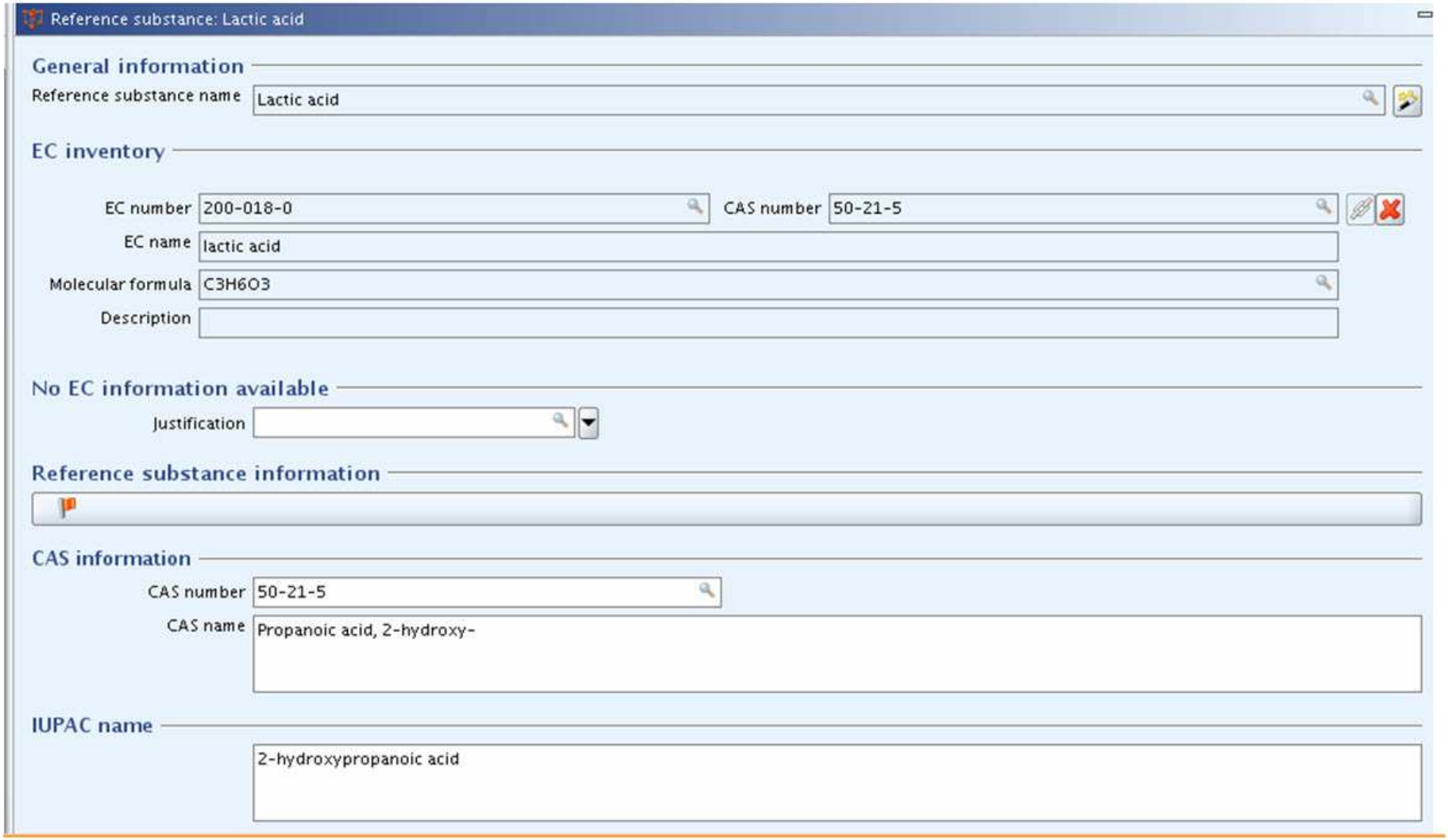
IUCLID 5 Dossiers

Dossier preparation for multi-constituent substances

