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Pre-release

EU-SRS

Polymers EU-SRS User Guide

Guidance on naming and building polymer records in EU-SRS

Disclaimer

This document is created as part of deliverable D2.8 EU-SRS Data Management Plan of Unicom Work Package 2: Implement IDMP – Substance Management in Europe.

This guide will be a living document, used by the Substances Validation Group (SVG) for creation and maintenance of substances in EU-SRS.

The current version is a pre-release. Your feedback, if any, is welcomed by **8 December 2022.** Comments can be sent to Steven de Wit (e-mail: s.d.wit@cbg-meb.nl).

Your feedback will be considered when preparing the official release which will be submitted as Unicom deliverable to the European Commission in January 2023.

Document control

This document is subject to a regular review by the Substance Validation Group (SVG). It is a living document, and changes will be captured in the version history section.

Document ownership

This document is owned by the SVG.

Revision history

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List of abbreviations

Abbreviation	Complete Form
BAN	British Approved Name
CAS	Chemical Abstracts Service
eAF	electronic Application Form
EDQM	European Directorate for the Quality of Medicines and HealthCare
EMA	European Medicines Agency
EU-SRS	European Substance Registration System
FDA	Food and Drug Administration
G-SRS	Global Substance Registration System
INN	International Nonproprietary Name
ISO IDMP	ISO Identification of Medicinal Products
IUPAC	International Union of Pure and Applied Chemistry
JAN	Japanese Accepted Name
OMS	Organisation Management Service
Ph. Eur.	European Pharmacopoeia
PMS	Product Management Service
SmPC	Summary of Product Characteristics
SMS	Substance Management Service
SMSID	SMS Identifier
SPOR	Substances, Products, Organisations, Referentials
SSG	Specified Substance Group
SVG	Substance Validation Group
SWG	Substance Working Group
UNII	Unique Ingredient Identifier
USAN	United States Adopted Name
USP	United States Pharmacopeia
WHO	World Health Organization
xEVMPD	Extended EudraVigilance Medicinal Product Dictionary

1 Introduction

The EU Network is currently implementing the ISO IDMP standards in a phased programme based on the four domains of master data in pharmaceutical regulatory processes: substance, product, organisation and referential (collectively referred to as “SPOR”) master data. ISO IDMP compliant business services for the central management and supervision of data in each of the four SPOR areas will be established through an iterative and incremental delivery approach. Through the Substance Management Services (SMS) of the SPOR programme EMA will provide the EU network centralised substance data management services.

EU-SRS will become the scientifically rigorous back-end for the Substance Management Services of SPOR. EU-SRS will be accessible to the EU regulatory network, enabling the unambiguous identification of substances used in medicinal products based on their scientific properties in accordance with ISO IDMP standard 11238 and ISO IDMP technical specification standard 19844. EU-SRS allows the unique identification of substances which will support various purposes including the enhancement of traceability of pharmacovigilance, non-clinical, clinical and quality findings with a high degree of precision to substances by their scientific identity.

The Substance Validation Group is responsible for building substance records in EU-SRS. In addition, the SVG defines guidance and best practices for substances management in EU-SRS (per substance type).

1.1 Purpose

The purpose of this document is to provide practical guidance for the registration of a polymer in EU-SRS.

1.2 Scope

Registration of human and veterinary polymer substances are in scope of this document.

This document is intended to be used together with the EU-SRS Substance Maintenance Process which describes the workflow between EMA and SVG (under development).

2 Defining a Polymer

In order to ensure that polymers are built in a harmonized way, rules and definitions have been established and agreed upon within the SVG and EMA.

The concepts required for the unique identification and description of substances are described in the ISO 11238 IDMP standard on substances. Guidelines for implementing ISO 11238 are provided in the technical specification ISO/TS 19844. Although ISO 11238 does not provide any guidance on substance nomenclature, it does provide a structure for the capture of names and codes that are used to refer to a substance. This section aims to provide supplementary guidance and should be read in conjunction with the standard and technical specification.

2.1 Definition

Placeholder for definition from ISO/TS 19844:2018 (approval pending).

Distinguishing characteristics for many polymers, such as molecular weight, degree of polymerisation, and viscosity, should be indicated in the names of these substances. Standardisation on such names to facilitate searching and identification of substances may be adopted within regions.

According to ISO 11238, the following elements are essential for defining polymers:

- Polymer Class: Homopolymer or Copolymer
- Polymer Geometry: Linear, Branched, Cross-linked, Network or Dendritic
- Copolymer Sequence Type: Random, Statistical, Alternating, Periodic, Block, Mixed, Graft or Cross
- Structural Repeat Units (SRU): The number and amounts of each structural repeat unit and the orientation of polymerisation. A structural representation of the polymer that indicates the connectivity within and between the structural repeat units and end groups.
- Degree of Polymerisation: The average and/or range of the number of times an SRU repeats in a homopolymer or the block size within a block copolymer.
- Monomers: Monomers are the starting materials or building blocks of polymers. The number of monomers and the amount or relative amount of each monomer should be given. Each monomer will be a substance in its own right and identified with a Substance ID.
- Molecular Weight: Molecular weight or mass of the polymer and the type of molecular weight and ranges or dispersity of molecular weights should be given. Molecular weights are often distinguishing characteristics of structurally related polymers.
- Property: Physical properties are often necessary to distinguish polymeric material. Viscosity is often given and can be required if the molecular weight is not given or known. Other physical properties such as density, glass transition temperature, interfacial or rheological properties should also be given, if relevant.
- Modification: Any modification that results in changes in the covalent structure of the polymer should be captured.
- Source: For biosynthetic polymers, the biological source of the polymers should also be indicated."

According to ISO 11238, the following substances can be registered as Polymer:

- Polymers refer to material that is polydisperse.
- Polymers have structural repeat units

Polymers shall be defined using a combination of the molecular structure of the structural repeating units, substituents that are attached to the structural repeating unit, molecular weight, and polydispersity of the polymer substance.

Monodisperse polymers will be classified as chemicals, proteins or nucleic acids.

According to the representation shown in Error! Reference source not found.**, some examples of related substance types are summarized in**

Table 1. The comment provides an explanation for the assignment of these substances to the respective substance type.

Substances closely related to polymers are monodisperse substances, mixtures and structurally diverse. To determine the correct substance type, the number of molecular entities should be considered. Figure 1 shows the workflow diagram for defining the substance type based on the number of molecular entities.

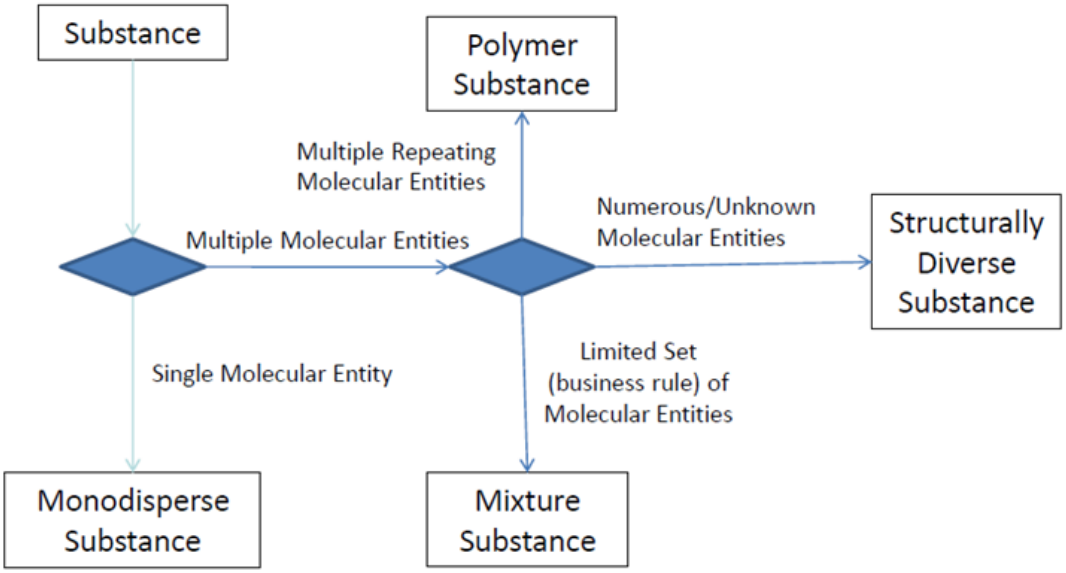


Figure 1. Workflow for determining if a substance should be classified as a polymer

Table 1. Examples of substances and their substances types (Mixture/SSG1/Structurally diverse/Concept) that are related to polymers.

Preferred Name	Substance Type	Comment
Cellulose, microcrystalline	Specified substance group 1	Specified substance of Cellulose
Maize starch	Mixture	Mixture of two polymers: amylose and amylopectin
Methacrylic acid - ethyl acrylate copolymer (1:1) dispersion 30 per cent	Specified substance group 1	Polymer dispersed in solvent
Polysorbate 60	Mixture	Mixture of partial esters of fatty acids. Main fatty acid components stearic acid and palmitic acid
Poly(vinyl alcohol), hydrolysed	Specified substance group 1	Polyvinyl alcohol hydrolysed is specified record of poly(vinyl alcohol)
Opadry OY-S-27203	Specified substance group 1	Multi-substance material: Multiple-Substances and/or Specified Substances of diverse origin.
Maltodextrin	Mixture	Mixture of glucose, disaccharides and polysaccharides, obtained by the partial hydrolysis of starch
Macrogol stearate	Mixture	Ph. Eur. definition: Mixture of monoesters and diesters of mainly stearic (octadecanoic) acid and/or palmitic (hexadecanoic) acid and macrogols. It may be obtained by ethoxylation or by esterification of macrogols with stearic acid 50 (type I) or stearic acid 95 (type II)
Siliconised polyester	Concept	Polymer substance in transdermal patch/medicated plaster material
Poly(ethylene terephthalate) film	Concept	Polymer substance in transdermal patch/medicated plaster material
Fluoropolymer coated polyester film Alias: Scotchpak 1022	Concept	Polymer substance in transdermal patch/medicated plaster material
Shellac	Structurally diverse	Purified material obtained from the resinous secretion of the female insect Kerria lacca (Kerr) Lindinger (Laccifer lacca Kerr).

3 Naming of Polymers

This chapter provides details around naming of Polymer substances in EU-SRS and SMS. Acceptable sources for naming of polymers are included in Appendix 4.

3.1 Name types

The EU-SRS system will contain name type information, such as:

- **Official names**: This name type contains comprehensive information about the name. It is chosen for names that are assigned by an official organisation. According to the EU Directive, the International Nonproprietary Name (INN) and the European Pharmacopoeia must be followed in the EU.
- **Systematic names:** The systematic names are formed according to the IUPAC rules. It can also be used for other systematic names (e.g. CAS).
- **Codes:** Aliases that represent company codes.
- **Common names:** Usage for first designation of recognised trivial names that have an additional systematic designation. An alternative for "official name".
- **Brand names**: Aliases that represent company brand name.
- **Scientific name**: Is based on the biological taxonomic nomenclature and reflects the current scientific knowledge based on acknowledged scientific/ taxonomic databases, which are however no official naming bodies (no jurisdiction applies) - applicable for substances coming from biological origin (e.g. microbial, botanical or animal)

3.2 Naming convention

In SMS, each unique substance receives an SMSID and each SMSID has one substance Preferred Term, which is characterised as “Display Name” in the system. The Preferred Term is the best substance name available at a given time and could change. The Preferred Term is used in several forms visible to industry. Going forward, it is planned that these forms (such as eAF) will also display the aliases.

3.2.1 Preferred term

The Preferred Term of a substance should be selected according to the priority ranking of the following reference sources and name types:

- European Pharmacopoeia (Ph. Eur.) (Official Name Type)

NOTE: There are cases were the Ph. Eur. name and the INN name are not aligned or where the monograph definition does not give sufficient level of depth. For these cases, what name reflects the substance best is determined case-by-case. Though, a general approach was decided on that is applicable for most cases, which was agreed with EDQM: In case only 1 monograph title exists currently, pointing to two or more substances, these need to be split up in SMS/EU-SRS. EDQM plans to update these monographs in the future as well.

NOTE: If the name in Ph. Eur. does not fully reflect the structure, then an alias is added to reflect the structure correctly.

- Recommended International Non-Proprietary Name (rINN) (Official Name Type)

NOTE: Modified INN will be generated according to the WHO publications “International Nonproprietary Names Modified” and “Names for radicals, groups & others Comprehensive list”.

- Other official name type with EU jurisdiction (INCI, BAN, etc.) (Official Name Type)
- International Union of Pure and Applied Chemistry (IUPAC) name (Systematic Name Type)
- Other systematic name (Systematic Name Type)
- Company code (Code Type)

NOTE: A company code can be temporarily used as a Preferred Term only if no other name is available in the public domain, e.g. for substances under development. Once another name becomes available, the company code should be changed into an alias and another term should become the Preferred Term.

3.2.2 Aliases

Aliases are valid alternative names for a Preferred Term, according to valid reference sources. SMS provides aliases when available. The EU-SRS Preferred Term should be written in European English. Any US English term is however to be kept as an alias.

In addition to the sources/name types used for preferred terms, the following sources can also be used for aliases:

- Proposed INN (pINN) (Official Name Type)
- United States Approved Name (USAN) (Official Name Type)
- United States Pharmacopoeia (USP) (Official Name Type)
- Japanese Approved Name (JAN) (Official Name Type)
- Official name in other jurisdiction, e.g. Australian Approved Name (AAN) (Official Name Type)

In addition, other names can be used as aliases when:

- The name is a brand name (Brand Name Type)
  Examples: Avicel, Eudragit, Methocel, Carbopol
- The name is presented differently based on order of the words or when there is a comma, hyphen or brackets in the substance name:
  Example: Poly(vinyl acohol) (Ph. Eur.), Polyvinyl alcohol (USP)
- Nomenclature defined by INCI (International Nomenclature of Cosmetic Ingredients) (Official Name type)
  Example: Cetomacrogol 1000 (INN), Ceteth-20 (INCI)
- The name contains an E number (Common Name Type)
  E numbers are acceptable as alias of an approved substance name and shall be written according to the Commission Regulation (EU) No 231/2012 (with a space between E and the following number).
  NOTE: specific E numbers should be used. E numbers should not be applied to a full group.
  Example:
  Preferred Term: Polysorbate 20.
  Alias: Polyoxyethene (20) sorbitan monolaurate (E 432)
- Systematic names (Systematic Name Type)
  - Accepted as an alias when following any official naming convention.
  - However, when a systematic name is newly added as a Preferred Term, it is preferred to follow IUPAC writing, as this format is often used by INN and applicants.
    - Alphabetical order of monomers
    - Conjuction, e.g. (-co-) between monomers
    - Ratio of monomers
  - Additionally, non-converted CAS writing of systematic names should be avoided.

  Example: Menfegol (INN)
  Preferred writing: α-[4-[methyl(1-methylethyl)cyclohexyl]phenyl]-ω-hydroxy-poly(oxy-1,2-ethanediyl)

3.2.3 Invalid substance name

Not acceptable names include:

- Company name should not be added behind the chemical names (e.g. HYPROMELLOSE (METHOCEL K100M)).
- E number, which refer to the whole polymer family (e.g. Macrogol), should not be added to the specified record (e.g. Macrogol 400).
- Non-converted CAS writing (e.g. ‘Poly(oxy-1,2-ethanediyl), α-[4-[methyl(1-methylethyl)cyclohexyl]phenyl]-ω-hydroxy-’).

