

# Substance identity - screening of the registration dossiers

## Inconsistent identifiers

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European Chemicals Agency



# Substance identity IT screening campaign

Scope defined by 10 Issue types:

1. Missing concentration ranges
2. Typical concentration outside of concentration range
3. Composition reported with no constituents
4. Low or ambiguous degree of purity for well-defined substances
5. Unidentified constituent or impurity present at significant concentration
6. Well-defined substance with inconsistency between degree of purity and constituent concentrations
7. Well-defined substance with inconsistency between degree of purity and impurity concentrations
8. No spectral and analytical information provided
9. Additives without stabilising function
10. **Inconsistent identifiers of constituents, impurities and additives**

## Why is this important?

- Chemical identifiers, such as IUPAC name and SMILES, are examined to establish the identity of the registered substance
  - when unclear ECHA may initiate a compliance check, or other regulatory processes such as testing proposal evaluation may be delayed
- Chemical identifiers are used by ECHA and Member State competent authorities to prioritise dossiers and substances for REACH and CLP processes
  - substance evaluation
  - risk management

## Why is this important?

- Chemical identifiers are also used to (automatically) derive structures that are subsequently used in various ways
  - structural alerts to predict fate and (eco)toxicological properties
  - examine substance sameness in categories
  - examine structural similarity of the registered substance to substances of known concern
- ➡ For ECHA and Member State authorities, chemical identifiers in the registration dossier are much more than text strings
  - automatic conversion into structures
  - chemo-informatics
  - establish links with regulatory lists, such as Annex VI of the CLP Regulation (EC) No 1272/2008

## Why is this important?



CAS number

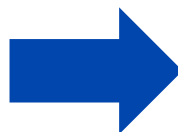
108-88-3

IUPAC name

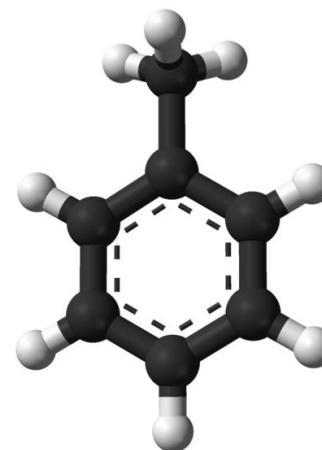
methylbenzene

synonym

toluene



chemical structure used in  
screening for REACH and CLP  
processes



# Which chemical identifiers are examined?

algorithms look in both the reference substance in section 1.1 and the individual constituents, impurities and additives in each composition in section 1.2

- 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
  - 1.8 Recipients
  - 1.9 Product and process oriented research and development
- 2 Classification & Labelling and PBT assessment
- 3 Manufacture, use and exposure
- 4 Physical and chemical properties
- 5 Environmental fate and pathways
- 6 Ecotoxicological Information
- 7 Toxicological information
- 8 Analytical methods
- 9 Residues in food and feedingstuffs
- 10 Effectiveness against target organisms
- 11 Guidance on safe use
- 12 Literature search
- 13 Assessment Reports
- 14 Information requirements

## IUCLID section 1.1

Reference substance

Reference substance flags

ECHA Substance / ECHA Substance / ECHA Substance / 11111-11-1

EC number	EC name
CAS number	CAS name
11111-11-1	ECHA Substance
IUPAC name	
ECHA Substance	

## IUCLID section 1.2

Substance composition

second composition

Name: second composition

Brief description

Composition ID: L-61afd0f3-3f45-4ecd-ac26-b041e05fac33

Degree of purity

> 23 <= 24 % (w/w)

Constituents

< 12 mg/L fenethazine / N,N-dimethyl-2-(10H-phenothiazin-10-yl)ethanamine / 522-24-7

Impurities

< 3 ppm zomepirac / [5-(4-chlorobenzoyl)-1,4-dimethyl-1H-pyrrol-2-yl]acetic acid / 33369-31-2