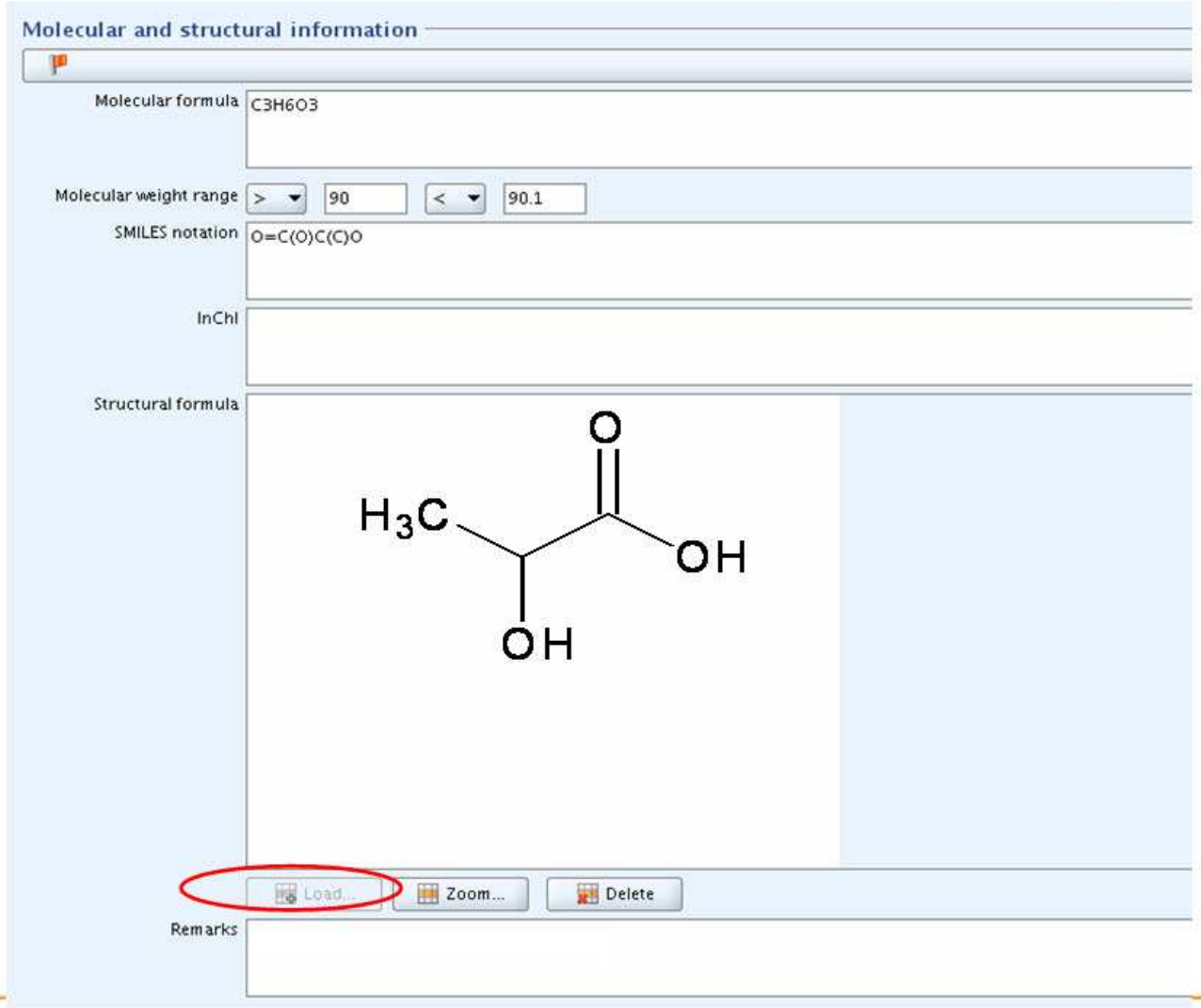
1.1 Identity


Substance identification
Chemical name
Lactic acid
Legal entity flags
Legal entity