For more examples, see the tables of the respective polymer families in section 4.4.

NOTE: Translations in all EU languages are valid substance names and are registered in SMS. However, translations are not included in EU-SRS.

3.3 Examples of Polymer Naming

This chapter contains specific information for naming of polymers.

3.3.1 General remarks

Greek letters should be written out in Latin as several consuming systems of SMS cannot display Greek letters. Beta instead of β and alpha instead of α. In EU-SRS system HTML coding (as listed in Appendix 2) should be used for the correct representation of Greek letter.

3.3.2 Copolymers

The Preferred Term for copolymers depends on whether they are in scope of Ph. Eur.:

- If the copolymer is in scope of Ph. Eur., then the Ph. Eur. Monograph title should be the Preferred Term and the systematic name should be an alias. Examples are included in the table below.

Table 2. Examples of naming of copolymers that are in scope of Ph. Eur.

Preferred Term (Ph. Eur. Monograph)	Alias (e.g. systematic name according to IUPAC, brand name)
Methacrylic acid-ethyl acrylate copolymer (1:1)	Poly(methacrylic acid-co-methyl methacrylate) (1:1) Poly(methacrylic acid, methyl methacrylate) (1:1)
Ammonio methacrylate copolymer (type A)	Poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonioethyl methacrylate chloride) (1:2:0.2) Eudragit RL 100
Basic butylated methacrylate copolymer	Poly(butylmethacrylate-co-(2-dimethylaminoethyl)methacrylate-co-methyl methacrylate) (1:2:1) EUDRAGIT E 100

- If the copolymer is not in scope of Ph. Eur., then the systematic name should be the Preferred Term. Examples are included in the table below.

Table 3. Examples of naming of copolymers that are out of scope of Ph. Eur.

Preferred Term (systematic name according to IUPAC)	Alias
Poly(methacrylic acid-co-methyl acrylate-co-methyl methacrylate-co-) (1:7:3)	Poly(methyl acrylate, methyl methacrylate, methacrylic acid) (7:3:1)
Poly(ethyl acrylate-co-methyl methacrylate) (2:1)	Poly(ethyl acrylate, methyl methacrylate) (2:1)

Same rules apply to all types of copolymers (naming rules explained on polymethacrylates).

3.3.3 Hypromellose

The monograph *Hypromellose* as found in Ph. Eur. includes different types of Hypromellose. In SMS and EU-SRS, each of these names should receive their own identifier. For example, the following names should receive their own identifier:

- Hypromellose — general record
- Hypromellose 2208, 10000 mPa.s — according to Ph. Eur. specifications
- Hypromellose 2506, 4000 mPa.s — out of Ph.Eur. specifications

Preferred Term in SMS/EU-SRS should include Ph. Eur. monograph title and related substitution type and viscosity:

- **PT: Hypromellose + substitution type, viscosity**
  - Hypromellose 2208, 10000 mPa.s
  - Hypromellose 2910, 4000 mPa.s
- Invalid names: 'Hypromellose' followed by only viscosity or only substitution type.
- Agreed naming rules are applicable for all hypromelloses regardless of whether they are in scope of Ph. Eur. or not.

NOTE: The unit for viscosity mPa.s is preferred before CP.

Table 4. Examples of naming of Hypromellose.

Preferred Term	Alias	Invalid Names
Hypromellose 2208, 10000 mPa.s Hypromellose 2506, 4000 mPa.s	Hydroxypropylmethylcellulose 2208, 10000 CPS Methocel K100 Premium LVEP Methocel E5 Premium LV	HYPROMELLOSE 100000 CP hypromellose (1500 MPAS) HYPROMELLOSE 2208 (E464) HYPROMELLOSE 2208 hypromellose 2200/15000 Hypromellose (Methocel K 15 M)

3.3.4 Macrogols

The monograph *Macrogols* as found in Ph. Eur. includes different types of macrogol. In SMS and EU-SRS, each of these names should receive their own identifier. For example, the following names should receive their own identifier:

- Macrogol
- Macrogol 400
- Macrogol 1000

Preferred Term in SMS/EU-SRS should include “macrogol” and type of macrogol expressed as average relative molecular mass.

- ***PT: Macrogol+type of macrogol expressed as average relative molecular mass***
- Agreed naming rules are applicable for all macrogols regardless of whether they are in scope of Ph. Eur. or not
- Macrogol can be also described by average number of oxyethylene groups (e.g. PEG-8)

Table 5. Examples of naming of Macrogols

Preferred Term	Alias	Invalid Names
Macrogol 400	PEG 400 Polyethylene glycol 400 Polyoxyethylene glycol 400 PEG-8	MACROGOL (PEG 400) MACROGOL 400 (PEG 400)

3.3.5 Hydroxypropylcellulose

- The monographs *Hydroxypopylcellulose* and *Hydroxypropylcellulose, low substituted* as found in Ph. Eur includes different types of hydroxypropylcelluloses. The content of hydroxypropoxy groups is the basic criterion on which the respective substances are distinguished from one another. Preferred Term for hydroxypropylcellulose depends on whether they are in scope of Ph. Eur.. If all specifications are according to Ph. Eur, then the Ph. Eur. Monograph title should be the Preferred Term. Examples are included in the table below.

Table 6. Examples of naming of Hydroxypropylcellulose that are in scope of Ph. Eur.

Preferred Term	Alias	Invalid Names
Hydroxypropylcellulose, low-substituted Hydroxypropylcellulose	Hyprolose (5-16%) Hyprolose (53.4-80.5%) Klucel LF Hydroxypropylcellulose (E 463)	HYDROXYPROPYLCELLULOSE LH-21 HYDROXYPROPYLCELLULOSE TYPE JF HYDROXYPROPYLCELLULOSE LOW SUBSTITUTED Hydroxypropylcellulose (E463)

- If the specification is not in scope of Ph. Eur., then the INN name should be the Preferred Term.
  - INN name: Hyprolose
  - INN name: Hyprolose (content (%) of hydroxypropoxy groups)

Table 7. Examples of naming of hydroxypropylcellulose that are out of scope of Ph. Eur

Preferred Term	Alias	Invalid Names
Hyprolose Hyprolose (71.0-76.9%)	Hydroxypropylcellulose (71.0% -76.9%)	Hydroxypropylcellulose 240 mpa.S

- Invalid names
  - Combination of the name hydroxypropylcellulose + brand name type e.g. LH and GF.

3.3.6 Poloxamer

The monograph *Poloxamers* as found in Ph. Eur. includes different types of poloxamer. In SMS and EU-SRS, each of these names should receive their own identifier. For example, the following names should receive their own identifier:

- Poloxamer
- Poloxamer 124
- Poloxamer 188

Preferred Term in SMS/EU-SRS should include “poloxamer” and type of poloxamer.

- **PT: Poloxamer + type**
- Agreed naming rules are applicable for all poloxamers regardless of whether they are in scope of Ph. Eur. or not

Each poloxamer name is followed by a number, e.g., poloxamer 188, 331, 407 etc. The first two digits multiplied by 100 correspond to the approximate average molecular weight of the poly(oxypropylene) portion; the third digit multiplied by 10 corresponds to the percentage by weight of the poly(oxypropylene) portion.

Table 8. Examples of naming of Poloxamer

Preferred Term	Alias	Invalid Names
Poloxamer 188	Kolliphor P 188	poloxamer 68 micronised

3.3.7 Povidone

The monograph *Povidone* as found in Ph. Eur. includes different types of povidone, which are characterised by their viscosity in solution expressed as a nominal K-value. The nominal K-value is 10 to 120.

Preferred Term in SMS/EU-SRS should include “Povidone” and K-value.

- **PT: Povidone + K-value/range of K-values**
- Agreed naming rules are applicable for all povidones regardless of whether they are in scope of Ph. Eur. or not

Table 9. Examples of naming of Povidone

Preferred Term	Alias	Invalid Names
Povidone Povidone K25 Povidone K29-32	Kollidon 25 Polyvinylpyrrolidone K90 Polyvidone K90 PVP K90	Povidon K90 (E1201) vinylpyrrolidone copolymer Kollidon K90 Povidone K-90 Povidone K29/32 Povidone K29 - 32

3.3.8 Crospovidone

Preferred Term in SMS/EU-SRS should include “Crospovidone” and type.

- **PT: Crospovidone (type)**
- Example: Crospovidone (type A)

3.3.9 Polysorbate

The monographs Polysorbate 20, Polysorbate 40, etc, as found in Ph. Eur. will receive their own identifier in SMS/EU-SRS, same as general record Polysorbate, which is INN name.

- Polysorbate
- Polysorbate 20
- Polysorbate 40

Preferred Term in SMS/EU-SRS should include “Polysorbate” and number.

- **PT in EU-SRS/SMS: Polysorbate + number**
- Agreed naming rules apply for all polysorbates (specification in/out of Ph. Eur.)

NOTE: Depending on main fatty acid component it could be mixture or polymer. Polysorbate 60 is a mixture and polysorbate 20, 40 and 80 are polymers.

Table 10. Examples of naming of Polysorbates

Preferred Term	Alias	Invalid names
Polysorbate 20	Polyoxyethylene 20 sorbitan monolaurate Tween 20	Polysorbate 20 (E432) POLYOXYETHYLENE SORBITAN MONOLAUREATE (TWEEN 20)
Polysorbate 40	Polyoxyethylene 20 sorbitan monopalmitate	
Polysorbate 65	Polyoxyethylene 20 sorbitan tristearate	

3.3.10 Carbomer

The monograph *Carbomers* as found in Ph. Eur. includes different types of carbomers. Preferred Term in SMS/EU-SRS should include “Carbomer” and number (letter).

- **PT: Carbomer + number (+letter if applicable)**

Table 11. Examples of naming of Carbomers

Preferred Term	Alias	Invalid Names
Carbomer 974P Carbomer 910	Carbopol 940	Carbomer 974 P Carbomer 29400-39400 mPa·s Carbomer 30750 mPa.s

4 Building Polymer Records

4.1 Duplicate check

The first step of any registration should be to ensure that the substance is not already in EU-SRS**,** to prevent from adding a duplicate. To ensure there is no duplicates, different elements can be used for verification, such as: different names, company codes, monomers, systematic name (or parts of systematic name in different order) and database IDs. The approach for duplicates check should be determined case-by-case. If duplicates are found, further investigation is required to determine if it's a true duplicate.

There are several ways to search for substances in EU-SRS: Global Search, Advanced Search, Structure Search, and Sequence Search.

4.2 General information

After verifying the substance is not registered in EU-SRS via the check of duplicates, use the Polymer Registration to register the new substance.

The Polymer registration form will be displayed. Section cards are collapsible to ease navigation, however the elements in this form are:

- Overview – definitional information
- Names
- Polymer Classification
- Monomers
- Idealized Structure
- Structural Units
- Agent modifications
- Structural modifications
- Physical modifications
- Codes
- Relationships
- Notes
- Properties
- References

According to ISO 11238, polymers shall be defined using a combination of the molecular structure of the structural repeating units, substituents that are attached to the structural repeating unit, molecular weight, and polydispersity of the polymer substance. Degree of polymerization, monomers used to synthesize synthetic polymers or copolymers, the source material for naturally derived polymers, polymeric end groups, and physical or biological properties shall also be captured when known and needed to distinguish material. Polymers shall be defined to the level of specificity needed to distinguish materials and broad polymeric definitions shall be disfavored.

Mandatory fields when registering a polymer are:

- A substance identity/molecular structure
- At least one name
- At least one definitional reference

4.3 Overview

For the registration of a new polymer in EU-SRS, some general information needs to be entered first (see **Error! Reference source not found.**). More information about the different fields is found in Appendix 5.

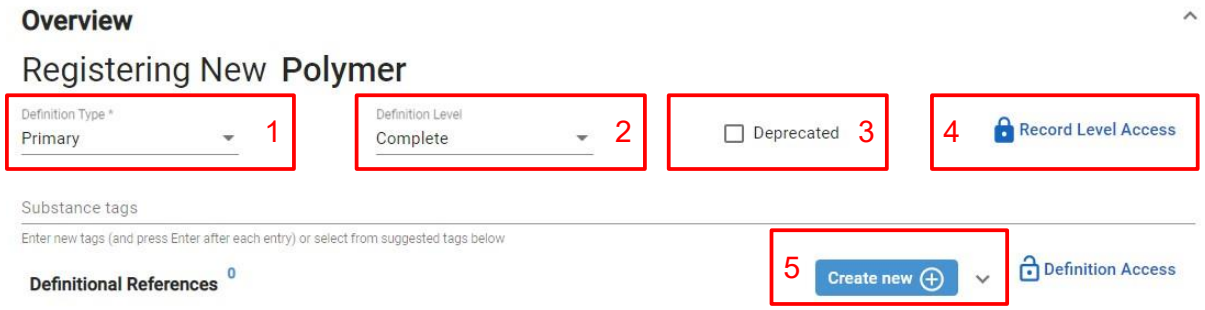


Figure 2. Overview of general information to be included when registering a new polymer

1. Definition Type - hover over and select the down arrow to activate the Edit drop-down. There are two options:
    a. Primary
    b. Alternative - Chemical alternative definition of a protein, nucleic acid, polymer, ring/open sugar etc. Once Alternative is selected a Primary Substance Search field appears

Note: Type the Primary Substance name in search box and select. As you begin, typing a list containing those letters will appear. Make a selection and then select search and the Primary Substance will populate. After submission, the system generates a relationship connecting both definitions. Alternative definition registration is similar to Primary definitions, but Names and Codes are not included.

2. Definition Level – select the down arrow to activate the Edit drop-down.
    a. Always try to enter a Complete definition
    b. Incomplete are allowed for incompletely defined substances.
    c. Representatives are too complex to define completely
3. Deprecated box: selecting this box means it is semi-deleted, or a candidate for deletion. There are other flags for deprecation elsewhere in EU-SRS, but that one also tells the browse/search functions not to show this record unless you specifically click the box allowing it to show.
4. Record Level Access: some substances are public in which case set the Record Level Access to Public by deselecting Protected. For non-public substances, select Protected. Protected means not readily available in public sources, domains, website, etc. (e.g., SciFinder, PubChem).
5. Definitional Reference(s):
    a. Select the Create new + button
    b. The Add Reference screen appears and additional fields will be displayed

Note: Select the down arrow next to Source Type. Use the scroll on the right to navigate and select a Source Type. Source Text/Citation – identifies where the information comes from. Based on the release sensitivity: Check Public Domain if public (If public, add Tags for Public-Domain-Release). Update the Access by deselecting PROTECTED, if applicable. Select Save.

In order to make something Public it has to be made public three times:

- Undo the lock
- Select the Public Domain checkbox
- Enter the Tag as Public Domain Release

Public Domain checkbox should be added for all public references. Every public name should have at least one reference with Public Domain checkbox. Public Domain Release Tag should be used for public records and added to the record when the lock is opened.

Click on Create new + to add more references or select a previously used ref by clicking on reuse to select a previous substance reference.