Additives

ECHA Substance

# Which chemical identifiers are examined?

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**General information**

Reference substance name: fenethazine

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**EC inventory**

EC number: 208-325-1    CAS number: 522-24-7

EC name: fenethazine

Molecular formula: C16H18N2S

Description:

---

**No EC information available**

Justification:

---

**Reference substance information**

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**CAS information**

CAS number: 522-24-7

CAS name:

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**IUPAC name**

N,N-dimethyl-2-(10H-phenothiazin-10-yl)ethanamine

EC number and EC name

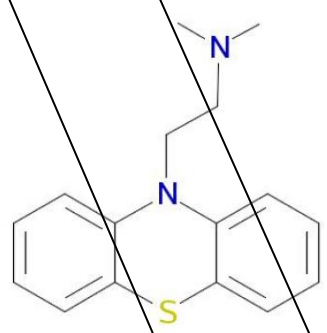
CAS number and CAS name

add here the correct CAS information if you disagree with the the EC inventory + explanation in the reference substance remarks

IUPAC name

# Which chemical identifiers are examined?

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- 1 General Information
  - 1.1 Identification**
  - 1.2 Composition
  - 1.3 Identifiers
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SMILES notation	<chem>CN(C)CCN1c2ccccc2Sc3ccccc13</chem>
InChI	InChI=1/C16H18N2S/c1-17(2)11-12-18-13-7-3-5-9-15(13)19-16-10-6-4-8-14(16)18/h3-10H,11-12H2,1-2H3
Structural formula	

SMILES

InChI

please note that a valid InChI starts with 'InChI=1' or 'InChI=1S'



# Which chemical identifiers are examined?

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**Synonyms**

Name
fenethazine

Add... View... Delete

---

**Related CAS information**

CAS name	CAS number	Justification
relatedCASNameExample	50-00-0	isomer

Add... View... Delete

synonyms

related CAS number(s) and related CAS name(s)

# Which chemical identifiers are examined?

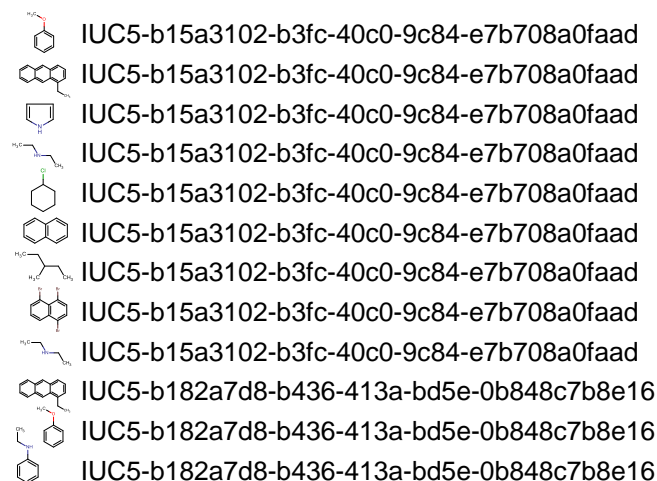


structure origin and conversion method	number of successful conversions
I5_CAS (I)	29566
I5_CAS (II)	106203
I5_CASNAME (I)	32217
I5_CASNAME (III)	35469
I5_EC (I)	28011
I5_ECNAME (I)	86405
I5_ECNAME (III)	94820
I5_ECNAME (IV)	118633
INCHI (I)	80762
INCHI (III)	76529
IUPACNAME (I)	84900
IUPACNAME (III)	87134
IUPACNAME (IV)	87323
REF_SUB_NAME (I)	89312
REF_SUB_NAME (III)	97986
REF_SUB_NAME (IV)	91449
SMILES (I)	94842
SMILES (III)	95670

Numbers are indicative



## chemical structures



...