Alberto-company / Helsinki / Finland
Third party flags
Third party
Role in the supply chain
Role flags
Role:
Manufacturer
Importer
Only representative
Downstream user
Reference substance
Type of substance
Composition
multi constituent substance
Origin
Trade names
Trade names flag
Name

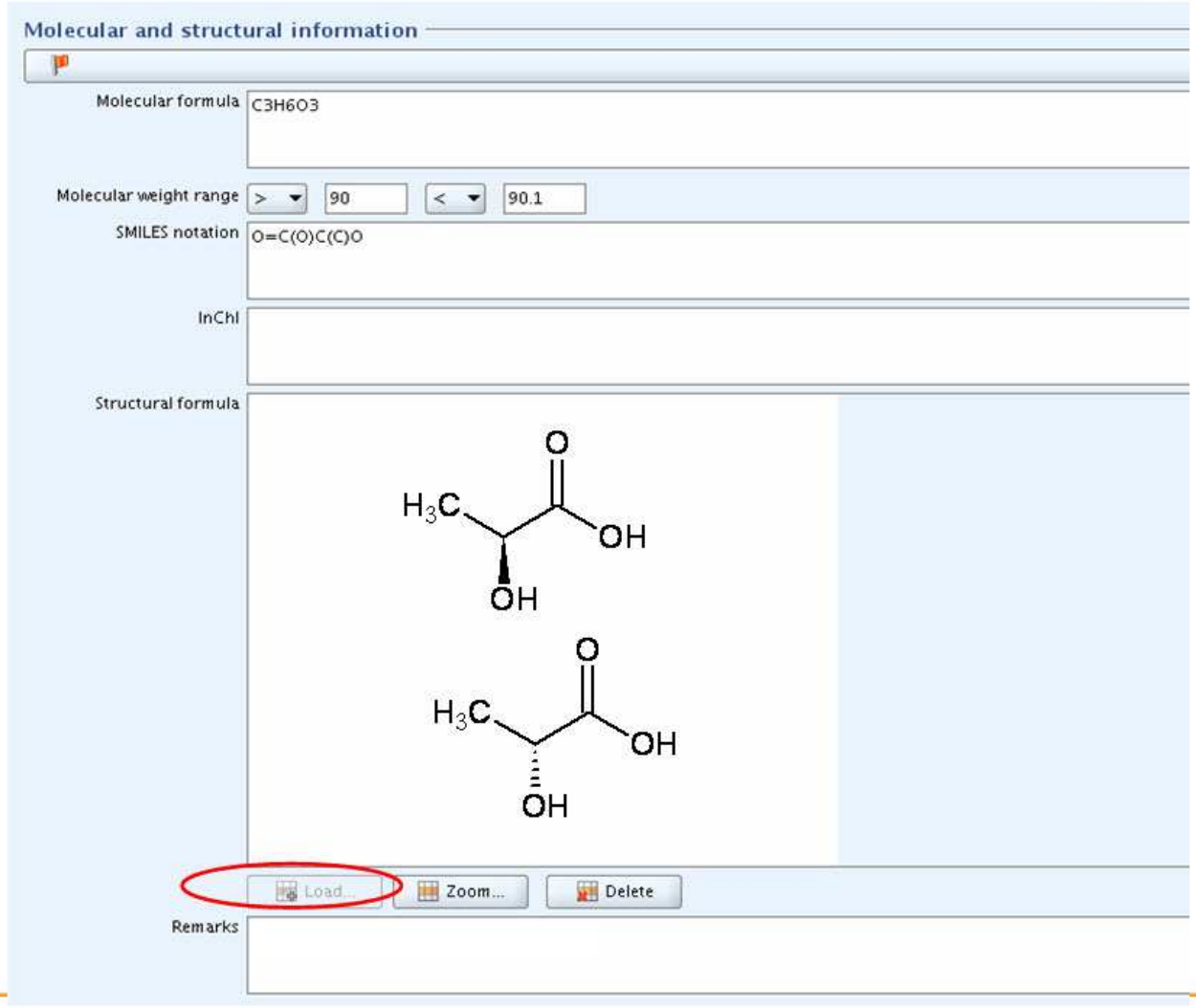
1.1 Identity (reference substance)



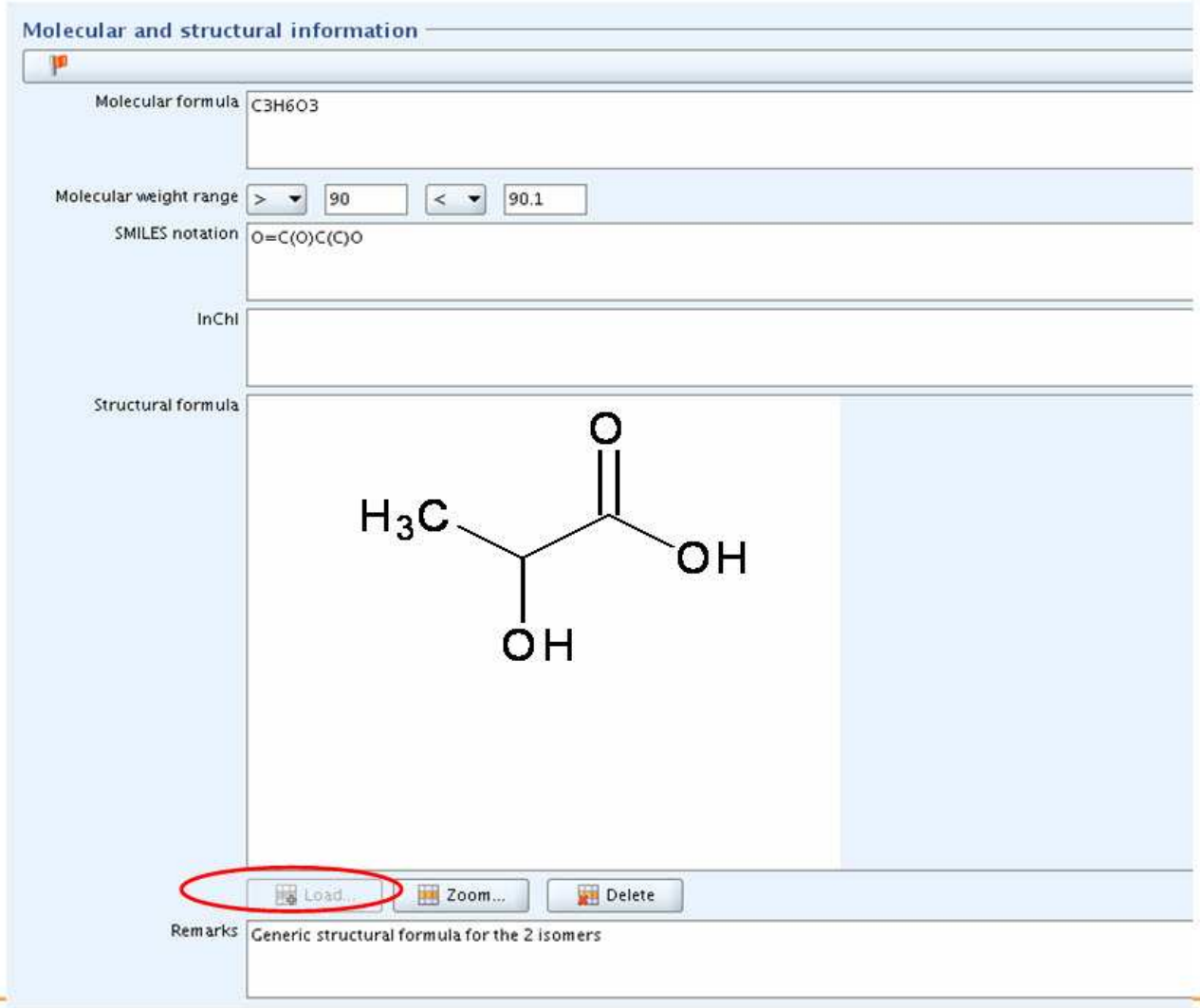