4.4 Entering of Names

Currently, the following name types are to be used:

- Official names
- Systematic names
- Common names
- Brand names
- Scientific names

Names can be added with "Add Names +". Depending on the type, additional information is displayed. The language of the names is set to English by default. At the same time, the name is always present as "public":

For the correct mapping of the Preferred Term, the correct ticking of display („DN“ Display Name) is crucial.**Option 1:** SMS Preferred Term and EU-SRS Preferred Term (= Display Name) are the same

- In EU-SRS, the Preferred Term is selected as Display Name, and the Additional Listing Name is also ticked

Option 2: SMS Preferred Term and EU-SRS Preferred Term (= Display Name) are not the same

- In EU-SRS:
  - Preferred term is indicated as Display Name
  - SMS Preferred Term is indicated as Additional Listing Name
- In SMS:
  - The public term is indicated as Preferred Term
  - The EU-SRS Preferred Term is indicated as alias, with name source “Substance Validation Group”

Note that there are several reasons why in SMS the Preferred term is not the EU-SRS Preferred Term:

- The action to change the Preferred Term is postponed due to technical reasons
- The EU-SRS Preferred Term is a confidential term, and can therefore not be marked as Preferred Term; in SMS the PT is always a public term

Table 12. Correct mapping of PT in SMS versus in EU-SRS

Options	SMS		EU-SRS	
	Name Reference	Name	Display Name (DN)	Additional Listing Name (AL)
SMS PT = EU-SRS PT	SMS PT = EU-SRS PT	-	Yes	Yes
SMS PT ≠ EU-SRS PT	Alias SMS = EU-SRS PT	Substance Validation Group	Yes	No
	SMS PT = EU-SRS alias		No	Yes

4.4.1 Official name

The name of the substance is entered under Name, then the name type is selected under Type. Languages ("Languages": English), Jurisdiction are selected from the drop-down lists.

Figure 3. Registering an official name

A polymer record can include more than one Official name, but just one name can be used as Display name (DN). The status of the official name is associated with the given jurisdiction. It is possible that an official name is a valid name in EU jurisdiction and other official name will be used in e.g. US jurisdiction.

For the official name, "Naming Organization" should be added. This is done with the "plus" sign next to "Naming Organization" when clicking on „Naming Organization“. If it is selected, the corresponding organization (e.g. BAN, EP, INCI, INN, JAN, USAN) can be selected.

If more than one organization is to be registered, additional "Naming Organizations" must be added using the "plus" sign:

Jurisdiction is registered only for official name. This always corresponds to the countries for which this designation can be used. The following table shows the jurisdiction for Preferred Term (Display name) and aliases.

Table 13. Listing of naming organizations and corresponding jurisdictions

Naming organization	Description	Jurisdiction if Official Name is included as	
		Display Name	Alias
EP	European Pharmacopeia	EU	-
INN	International Nonpriority Name	EU	EU
USAN	United Sates Adopted Name	US*	US
USP	United States Pharmacopeia	US*	US
BAN	British Adopted Name	EU	GB
BP	British Pharmacopeia	EU	GB
JAN	Japanese Adopted Name	JP**	JP
INCI	International Nomenclature of Cosmetic Ingredients	EU	-

*If USAN/USP is the same as INN: then substance will get 2 Naming Organizations:

1. INN (Jurisdiction EU)

2. USAN (Jurisdiction US)

If USAN/USP is not the same as INN, then INN will be included as DN (Jurisdiction EU), USAN/USP will be included as Alias (Jurisdiction US)

**If JAN is the same as INN: then substance will get 2 Naming Organizations:

1. INN (Jurisdiction EU)

2. JAN (Jurisdiction JP)

If JAN is not the same as INN, then INN will be included as DN (Jurisdiction EU), JAP will be included as Alias (Jurisdiction JP)

Subsequently, the references for the corresponding name must be entered. References can be added with "Create new +". A dialogue window opens for this purpose. Using "add reference", the information on the source type (see the list of "Source types" used at the end of the document) and the "Citation" (free text for the actual citation) can be inserted. A checkmark should be placed next to "Public Domain" for the public names.

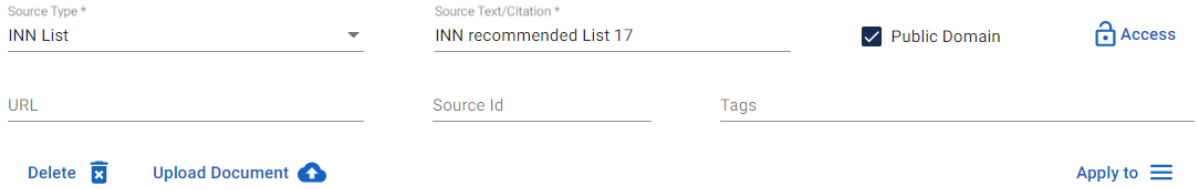


Figure 4. Registering references

Once all the information for the respective Name has been entered, it can be checked directly in the display:

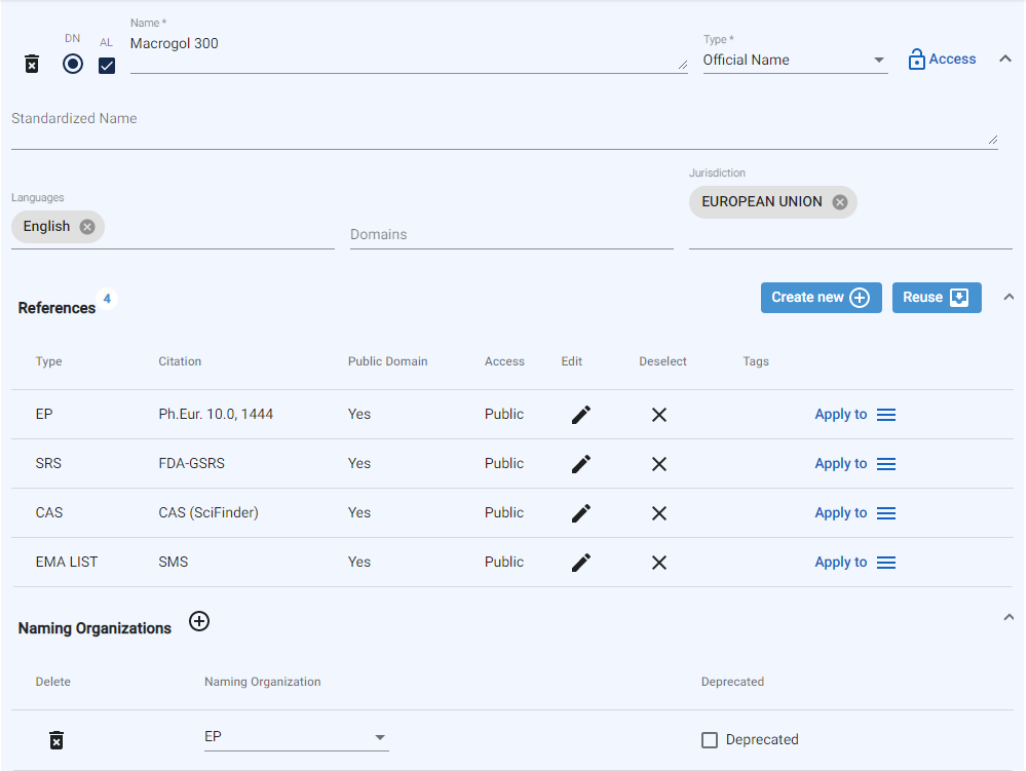


Figure 5. Official name including references and naming organization

4.4.2 Systematic Name

The systematic name of the substance is entered under the tab "Name", then the name type is selected under "Type". As with the first name, the references are opened and saved in a new dialogue window ("reuse"). When entering systematic names and aliases, care must be taken to ensure IUPAC-compliant display. The use of HTML meta-language ensures the correct use of Greek letters, Roman numerals, superscript and subscript, among others. The list of HTML codes to be used can be found at the end of this document (see Appendix 1).

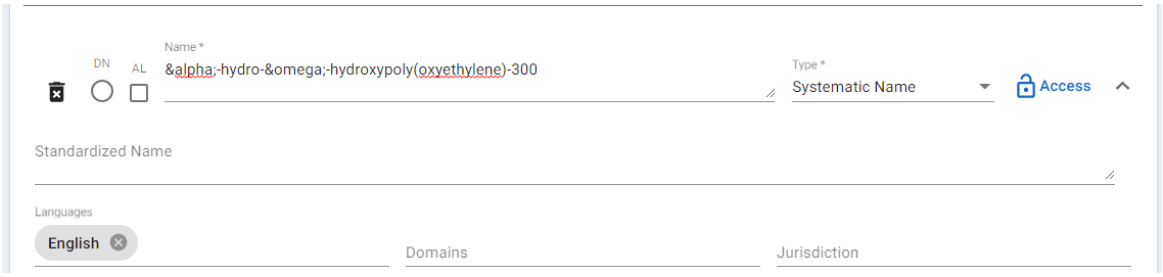


Figure 6. Registering systematic name in HTML format

Name registered with html (Figure 6) is displayed in browse mode as follows: α-hydro-ω-hydroxypoly(oxyethylene)-300. The IUPAC (= INN description: systematic name in the INN list) are mapped as references. Other systematic names (e.g. CAS name) can also be entered. This is the preferred designation in SciFinder. The relevant references are attached. Non-coverted CAS names should not be used.

4.4.3 Alias

Under the tab "Name" the name of the substance is added, then the name type is selected under "Type". Under "Languages" the language ("Languages": English) must be used for this name type (English is set by the program). No tick must be set for „DN“ or Additional Listing Name „AL“. The company codes can be entered with different spellings, depending on the reference database used. Brand names can also be registered for polymers in the same way.

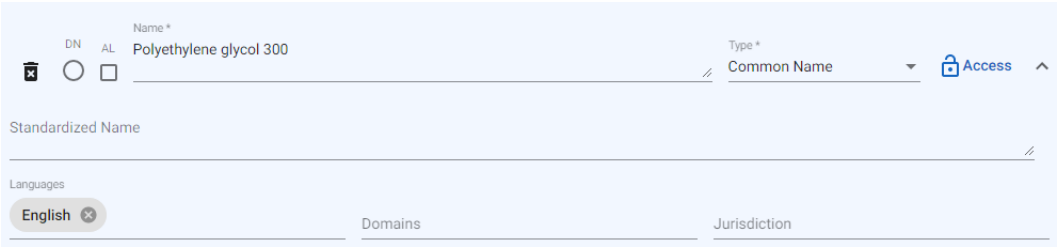


Figure 7. Registering alias

For the locked aliases (protected, non-public), the access lock must be closed, and in the options under the lock symbol, a tick is set for "Protected".

4.5 Polymer classification

The data under this section provide additional information on the structure of the polymer (copolymer, homopolymer), its geometry (linear, cyclic, ...) and origin (synthetic, biosynthetic).

Polymer class, source type and polymer geometry are drop-down driven by the CV. Only one position from CV can be selected. In contrast, polymer subclass includes multi-select drop-down list driven by the CV. Parent substance can be added, if needed, by substance search/selector. For this purpose use the substance search box and select the Parent substance which should be pre-registered.

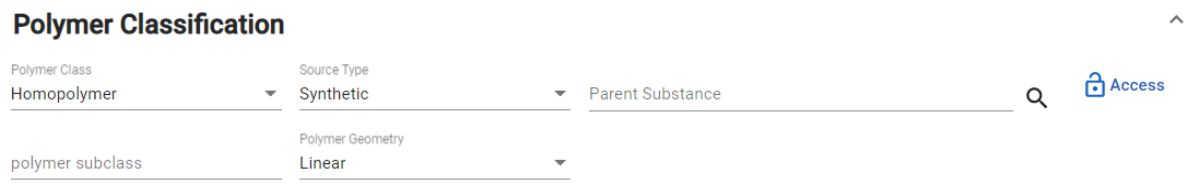


Figure 8. Registering Polymer Classification

4.6 Monomers and Starting Materials

Monomers must be pre-registered. To expand the monomers card, select Monomers. If a monomer already exists in the database, it is entered by searching under "monomer substance". The search can be performed by CAS No. or chemical name.

Monomer type includes drop-down list driven by CV.

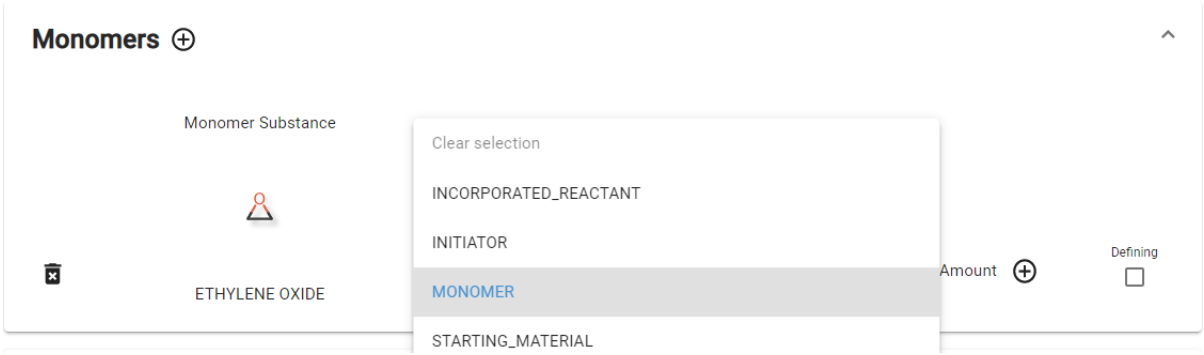


Figure 9. Registering of Monomers

The information under amount is used to determine the mol ratio or weight ration of the respective monomer in the polymer. The amount parameter can be edited in the pop-up window. The units should be per polymer for homopolymers and no units for copolymers. The amount could be a range, average or limits.

Figure 10. Registering of Amount

After select save, you are returned to the Polymer registration form and the amount details are displayed on the Monomers card.

4.7 Structure

A molecular structure should be included for registering a polymer. This can be done in two ways:

- By using relevant SMILES
- By drawing the molecular structure

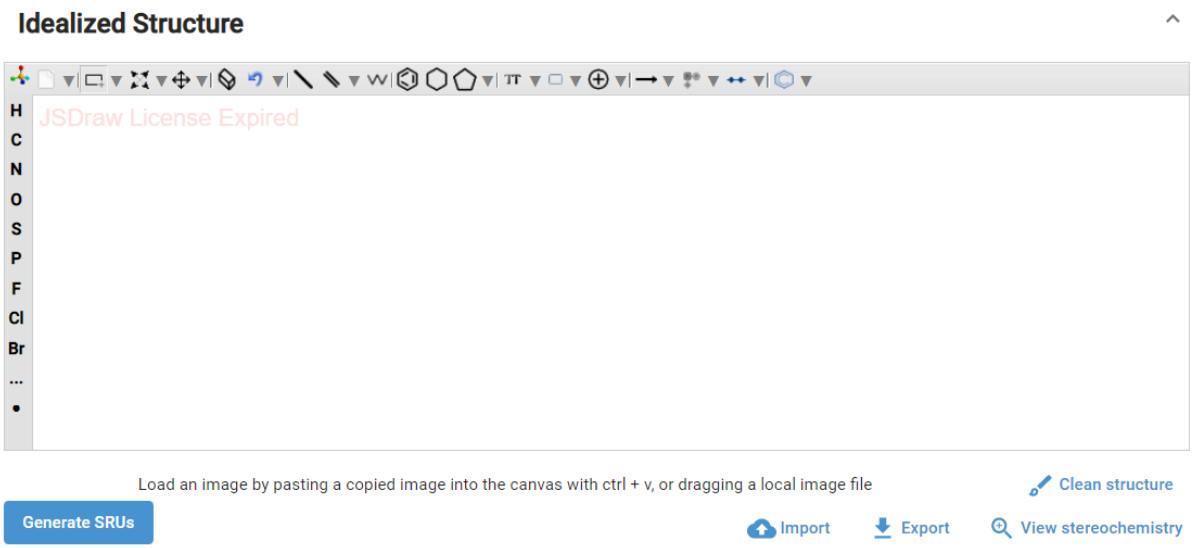


Figure 11. Drawing tool for registering a molecular structure

4.7.1 Drawing tool for molecular structures

For polymers, it is required to insert the molecular structure by using the drawing tool. Instructions for using the drawing tool are included below.