**Erroneous identifiers, such as invalid IUPAC names, or inconsistent identifiers cause issues and can be one of the reasons to manually examine the dossier in greater detail**

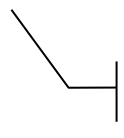
## Messages in information letters

### Excerpt from the information letter:

#### "Inconsistent identifiers of constituents, impurities and additives"

The impurity with reference substance name "*Reference Substance Name*" and IUPAC name "*IUPAC Name*" empty in the composition with name "*Reference Substance Name*" and local UUID "*Lf5cecc8b-2bce-4f0d-a552-45801ccc6785*" seems to have two sets of inconsistent identifiers leading to different molecular structures:

- molecular structure 1 is derived from the identifier SMILES "CCCCCO...CCCC(=O)O"
- molecular structure 2 is derived from the following two identifiers CAS number "*123-123-12*" and InChI "*InChI=1/C17H34O2/c1-2-... (H,18,19)*"

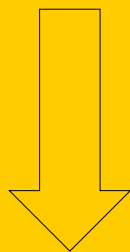


two groups of chemical identifiers leading to different molecular structures

# Automatic identification of inconsistent identifiers

- All reference substances, in all compositions are checked separately
- The chemical identifiers are processed and used to generate a molecular structure
  - 'textual' identifiers, such as IUPAC names are also used and automatically converted to structures
  - 'numerical' identifiers, such as CAS numbers are also used to generate a molecular structure using reliable, external sources
  - SMILES and InChIs are directly used as they provide structural information
- The molecular structures produced by the different identifiers are checked for consistency
  - inconsistencies are grouped in terms of severity
  - type of inconsistency, and
  - number of distinct molecular structures derived

severity decreases



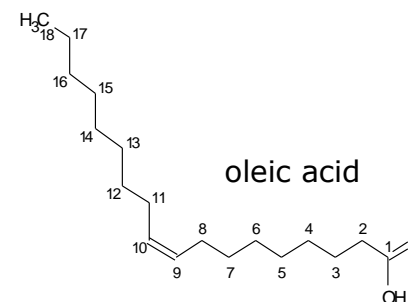
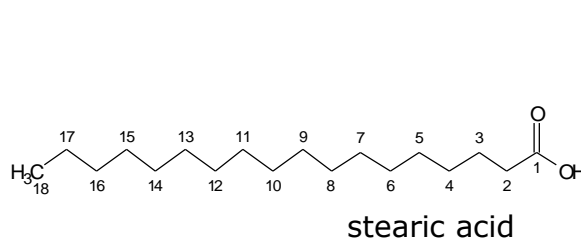
grossly different structures (e.g. incorrect CAS number)  
differences in counter ions for salts  
mixture vs. pure substance  
positional isomerism (substituents or bonding)  
...  
differences in the configuration of a single chiral centre

## Key messages I

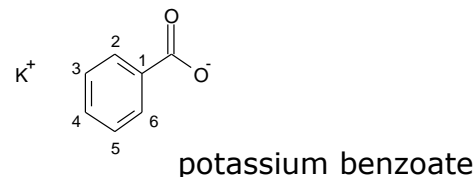
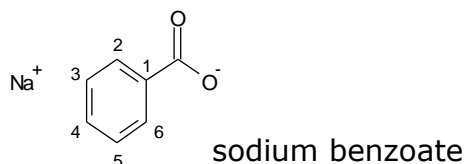
- Check the identifiers for all reference substances in all compositions in your registration dossier, regardless of their concentration
  - even if you have not received an information letter
- Do not use generic identifiers (e.g. EC number or CAS number), if your reference substance can be identified with a more specific identifier
- On some occasions, the identifiers in the EC inventory or prefilled reference substances may not be perfectly accurate; it is your responsibility to check their correctness
  - IUCLID allows a different CAS number than the one in the EC inventory to be specified
  - IUCLID allows the imported reference substance to be edited, e.g. to change the SMILES
- **Please pay attention to all aspects**
  - enantiomers (R/S), or other isomers (e.g. cis/trans), are not the same structure, although a CAS number does not necessarily specify the isomerism
  - for further information, please consult the Guidance on substance identification<sup>1</sup> (Chapter 5) and the Dossier Submission Manual, part 182 (DSM 18, Q&A 4, Q&A 7)
  - SMILES and InChI discriminate among isomers if used properly