1.1 Identity (reference substance)



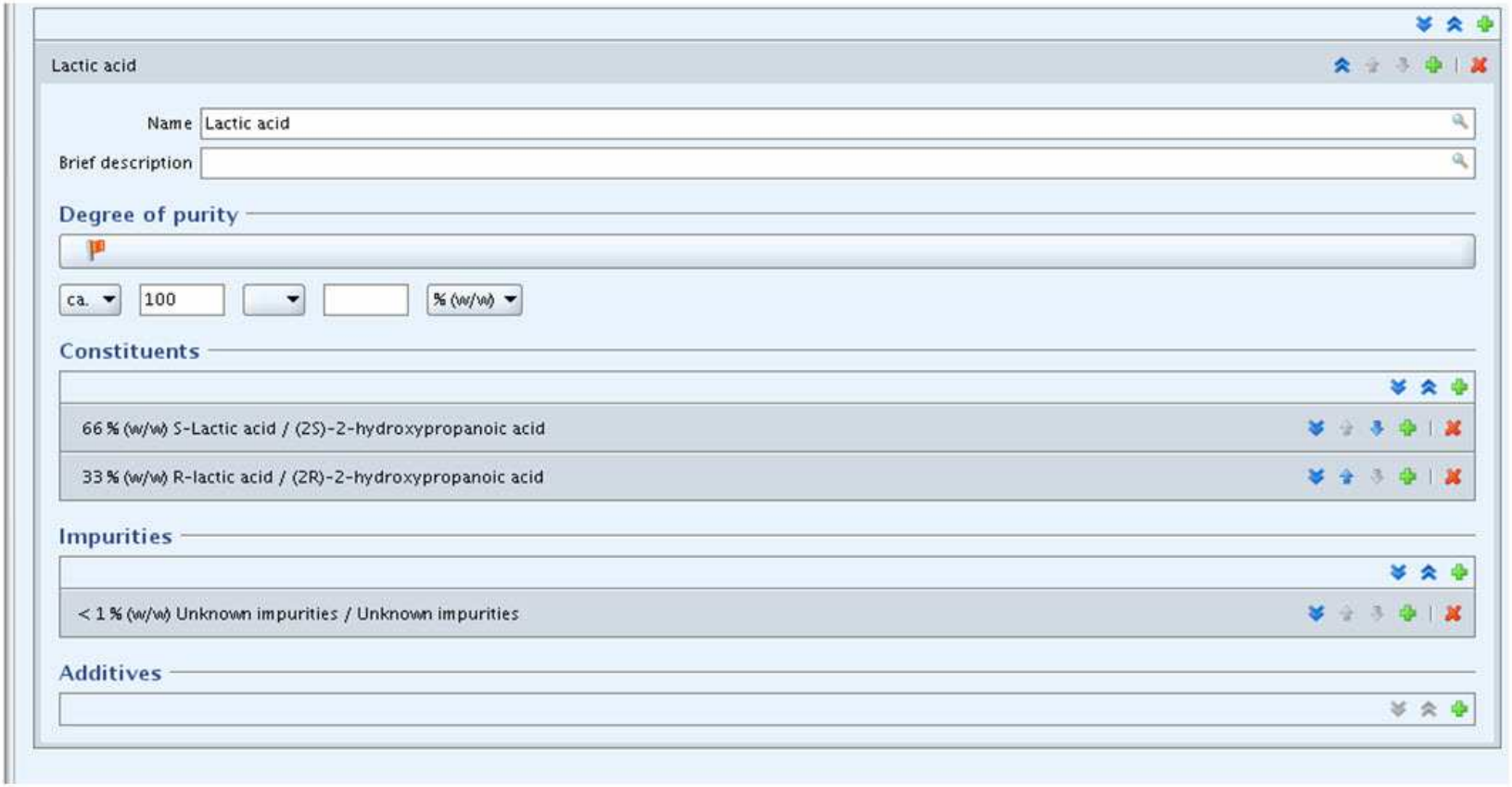
1.1 Identity (reference substance)