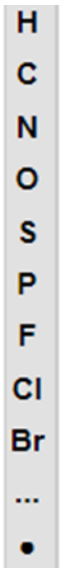
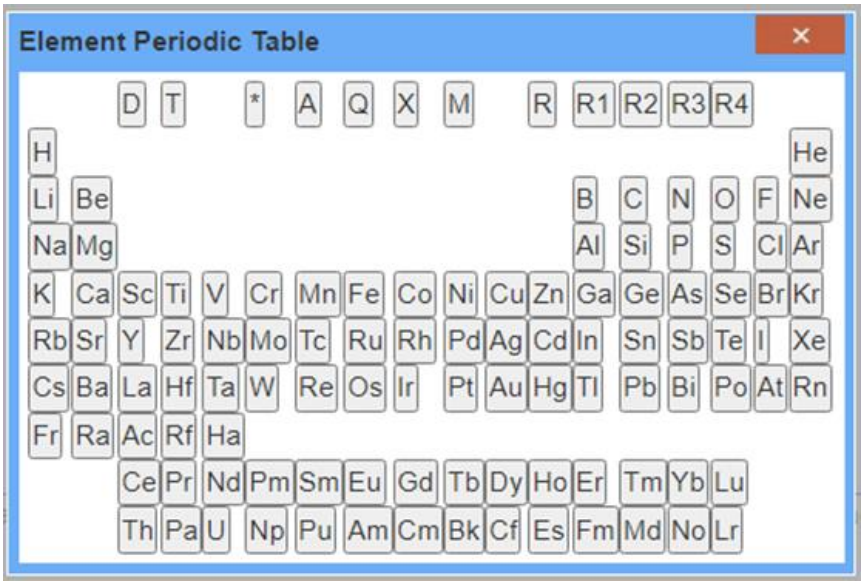
Table 14. Instructions for the horizontal part of the drawing tool

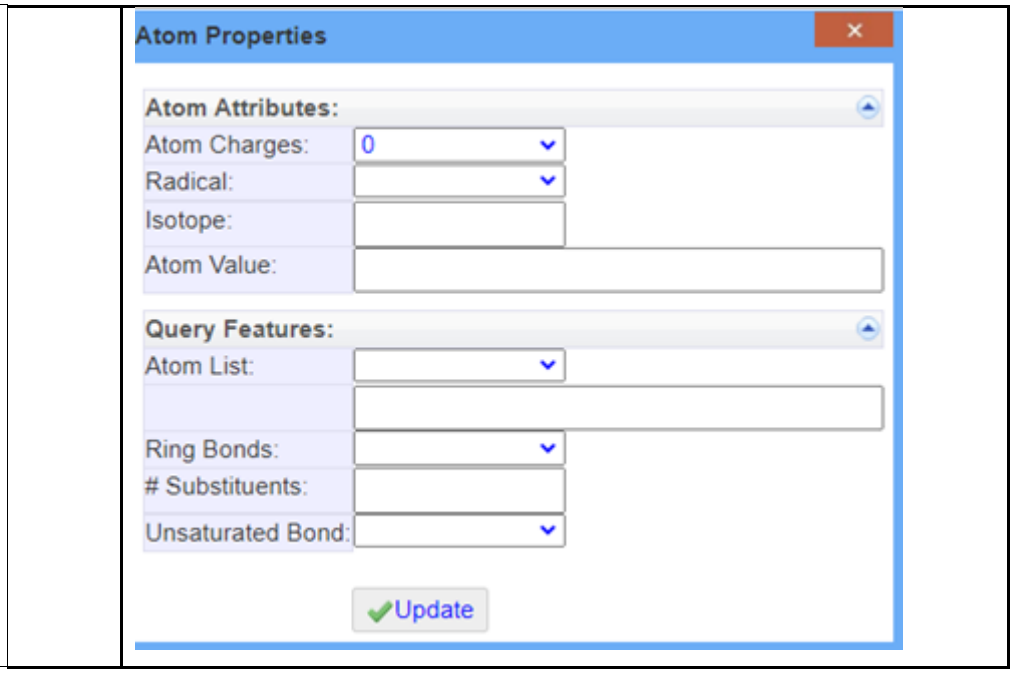
	
	JSDraw V5.2.0 (java script editor for chemical structure and biologics)
	Clear all contents (new page)
	„Triangle“ for whole list of different tasks mainly for the selection of the structure
	„Triangle“ for whole list of different tasks changing the position of the structure (up to the middle), increasing, reducing, rotation

	„Triangle“ for whole list of different tasks changing the position of the structure, every direction possible
	Eraser
	„Triangle“ for whole list of different tasks back / forward arrow
	Single bond
	„Triangle“ for whole list of different tasks Other bonds
	Chain tool
	+ „Triangle“ for whole list of different tasks
	
	

	„Triangle“ for whole list of different tasks Brackets for e.g. polymers
	„Triangle“ for whole list of different tasks + and – for ions

Table 15. Instructions for the vertical part of the drawing tool

		Element periodic table: 
		Atom properties:



4.7.2 Entering of the Structure

The structure can be drawn using the editor (see chemical section) or inserted as SMILES. For this purpose, SMILES can be copied from reference databases (e.g. CAS SciFinder, G-SRS).

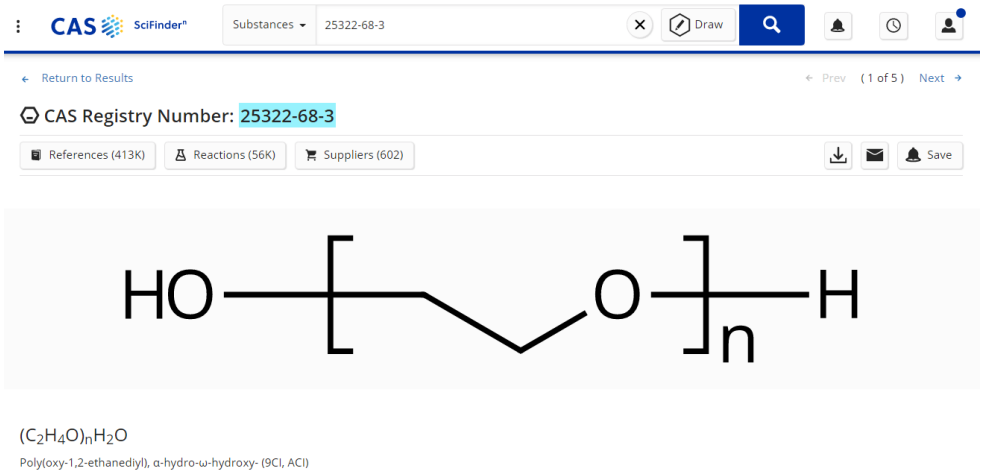


Figure 12. Structure as found in SciFinder

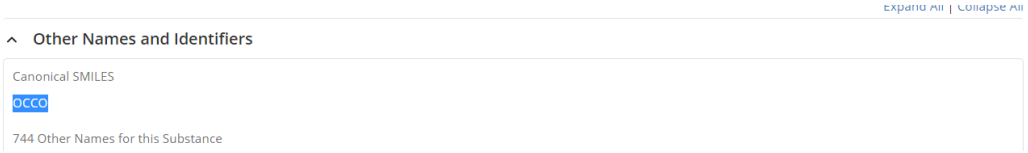


Figure 13. SMILES as found in SciFinder

and then simply inserted directly in the structure area with 'Crl+v':

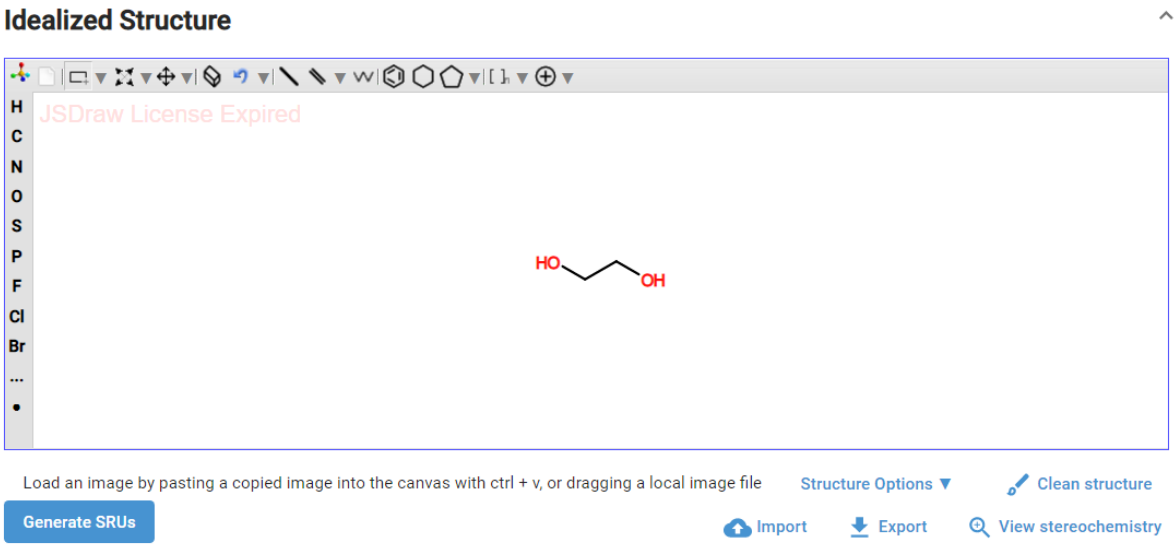


Figure 14. Structure pasted in the drawing canvas

If necessary, the structure can be edited manually to ensure the best representation of the polymer. It is important to know that the brackets are not imported and must be added manually. The bracket types [ ] can be found in the JS Draw Canvas.

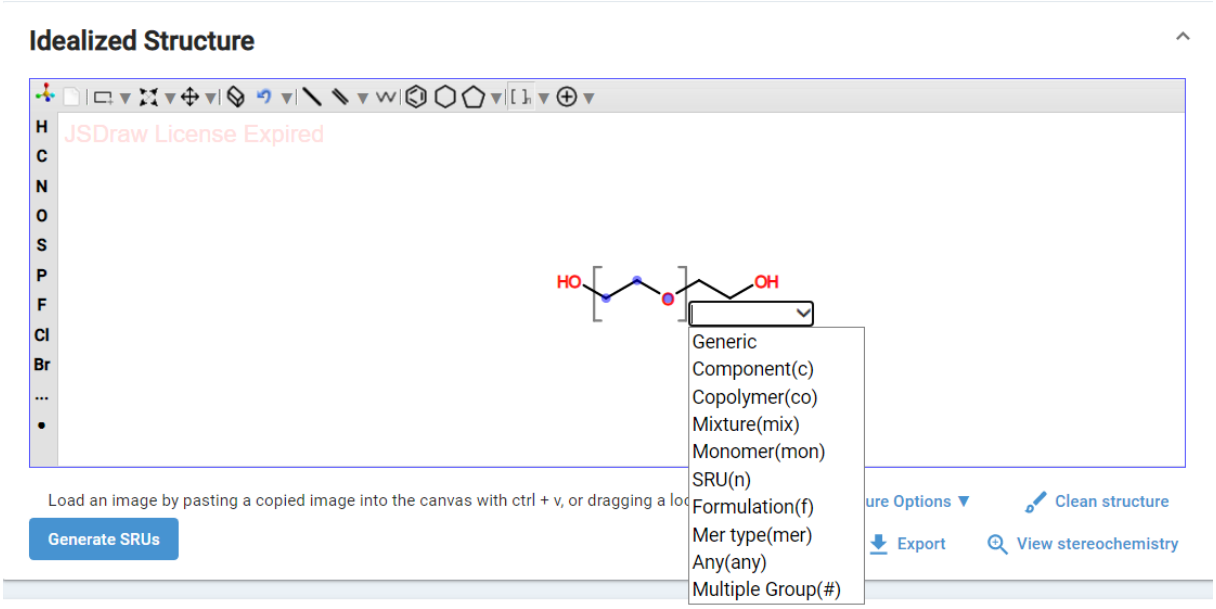


Figure 15. Adding brackets in polymer structure

When a bracket is inserted, a drop-down list is automatically generated, in which you can specify the type of bracketing. Copolymer(co) and SRU(n) play the most important role here.

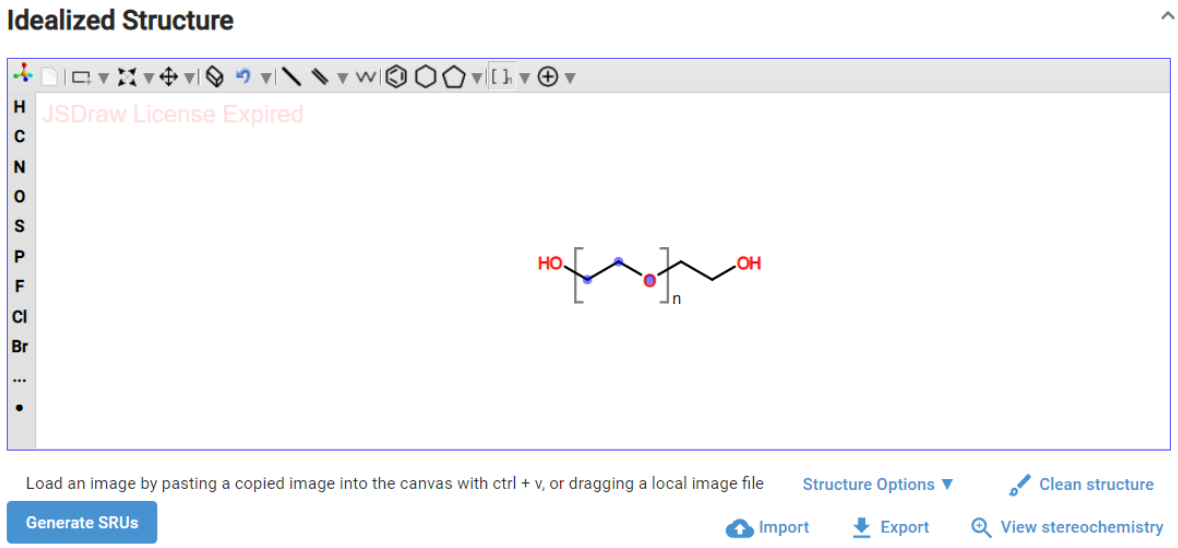


Figure 16. Selecting of bracket type in structure

If the structure is to be rotated, it is selected in the upper bar  . An atom in the structure is marked by clicking on it. With a further click (+hold) in the image, the structure can be rotated as desired.