## Key messages II

- Differences in branching, or differences in the position of an unsaturated bond, mean different substances, e.g.
  - EC number 200-313-4, stearic acid ( $C_{18}H_{36}O_2$ )  $\neq$  EC number 204-007-1, oleic acid ( $C_{18}H_{34}O_2$ )



- A neutral acid or base is not the same with an individual salt
- Salts with different counterions are different substances, e.g.
  - EC number 208-534-8, sodium benzoate ( $C_7H_5O_2.Na$ )  $\neq$  EC number 209-481-3, potassium benzoate ( $C_7H_5O_2.Ka$ )



<sup>1</sup> Data Submission Manual, part 18, how to report the substance identity in IUCLID 5 for registration under REACH, [echa.europa.eu/documents/10162/13653/substance\\_id\\_report\\_iuclid\\_en.pdf](http://echa.europa.eu/documents/10162/13653/substance_id_report_iuclid_en.pdf)

<sup>2</sup> Guidance for identification and naming of substances under REACH and CLP, [echa.europa.eu/documents/10162/13643/substance\\_id\\_en.pdf](http://echa.europa.eu/documents/10162/13643/substance_id_en.pdf)

## References

- **Guidance for identification and naming of substances under REACH and CLP**  
[echa.europa.eu/documents/10162/13643/substance\\_id\\_en.pdf](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**  
[echa.europa.eu/documents/10162/13653/substance\\_id\\_report\\_iuclid\\_en.pdf](http://echa.europa.eu/documents/10162/13653/substance_id_report_iuclid_en.pdf)
- **Questions and answers on substance identification**  
[echa.europa.eu/qa-display/-/qadisplay/5s1R/view/REACH/SubstanceIdentification](http://echa.europa.eu/qa-display/-/qadisplay/5s1R/view/REACH/SubstanceIdentification)
- **How to improve your dossier webpages**  
[echa.europa.eu/support/how-to-improve-your-dossier](http://echa.europa.eu/support/how-to-improve-your-dossier)



The screenshot shows the ECHA website page titled "How to improve your dossier". The page features a navigation menu on the left with categories like "Regulations", "Information on Chemicals", and "Support". The main content area includes a sub-header "How to improve your dossier" and a paragraph explaining that ECHA has published a wide range of information and tools to help registrants prepare high-quality dossiers. Below this, there are several sections: "Concrete support to improve their dossiers", "Dossier Quality Assistant", and "Related news". A large blue arrow points from this screenshot towards the right, indicating a transition to a more detailed view of the content.

### Substance identification

Correct and consistent substance identification (SID) is the basis for all REACH processes. It is the obligation of each registrant to provide a detailed characterisation of the identity of the substance they manufacture or import; this responsibility cannot be solely on the lead of the joint submission in the substance information exchange forum (SIEF).

The annual progress reports on evaluation under REACH point to substance identification as one of the most frequent shortcomings in registrations submitted to the Agency. ECHA has therefore conducted an IT-based screening on required information elements for substance identity of all REACH registrations.

#### Supporting material

- › [Technical annex provided with SID screening letters](#) [PDF] [EN]
- › [Substance identity](#)
- › [Data Submission Manual – Part 18 – How to report the substance identity in IUCLID 5 for registration under REACH](#) [PDF] [EN]

#### Related news

- › e-News 09 April 2014  
ECHA targets substance identity – letters sent to companies with shortcomings in their registrations
- › News Alert 11 December 2013  
Is your substance identity information up-to-date?
- › e-News 24 April 2013  
ECHA to check substance identity of REACH 2013 registrations

# Thank you

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