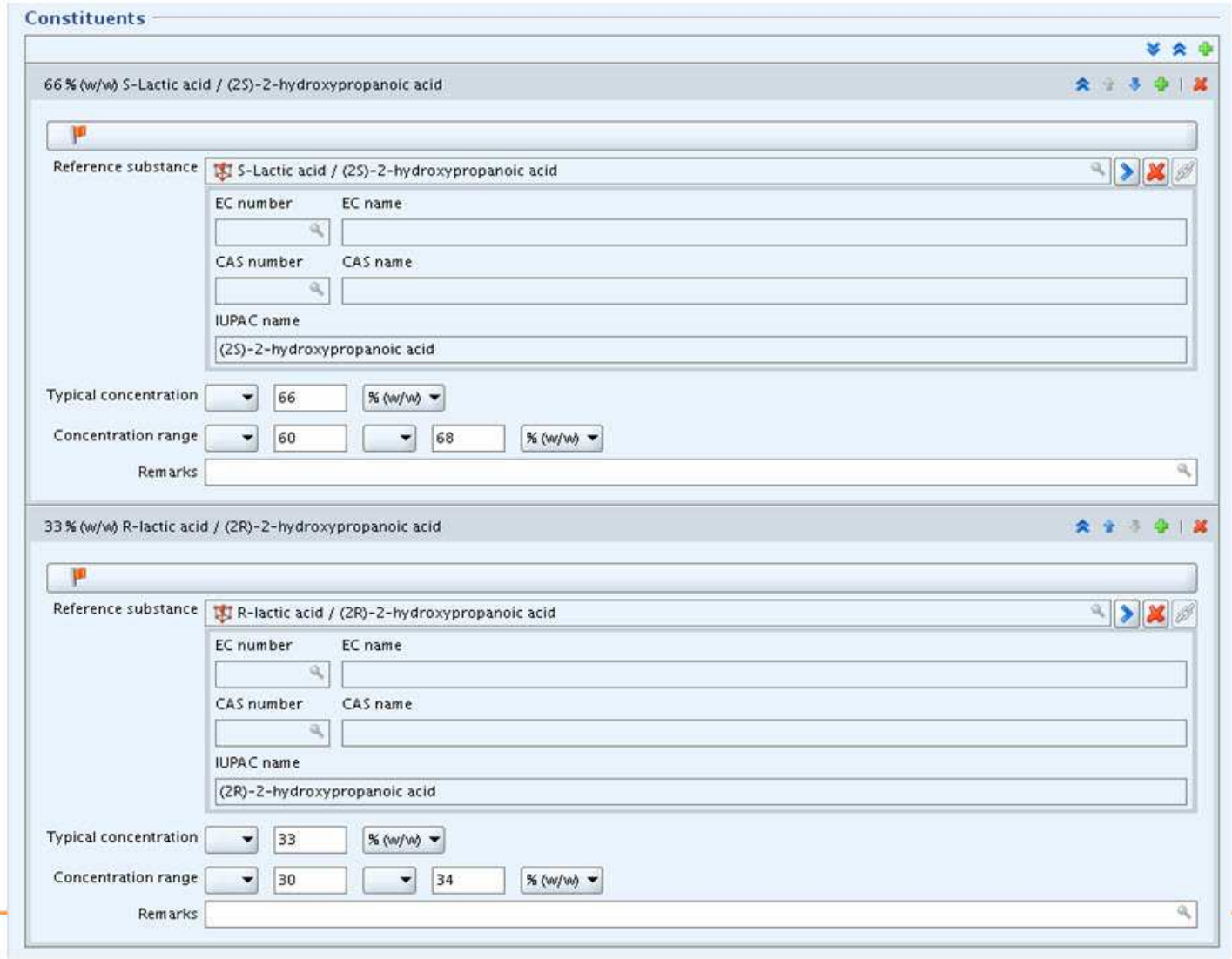
1.1 Identity (reference substance)



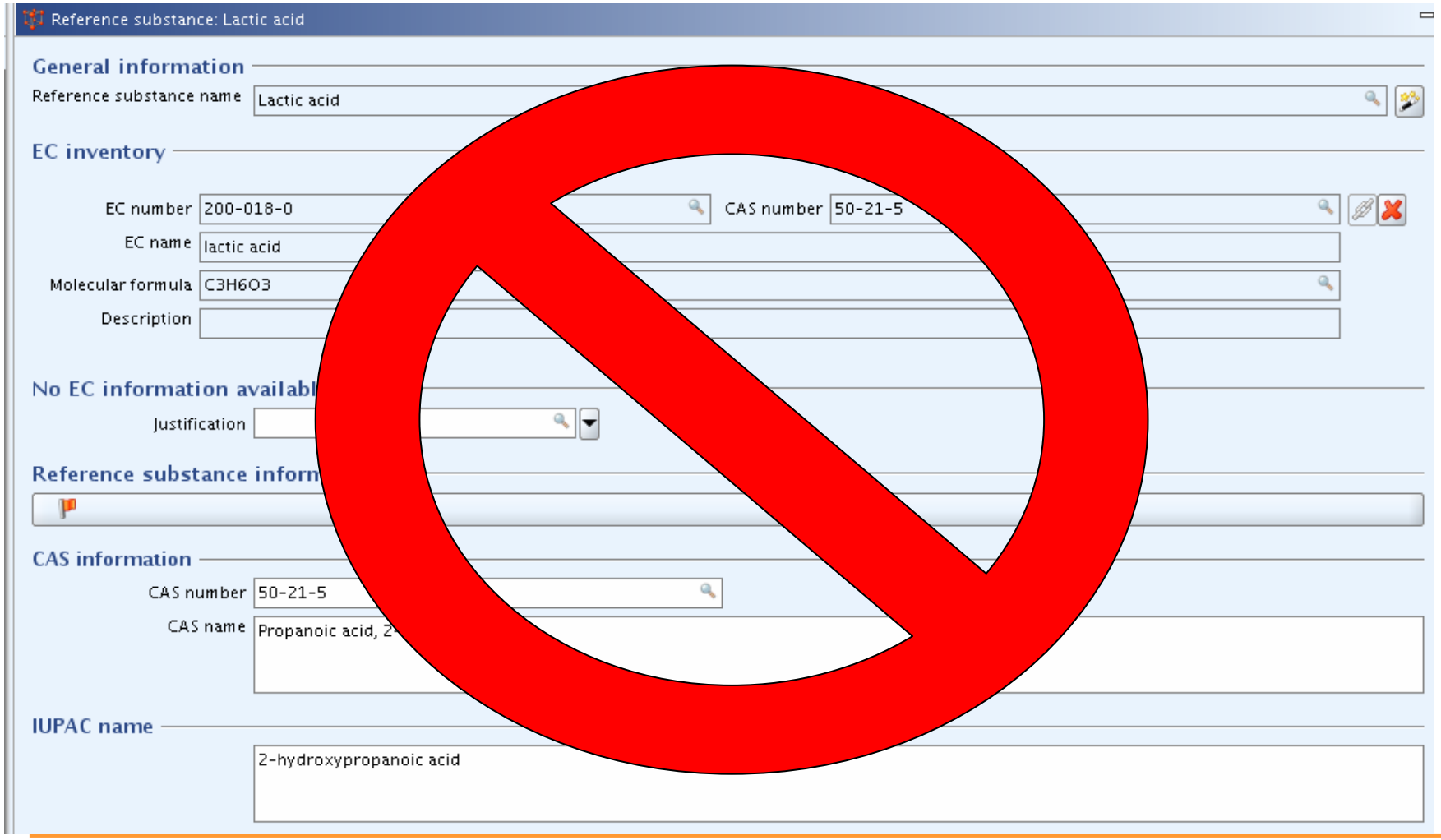