The structure must always be assigned a reference. However, this reference is not entered in the structure, but at the very top of the data set under "Definitional Reference":

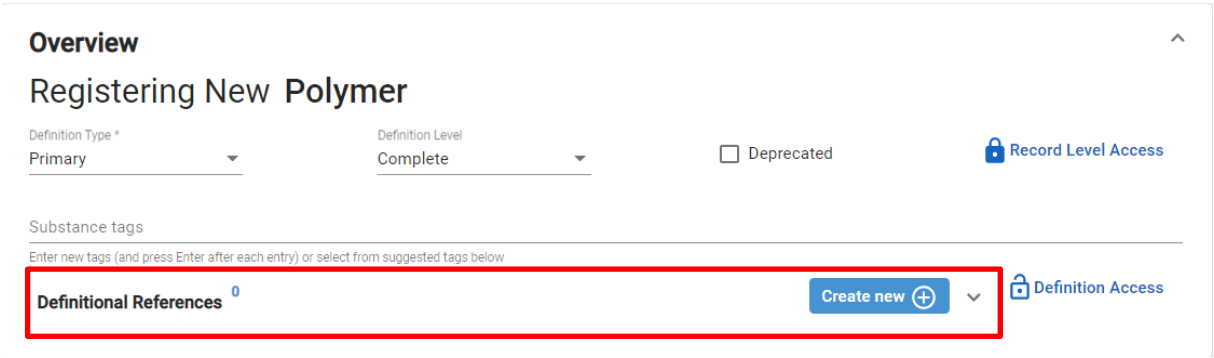


Figure 17. Registering a definitional reference

If the structure can be released, "Public Access" reference to it should be inserted, then further reference which occupy this structure.

Compilation of possible references for the definition:

- For INNs — INN list reference
- For Pharmacopoeia — Pharmacopoeia reference
- General reference — confirmation of the structure (e.g. CAS, G-SRS)

If publication of the dataset is allowed, the Access lock icon should be opened. To enable the release, a tag Public Domain Release must be inserted at a definitional reference at this time. The release of the record should only be done finally when all information on the substance has already been entered (see section 5.13).

4.8 Structural units

Structural units will be generated automatically from the Idealized Structure canvas. To get the structural units select the Generate SRUs button.

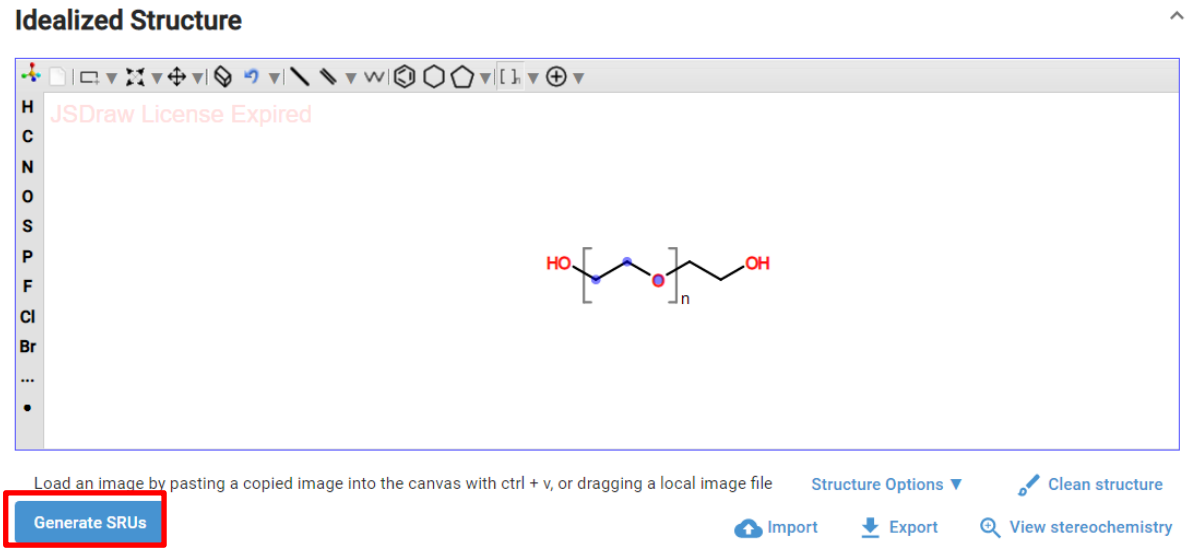


Figure 18. Generation of Structural units

The generated values can be manually updated.

Figure 19. Edit Structural units

Each Structural Units has a field for:

1. SRU type, which is drop-down list driven by the CV
2. Label
3. Attachment count – this value is computed and cannot be changed
4. Amount – to add amount, select +. A pop-up window will be displayed to edit the parameter

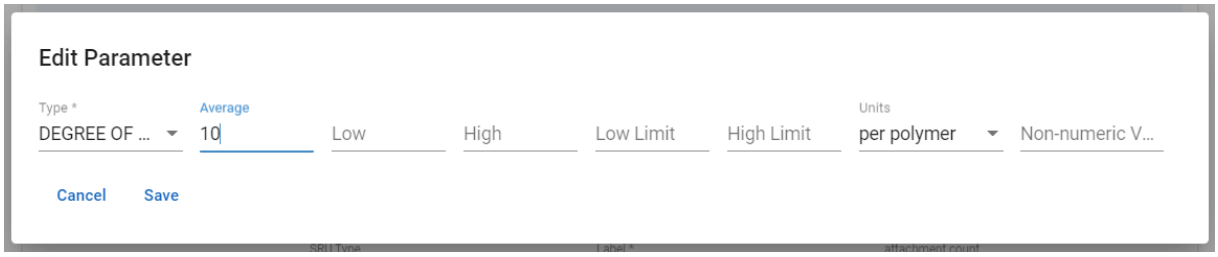


Figure 20. Registration of Amount

Degree of polymerization for structural units and degree of Substitution for substituents can be determined. The amount can be a range, average or low/high limits. Any additional information can be captured under Non numerical values. Select save to be returned to the polymer registration form.

5. Connectivity

4.9 Agent Modification

Agent Modification is only added if relevant for the respective polymer.

4.10 Structural Modification

Structural Modification is only added if relevant for the respective polymer.

4.11 Physical Modification

Physical Modification is only added if relevant for the respective polymer.

4.12 Codes

The code section in edit mode includes substance identifiers from other databases, RMS category, RMS domain and ATC code. In browse mode all those codes will be displayed in two different sections. Substance identifiers from other databases will be displayed as identifier. RMS category, RMS domain and ATC code will be shown as classifications.

4.12.1 Substance identifiers from other databases

The codes of the substance can be selected from the code system drop down list. Type of the code is also defined by the drop-down list. There are several types that can be selected from the list:

- Primary: to be used if the code uniquely describes the structure
- Generic (family): is selected if the code is not precisely specified and can be assigned to several substances, whole family
- Superseded: is set if the code numbers is already deprecated
- Alternative: is used when there are two codes that correctly describe the same structure. It is often found on SciFinder for recently recorded substance.

To enter the CAS No., CAS is selected from the "Code System" drop-down list. The type is set as described above. Cas No. is then inserted under Code.

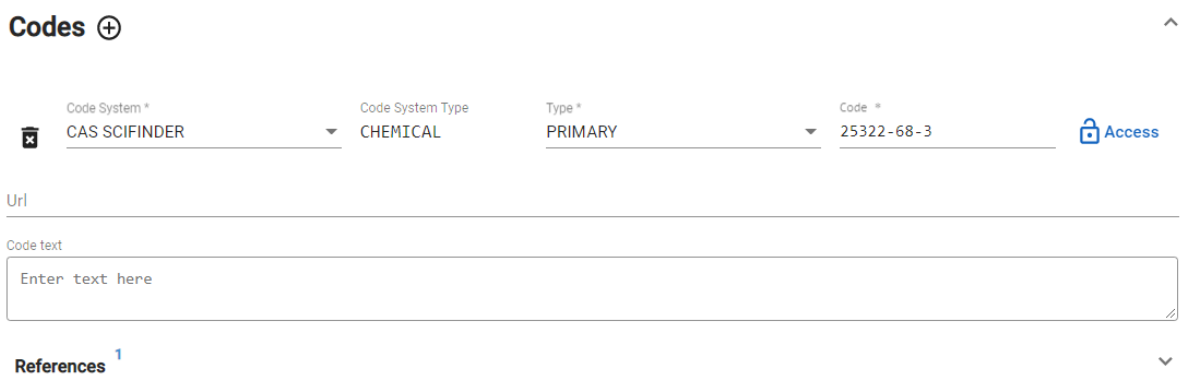


Figure 21. Registration of CAS ID

CAS is a single identifier that requires a reference. The reference is to be entered as follows:

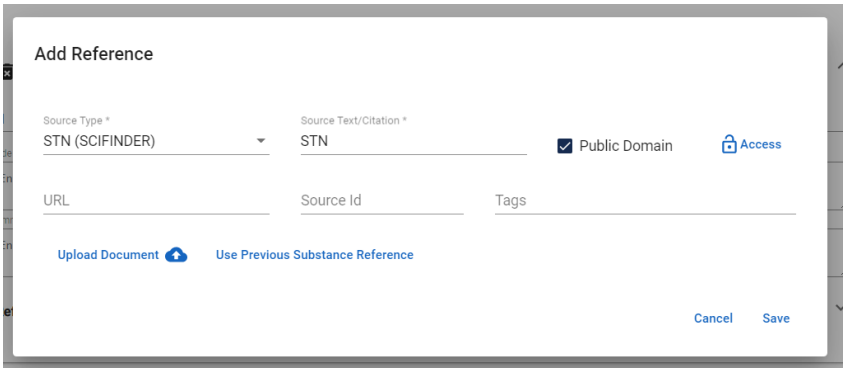


Figure 22. Reference for CAS ID

Other codes are included in the same way (e.g. UNII, SMSID, xEVMPD, INN, EDQM), but they do not require a reference. EU-SRS will automatically construct URLs for the following Code Systems which can be accessed in the hyperlink on the view page:

Table 16. Code systems and associated hyperlinks

Code System	Hyperlink
CAS	ChemIDplus
FDA-UNII	G-SRS
PubChem	PubChem
INN	The School of INN
EDQM	Knowledge Database EDQM
NCI Thesaurus	NIH National cancer institute

SVGID is EU-SRS own identifier and will be generated automatically for each new record.

4.12.2 RMS category and domain

The classification of the substance is entered under code section. To enter the “category” or “domain”, RMS is selected from the "Code System" drop-down list. The type is set to "Generic (family)" and the number of the category is added under “Code”.

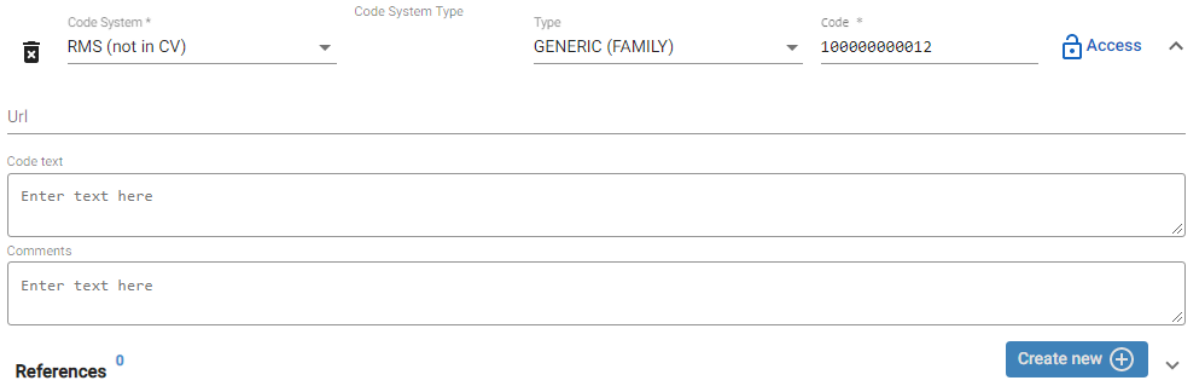


Figure 23. Entering RMS category and domain

Neither category nor domain need a reference.

RMS categories and domains relevant for polymer registration are shown in the table below. A complete list is available in the General EU-SRS User Guide.

Table 17. Applicable RMS codes for Domain and Category for polymers

RMS Code	Domain
100000000012	Human use
100000000013	Veterinary use
RMS Code	**Category**
200000005022	Polymer

4.12.3 ATC Code

The ATC Code level 5 of the substance is entered under code section. The “WHO-ATC” is selected from the “Code System” drop-down list. The type is set to “Generic (family)” and the number of the category is added under “Code”.

ATC code does not require a reference. The use of the type “Generic (family)” is mandatory. “Code system type”: ”Pharmclass” is generated by the system.

NOTE: Check the information in the browse mode. If ATC code is shown there under tab Identifier, it means that this code is not yet stored. In such a case inform the key user.

In such cases it is also possible to build the hierarchy tree from the WHO-ATC hierarchy itself by adding the levels in ‘Code text’ one after the other in the following way: ”ATC| Level 1| Level 2| Level 3| Level 4| Level 5”. In this way ATC Code will also be displayed as Classification in browse mode.

4.13 Notes

Notes are generated automatically and includes system validation messages.

4.14 Properties

Depending on the polymer, additional substance information can be included to the Properties card. Density, Mol_Weight:Number Average, Mol_Weight:Weight Average, Particle size, Viscosity:Dynamic, Viscosity:Kinematic can be selected from the Name drop-down list.

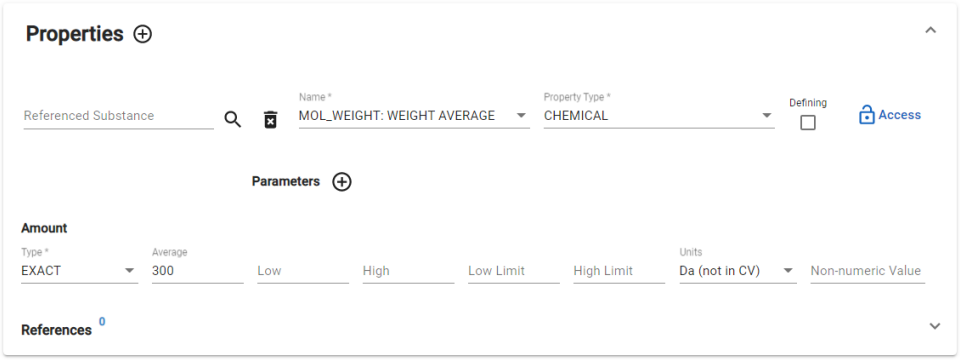


Figure 24. Entering of Properties

Property type can be Chemical, Enzymatic or Physical. Default is empty Tick box of Defining. The check mark can be set if the requirements are mandatory. It is also used in the family of substances that differ in their certain properties (e.g. hypromellose and viscosity). Amount can be registered with type information “mol ratio” or ”weight ratio” can be registered, as mean value (Average), or range (Low Limit and High Limit). Units can be selected, but it is not mandatory.

4.15 Relationships

Relationships can only be generated for existing data sets. If a salt is entered, the basic substance must therefore be entered first. In the case of polymers, the generation of the hierarchy of whole families plays an important role. In this way, the general polymers (e.g. Macrogol) and specified data sets (e.g. Macrogol 300) can be linked to each other. The link is generated from the parent record – Macrogol:

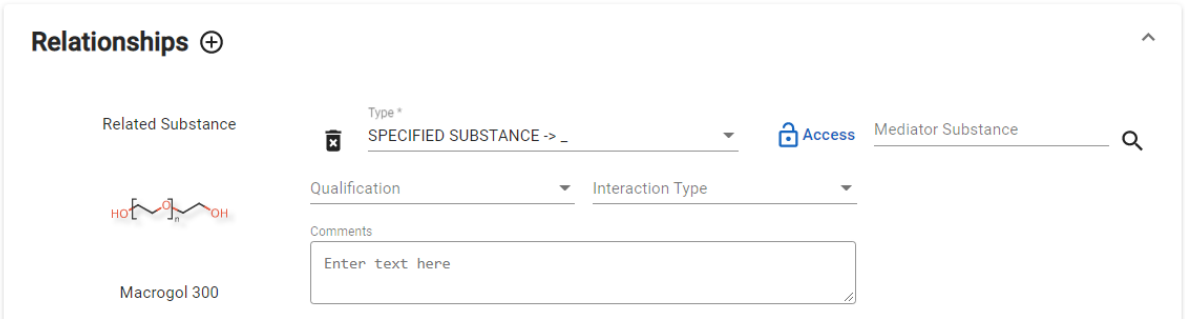


Figure 25. Entering of Relationships

For this purpose Type: “Specified substance ->_” will be selected in edit mode of Macrogol. This linkage appears automatic at the specified subordinate record Macrogol 300.

NOTE: Starting from Macrogol 300, this link cannot be generated. This relationship allows switching from Macrogol data set to the respective specified child record in browse mode.

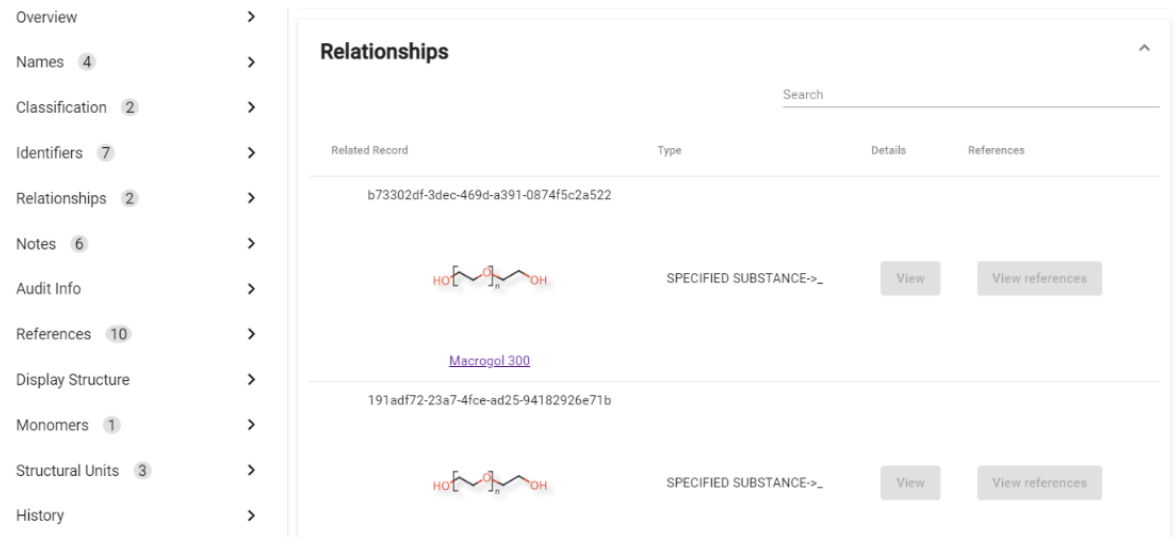


Figure 26. Entered Relationship in browse mode on parent substance level

In the record Macrogol 300 must be added another relationship. Here Macrogol is selected under related substance. "Active moiety" from the CV is selected as the type:

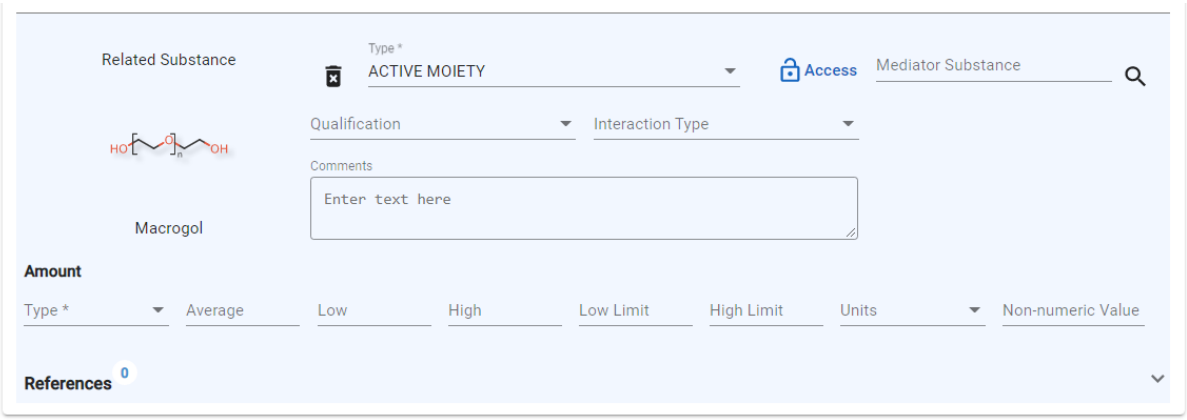


Figure 27. Entering Relationship „Active Moiety" on child record level

NOTE: Starting from Macrogol, this link can not be generated. This relationship enables the generation of the hierarchy for all records of the respective family:

Figure 28. Hierarchy which results from „Active Moiety" relationship as displayed in browse mode

4.16 References

References can be included directly during the registration of names, codes or relationships, etc. Alternatively, registration can be started by recording all references, which are then used in the course of registering further information. References can be added, updated, or removed from this card. Public Domain checkbox should be added for all public references. All References should include Public Domain checkbox. Public Domain Release Tag should be used for public records and added to the record when the lock for the full dataset is opened. This is then equivalent to the release for public of the dataset. The complete list of valid references can be found in Appendix 3.

4.17 Completion of Registration

To complete the registration of "Polymer", a "Definition Reference" (see also 5.2.2) must be inserted. If the record is allowed to be published, the Access lock icon should be opened.

The data set is not saved and inserted into the database until "Submit" is clicked. A dialogue window appears. If all messages are highlighted in green, click on "Dismiss All" and then on "Submit". The data set can now be viewed with "View Substance" in the browse mode.

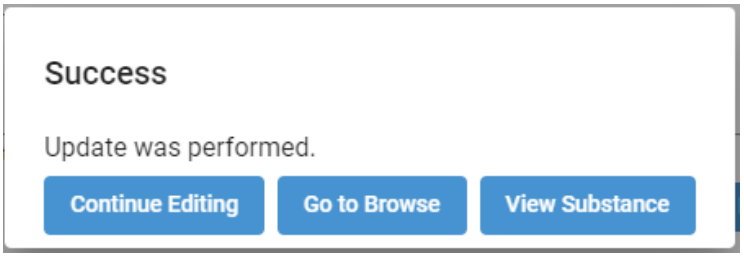


Figure 29. Notification of completed substance registration

If messages with a yellow background appear, these details must first be checked for correctness. Registration can still take place. Messages with a red background do not allow registration. These errors must first be corrected in the data set so that registration can subsequently take place.

NOTE: Please make sure that the editing of the substance mode does not exceed 120 min. If this time is exceeded, submission is not possible.

4.18 Verification of completed record

The final check of the registration shall be performed in the browse mode:

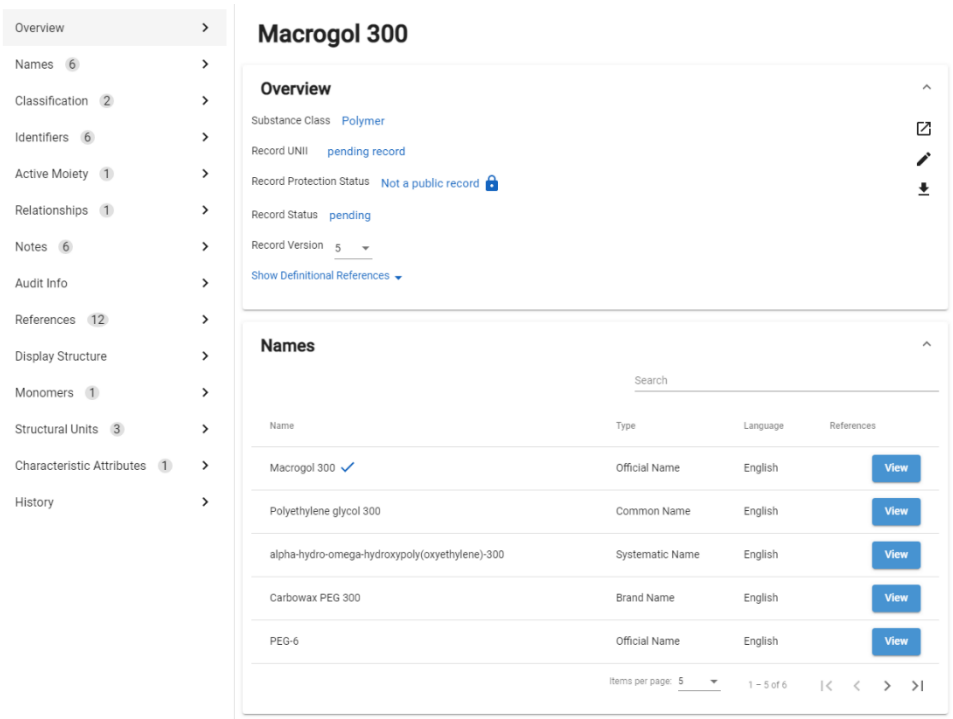


Figure 30. Extract from the browse mode

4.19 Concept upgrade

Some polymers were registered as concepts during data load in EU-SRS. Under Concept, polymers can also be registered in the simplified registration procedure. These records can be found in Browse mode in this way by using of RMS Polymer Category: 200000005022. The data sets under Concept can be upgraded to correct polymer record when the complete information on the substance is available.

For the Concept upgrade to “Polymer” the following steps are necessary:

1. Go to the field “Advanced Features” in the headline.
2. Click in the scroll down menu on ”Change Substance Class”.
3. Choose the applicable substance class in the field ”New Class”.
4. Check the names under Names after which the polymer record was opened.
5. Continue with the steps described from section 5.3 above.

4.20 Change Reason

If a substance is updated (e.g. new name added), the reason for creating a new version must be recorded under Change reason. This tab appears only from the second version. So, it is not present at the first registration. In order to simplify the future search, a short valid reason should be given if possible. Examples are summarized in the table:

Table 18. Examples of change reasons

Change reason	Comment
Name	Name was added/removed
RMS	RMS was added/exchanged
Identifier	Identifier was added/removed
PT	Preferred Term was changed
Relationships	Relationship was added/removed
Properties	Properties was added/removed
Modification	Modification was added/removed

Multiple use of different reasons is possible, e.g. name, identifier, RMS.

4.21 Registration of complex polymers

The example of *Neisseria meningiditis, Serogroup W135, oligosaccharide, spacer modified* is used to summarise the registration of complex polymer. In this chapter, only sections that deviate from the previous approach are discussed.

1. The structure can be copied from a similar dataset. For this purpose, select the structure from existing record (“ctr+c”) and past it into the new record registration (“ctl+v”). SMILEs from other databases can also be used.

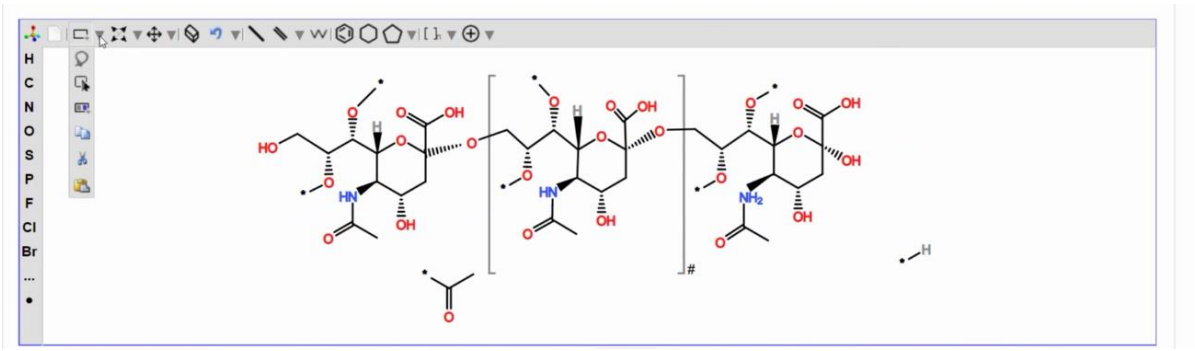


Figure 31. Step 1 of building complex polymers - adding the main structure

2. To be able to make further modifications of the copied structure, the structure must be reduced in size, select the whole structure and make it smaller:

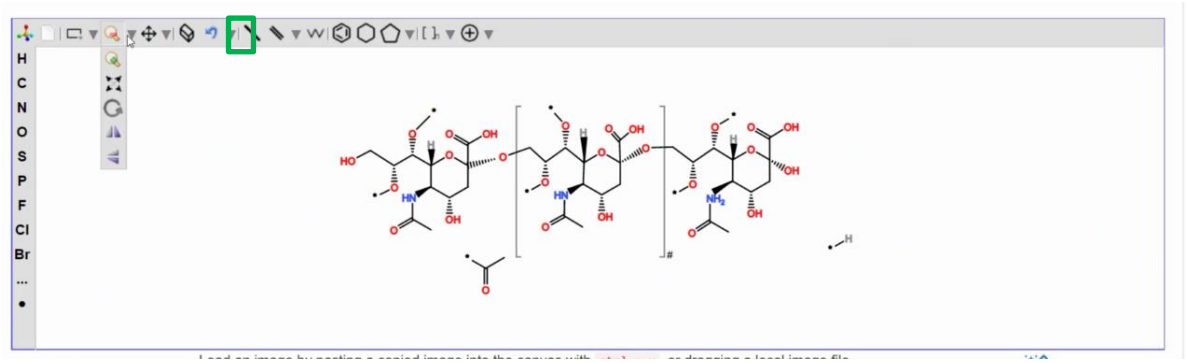


Figure 32. Step 2 of building complex polymers - resizing of the main structure

3. In the next step, the structure can be moved to the side so that there is still enough space for the side chain. Select all and move to the left. The best way to move the structure is by using the navigation arrows on the keyboard.