1.2 Composition



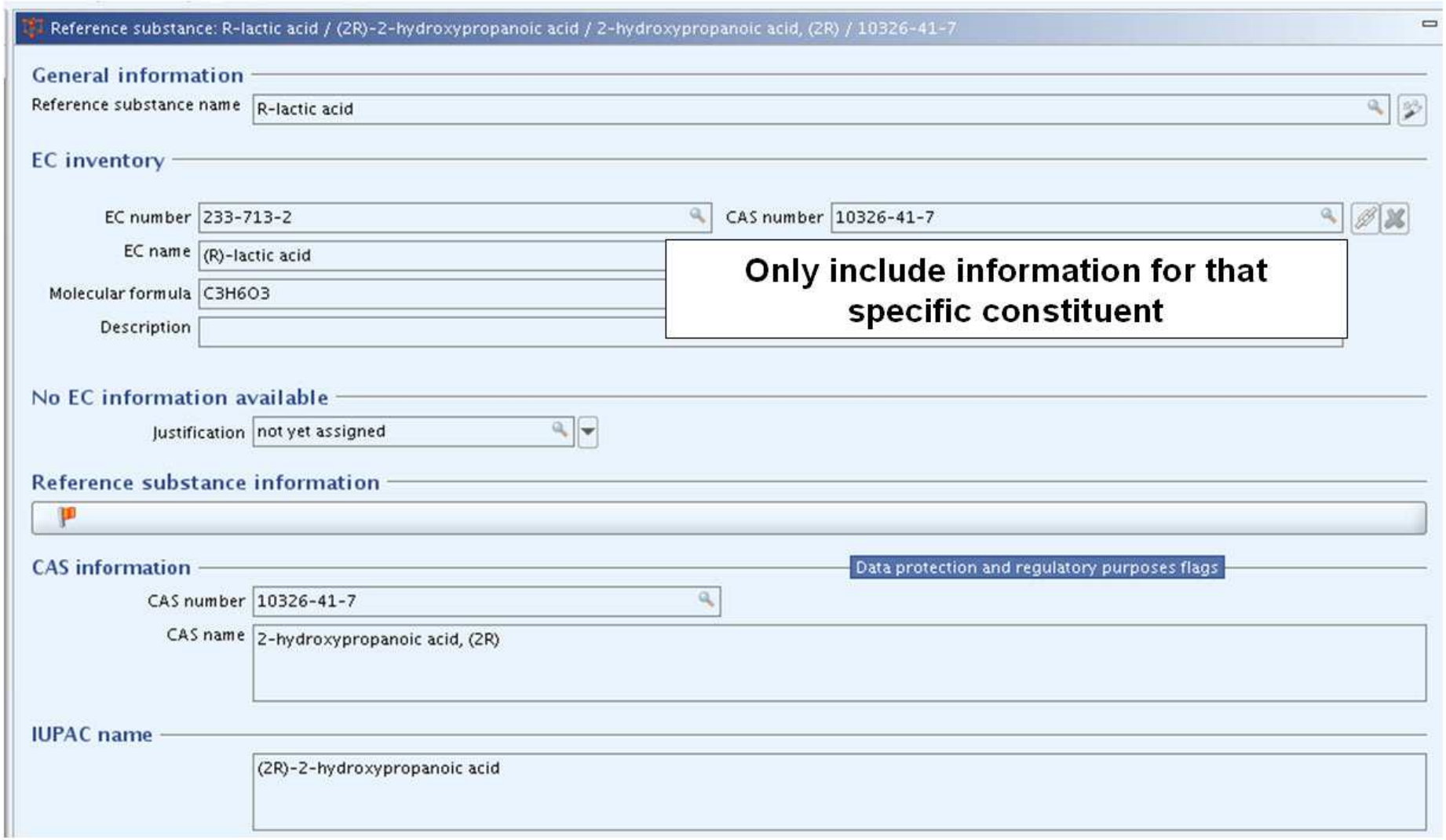
1.2 Composition



1.2 Composition



1.2 Composition



1.2 Composition