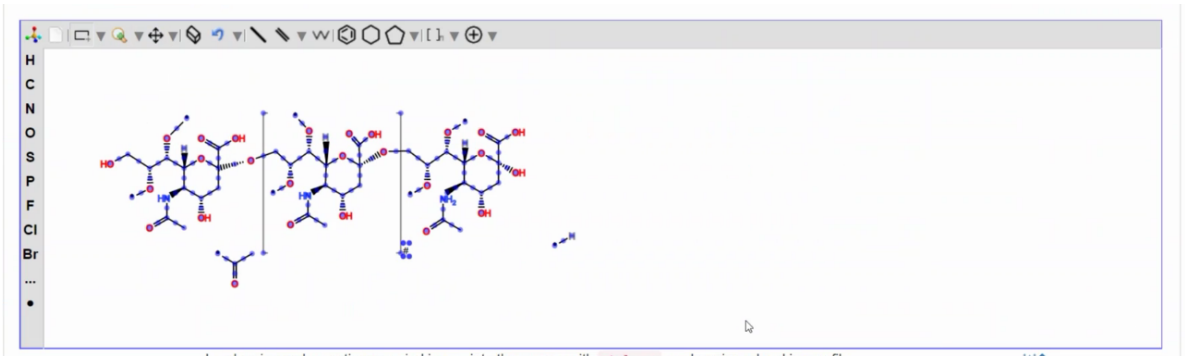


Figure 33. Step 3 of building complex polymers - repositioning of the main structure

4. According to the documentation, the structure is updated:

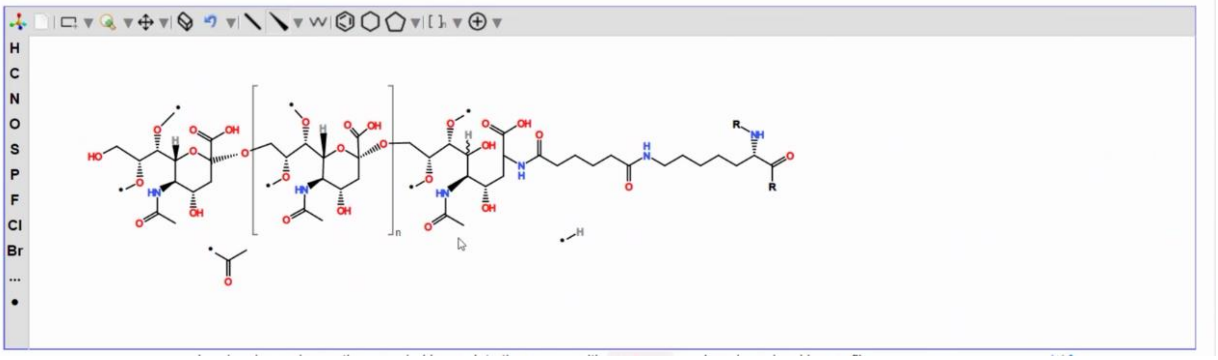


Figure 34. Step 4 of building complex polymers - adding the side structure(s)

To check the structure for correctness, Generate SRUs should always be selected.

5. Registration of Structural modifications:

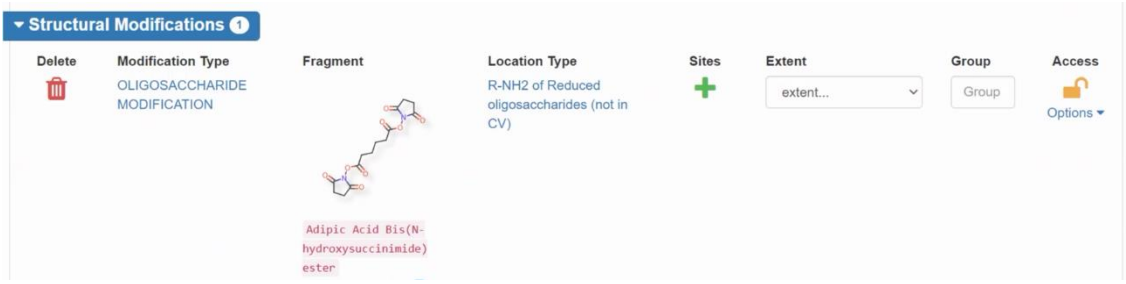


Figure 35. Registration of Structural modifications

the chemical substance *Adipic Acid Bis(N-hydroxsuccinimide)adipate* is used in the production of our polymer.

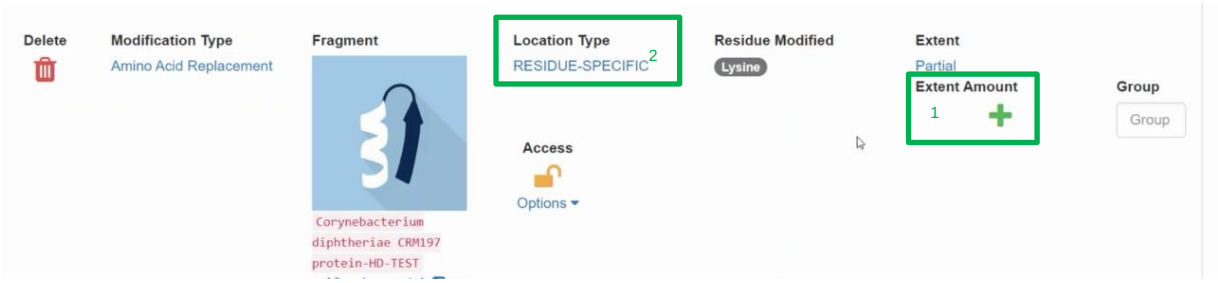


Figure 36. Registration of the modified polymer

if needed amount will be defined in the pop-up window (1):

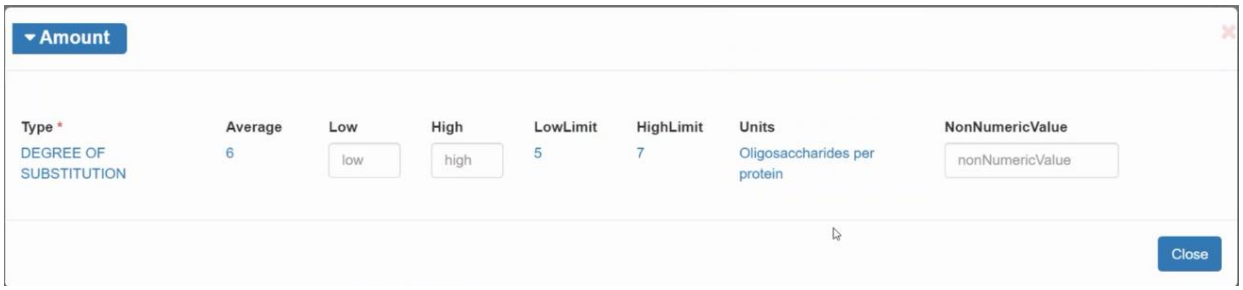


Figure 37. Registration of details of the fragment amount

Location type: residue specific and site specific (2)

Residue specific: there are 49 lysin in the structure, but just 5-7 lysine residues will be populated with the structure

Site specific: to use if you know exactly the position of lysine

6. Add Relationships:

Figure 38. Registration of relationships

make relationship to Structurally Diverse definition of this record

7. Add Properties:

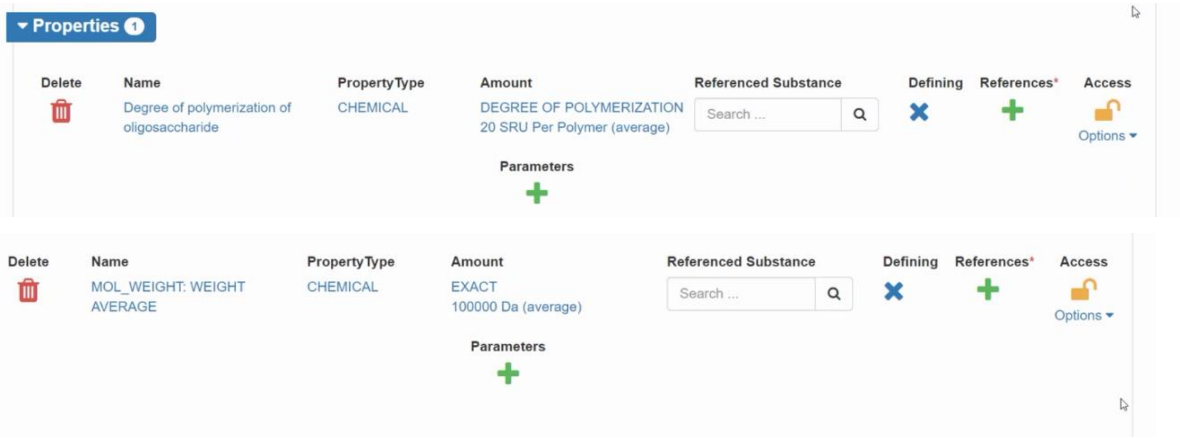


Figure 39. Adding properties

8. Finally submit the record. When registering a substance for the first time, a single version should be generated if possible. For this reason, it is recommended to prepare all necessary information in advance and only then to register a substance.

4.22 Most common mistakes – troubleshoot

1. New bonds are not accepted by the system.

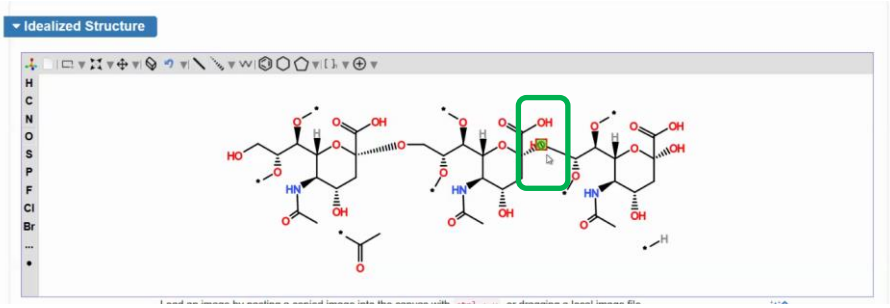


Figure 40. Example of wrong group

OH is still displayed, but it shoud be an ether

In such situation try to draw the bond from different direction

2. Bond lengthening

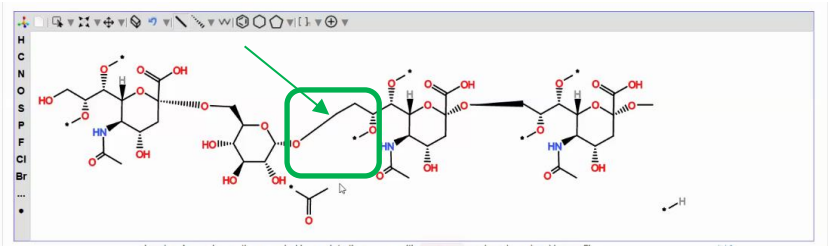


Figure 41. Example of wrong bond lenght

A connection between two units should be extended, instead additional carbon atom was added

However, this atom is difficult to recognise. Always check SRUs!

3. Too many SRUs were generated

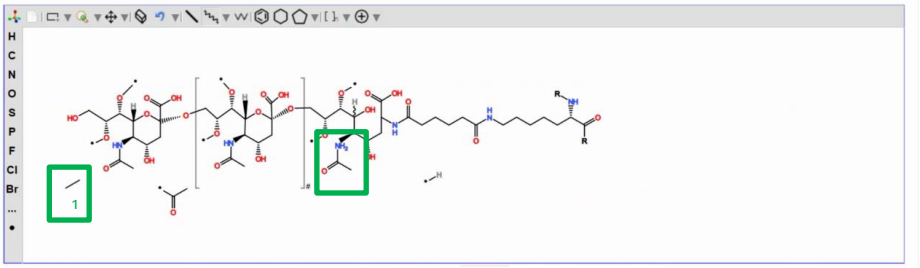


Figure 42. Example of exceeding atoms added by mistake

check that additional atoms have not been added by mistake (1)

amid as SRU was too much. You can see error in the structure: „NH_2“ for amid bond instead of „NH“. Sometimes the system doesn‘t accept the new bond. In such situation try to draw it from different direction

4. wrong annotation behind brackets

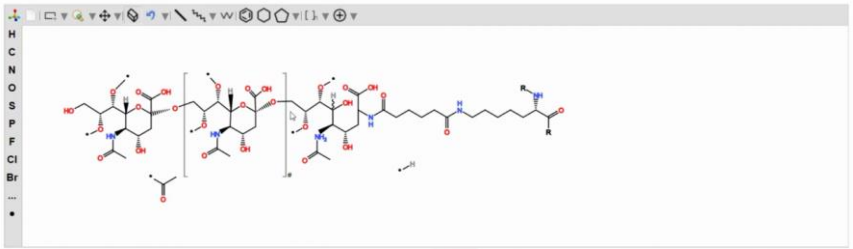


Figure 43. Example of wrong annotation

remove brackets and add new one, put „n“ for SRU

5. connection of residue to the structure

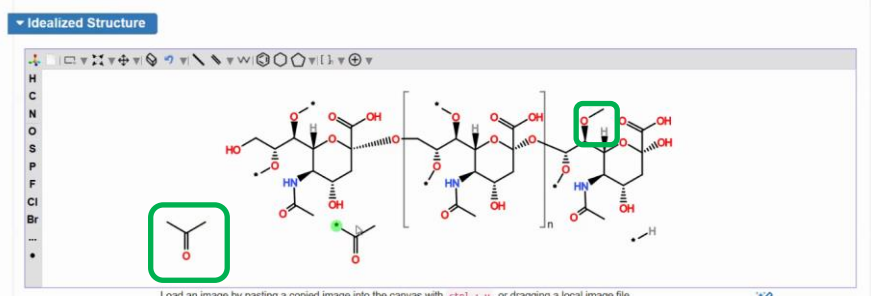


Figure 44. Example of residue misplacing

Use right mouse button and select „attach point“ from the „pop-up window“

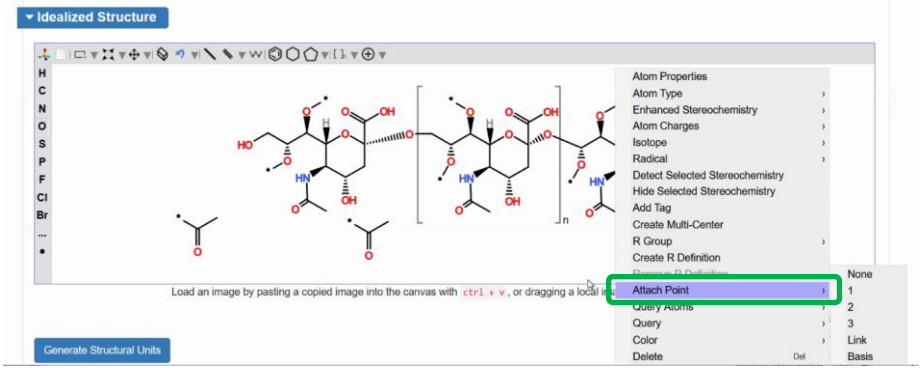


Figure 45. Correction of residue misplacing

You can use „link“ or „number“, by using of „link“:

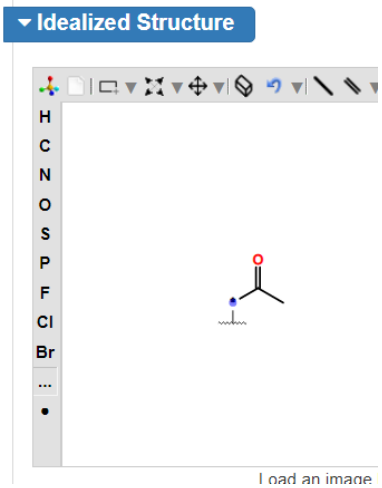


Figure 46. Checking the residue appropriateness

Check the structural units, after the groups are allocated

5 Appendix

5.1 HTML code elements for displaying special characters

HTML Code	HTML View
₂	x_2
²	x^2
←	←
→	→
<	<
>	>
±	±
Α	Α
α	α
Β	Β
β	β
Γ	Γ
γ	γ
Δ	Δ
δ	δ
Ε	Ε
ε	ε
Ζ	Ζ
ζ	ζ
Η	Η
η	η
Θ	Θ
θ	θ
Ι	Ι

HTML Code	HTML View
ι	ι
Κ	K
κ	κ
Λ	Λ
λ	λ
Μ	M
μ	μ
Ν	N
ν	ν
Ξ	Ξ
ξ	ξ
Ο	O
ο	ο
Π	Π
π	π
Ρ	P
ρ	ρ
Σ	Σ
σ	σ
Τ	T
τ	τ
Υ	Y
υ	υ
Φ	Φ
φ	φ
Χ	X

HTML Code	HTML View
χ	χ
Ψ	Ψ
ψ	ψ
Ω	Ω
ω	ω
±	±
ß	ß
Ä	Ä
ä	ä
Ö	Ö
ö	ö
Ü	Ü
ü	ü
§	§
¯	¯
Ⅰ	Ⅰ
Ⅱ	Ⅱ
Ⅲ	Ⅲ
Ⅳ	Ⅳ
Ⅴ	Ⅴ
Ⅵ	Ⅵ
Ⅶ	Ⅶ
Ⅷ	Ⅷ
Ⅸ	Ⅸ
Ⅹ	Ⅹ
Ⅺ	Ⅺ

HTML Code	HTML View
Ⅻ	℻
ⅩⅢ	Ⅹⅲ
ⅩⅣ	Ⅹⅳ
ⅩⅤ	Ⅹⅴ
ⅩⅥ	Ⅹⅵ
ⅩⅦ	Ⅹⅶ
ⅩⅧ	Ⅹⅷ
ⅩⅨ	Ⅹⅸ
ⅩⅩ	ⅩⅩ

5.2 Valid source types and citations

Source Type	Citation	Comment
EMA LIST	SMS	Reference for SMS Names Tag: Public domain release for Public dataset
EMA LIST	SVG	Reference for Public names without valid public soruce Tag: Public domain release for Public dataset
CAS	CAS (SciFinder)	Reference for Names
STN (SCIFINDER)	STN	Reference for CAS ID in tab Codes
CHEMID	ChemIDplus	
CHEMSPIDER	ChemSpider	
PUBCHEM	PubChem	
FDA_SRS	FDA-GSRS	
FDA_SRS	G-SRS (NCATS)	
CLINICALTRIALS	AdisInsight or USNCT or ICTRP	
IUPAC	IUPAC Name	
INN List	INN description	INN chemical name, definitional name from INN list. The chemical substances are supposed to be IUPAC names.
INN List	INN recommended List No	the number of the published recommended INN list. Tag: Public domain release can be added for Public dataset. Link to pdf file of list can be also added.
INN List	INN proposed List No.	the number of the published proposed INN list. Tag: Public domain release can be added for Public dataset. Link to pdf file of list can be also added.
EUROPEAN PHARMACOPOEIA	Ph. Eur.: Issue, monograph number	e.g. Ph. Eur.: 10.0, 2118
BRITISH PHARMACOPOEIA	BP year	e.g. BP2022
USP/NF	USP issue	e.g. USP42

Source Type	Citation	Comment
MARTINDALE	Martindale year	e.g. Martindale 2022
BAN	BAN	British Approved Name
JAN	JAN	Japanese Accepted Names
AAN	AAN	Australian Approved Name
USAN Coun	USAN	To be used for the USAN designation
USAN Coun	USAN description	To be used for USAN chemical names
International nomenclature of cosmetic ingredients	INCI	
NCI DRUG DICTIONARY	NCI drug dictionary	
NCI THESAURUS	NCI thesaurus	
ORPHAN DRUG	Orphan.desig:FDA Orphan.desig:EU	

5.3 Appendix 4: List of relevant databases for substances

When additional information concerning a substance is needed, the following databases can be used as a reference:

Database	Description
INN	The INN Programme assigns International Nonproprietary Names to medicinal substances through a broad consultative process. WHO is responsible for the INNs.
European Pharmacopoeia	The purpose of the European Pharmacopoeia is to promote public health by the provision of recognised common standards for the quality of medicines and their components. As these standards ensure that medicines reaching the market are safe for use by patients, it is essential that they are appropriate. Their existence also facilitates the free movement of medicinal products in Europe and beyond.
Medicines Complete	A site which guides on to several different publications, databases containing information about medicines.
Inxight: Drugs	Site provided by NIH, National Center for Advancing Translational Sciences. Information about e.g. treatment and pharmacology.
FDA Substance Registration System	Registration system in the U.S. by FDA and the U.S. National Library of Medicine (NIH), provides UNII-codes, Unique Ingredient Identifier.
G-SRS	Database built by GiNAS, NIH. This is the basis for the EU-SRS.
United States Approved Names	This is a site for USAN, where to find the approved names, provided by American Medical Association, AMA.
Japanese Accepted Names	This is a site for JAN, where to find the approved names, as part of the Japanese Pharmacopoeia.
PubChem	Chemical information from authoritative sources provided by U.S. National Library of medicine, NIH
European Union Food Additives	This database can serve as a tool to inform about the food additives approved for use in food in the EU and their conditions of use. It is based on the Union list of food.
EU CosIng	CosIng is the European Commission database for information on cosmetic substances and ingredients.
European Chemicals Agency	ECHA is an agency of the European Union and the site provides data from registration dossiers.

Database	Description
EC Active substance database	Site from the European Commission and it provides General index of products by active substance.
Merck Index	Online version of the Merck index, regarded as the most authoritative and reliable source of information on chemicals, drugs and biologicals. Now this trusted resource is available online from the Royal Society of Chemistry.
EU Orphan Database	Site from the European Commission and it provides The Community Register of orphan medicinal products.
FDA Orphan substance database	Site from FDA and it provides The Community Register of orphan medicinal products.
Index Nominum	This is an International Database of Pharmaceutical Substances and Preparations, provided by Wissenschaftliche Verlagsgesellschaft Stuttgart
International Pharmacopoeia	International Pharmacopoeia provided by WHO.
Scifinder	Research discovery application that provides integrated access to the world's most comprehensive and authoritative source of references, substances and reactions in chemistry and related sciences.
FDA Inactive Database	Site provided by FDA with a database of Inactive ingredients.

5.4 EU-SRS guidance for registering and/or editing of a Polymer

EU-SRS field name	Field details
Overview	
Preferred Term	Decide if the name complies to the PT rules
Definition Type	Always Primary.
Definition Level	Always Complete.
Deprecated	Relevant for a Deprecated Record.
Record Level Access	If no box is ticked the record is public. If it should be non public choose 'PROTECTED'. 'PROTECTD' means that the record cannot be exported.
Substance tags	*Not applicable.*
Definitional References	Definitional reference apply to the whole substance/record and to the structure. Field linked to Reference section. The definitional reference(s) are listed togheter with the other referenses and might be "reused" for names.
Names	
Name (Display *Name/Preferred Term in EU-SRS)*	Each record needs a Preferred term, which is the displayed name in EU-SRS. Necessary details: Choose a name type, Language always 'English', tick 'DN' (=Display Name)', choose a naming organisation, check if a public reference is given. Detailed information on the single fields can be found below.
Name (*Additional name in EU-SRS, could be PT in SMS)*	May be added, but the Display Name is sufficient. If there is a record in SMS (which is not necessarily the case), the common name used as PT in SMS should always be included as alias in the record as an Additional Listing Name ('Common Name').
Type	Each name type can be chosen, as appropriate. If it is possible to choose between more than one name type, the following priorisation should be used: Official Name, Common Name, Systematic Name, Company Code, Brand Name . The Official Name is any name used by an Official Naming body. An Official Naming Body is any organization allowed to Name a Substance PT = appropriate name type (e.g., 'Official Name', 'Systematic Name'), Alias = PT in SMS = 'Common Name', Other Alias = 'Common Name' or other name type
Access	If the information in the record is confidential, *Access* can be set to 'PROTECTED', but the name should have a public and a confidential reference.
DN	DN = Display Name: Tick box to indicate what name should be the *Display Name* in EU-SRS (= Preferred Term in EU-SRS). Mandatory for the EU-SRS-PT.
AL	AL = Additional Listing Name: Field is mandatory for the SMS-PT (not to be ticked for other aliases).

EU-SRS field name	Field details
	If EU-SRS-PT is the same as SMS-PT both check boxes should be used.
Standardized Name	*Not applicable.*
Languages	Always English.
Domains	*Not applicable.*
Jurisdiction	Field is optional when an 'Official Name' type is selected. Example: USAN would have Jurisdiction *United States*.
References	At least one public reference is needed per name. References can be newly created or reused.
Naming Organization	Field is only displayed if 'Official Name' type is chosen. If displayed it is conditional. Mandatory when the organization are INN, EP., USAN, BAN, JAN, AAN, INCI.
Polymer Classification	
Polymer Class	Copolymer or Homopolymer can be selected from drop-down list
Source type	Biosynthetic or Synthetic can be selected from drop-down list
Parent Substance	The Substance can be selected directly by the search from the dataset
Polymer subclass	Block, Cross-linked, Random or Substituted can be selected from drop-down list
Polymer Geometry	Branched, Cyclic, Linear or Network can be selected from drop-down list
Monomers	
Monomer Substance	Monomer can be selected directly by the search from the dataset
Monomer Type	Incorporated reactant, Initiator, Monomer or Starting Material can be selected from drop-down list
Amount	appears as a pop-up window. The type information 'mol ratio' or 'weight ratio' can be registered, as mean value (Average), or range (Low Limit and High Limit). Units can be selected (e.g. 'per polymer'), but it is not mandatory. Access is set to Public from the system after the import from SMS (standard = Public).
Idealized Structure	
Structure	Load an image by pasting a copied image into the canvas with ctrl + v, or dragging a local image file.
Generate SRUs	The button is selected when the structure is created. In this way, the information is filled into the new tab: Structural units.
Structural Units	
Structural Units	*This is a automatically filled by the system from Idealized structure*
Agent Modifications	
Agent Substance	*Not applicable.*

EU-SRS field name	Field details
Modification Process	*Not applicable.*
Modification Type	*Not applicable.*
Modification Role	*Not applicable.*
Amount	*Not applicable.*
Group	*Not applicable.*
Access	*Not applicable.*
Structural Modifications	
Molecular Fragment	Fragment can be selected directly by the search from the dataset
Modification Type	Modification can be selected from drop-down list
Residue Modified	*Not applicable.*
Extent	Complete or partial can be selected from drop-down list, depending on whether the modification was complete or incomplete.
Location	*Not applicable.*
Group	If the performed modifications run consecutively, they are defined numerically here (step 1 → group 1).
Access	Standard = Public
Extent Amount	appears as a pop-up window. The type information 'mol ratio' or 'weight ratio' can be registered, as mean value (Average), or range (Low Limit and High Limit). Units can be selected (e.g. 'per polymer'), but it is not mandatory. Access is set to Public from the system after the import from SMS (standard = Public).
Physical Modifications	
Modification Role	*Not applicable.*
Parameters	*Not applicable.*
Group	*Not applicable.*
Access	*Not applicable.*
Codes	
Code system	SMSID is always mandatory unless an SMSID is not available - then the SMS team will be asked for. Preferably other public sources are added when available, e.g., INN, EDQM, CAS, PubChem, Wikipedia. Classification: Besides the codes from the source databases used, the classification of the substance is entered under code section, which is relevant for searching. To enter the 'category' or 'domain', RMS is selected from the drop-down list.
Code System Type	*This is a default value (automatically filled in and managed by Admin).*

EU-SRS field name	Field details
Type	In nearly all cases default 'Primary' (code uniquely describes the substance). When the code is tied to a group/used for classification (Code system 'RMS') use 'Generic (Family)'. Superceeded is set if the code is already deprecated.
Code	Alpha numeric value. Classification: Relevant is the code for the domain 'Human use' or 'Veterinary use' and the category 'Polymer'
Access	Set to Public from the system after the import from SMS (standard = Public).
URL	Will be generated atomatically
Code Text	*Not applicable.*
Comments	*Not applicable.*
References	For CAS ID add STN reference
Relationships	
Related Substance	can be selected directly by the search from the dataset
Type (purpose *hierarchy)*	'Active Moiety' is selected if the substance is to be assigned to a higher-level data set (e.g. Macrogol is the active moiety of Macrogol 300)
Type (purpose not *hierarchy)*	'Specified substance -> _' It is selected to create a link to subordinate record. (e.g. Relationship between macrogol and x, this relationship can only be included for parent data set, i.e. Macrogol and is automatically generated for the child record Macrogol 300).
Access	*Not applicable.*
Mediator Substance	*Not applicable.*
Qualification	*Not applicable.*
Interaction Type	*Not applicable.*
Comments	*Not applicable.*
Amount	*Not applicable.*
References	*Not applicable.*
Notes	
Note	Field is optional and automatically populated by the system.
References	*Not applicable*
Access	*Not applicable*

EU-SRS field name	Field details
Properties	
Name	Density, Mol_Weight: Number Average, Mol_Weight:Weight Average, Particle size, Viscosity:Dynamic, Viscosity:Kinematic can be selected from the drop-down list.
Property Type	Chemical, Enzymatic or Physical can be selected as Property type from the drop-down list
Defining	Default is empty Tick box. The check mark can be set if the requirements are mandatory. It is also used in the family of substances that differ in their certain properties (e.g. hypromellose and viscosity).
Referenced Substance	*Not applicable*
Parameters	*Not applicable*
Amount	appears as a pop-up window. The type information 'mol ratio' or 'weight ratio' can be registered, as mean value (Average), or range (Low Limit and High Limit). Units can be selected, but it is not mandatory. Access is set to Public from the system after the import from SMS (standard = Public).
References	*Not applicable*
Access	*Not applicable*
References	
Source Type	CV-List; Mandatory field; Additional value not in CV is possible as temporary value (note: be careful with adding a new value, this needs to be communicated with the technical team).
Source text/Citation	Mandatory field and should represent the related value of the type.
Public Domain	Default is Public (Tick box), but it may be set 'Non-Public' in combination with a public reference.
Access	Default is 'Public'. Confidential = tick 'PROTECTED'.
URL	This field is optional .
Source Id	*Not applicable*.
Upload a Document	This field is optional.
Tags	This field should be populated by at least one value ('Public domain release') and if applicable other values. When reference is made to the SMSID database entry should be chosen.
Change Reason	
Change Reason	Add the reason of the change of the record that led to the creation of a new version.Use short notes (if something was added, edited or removed), e.g. Name , Code, RMS, Reference, Naming organization.