EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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SMS Guidance for external users

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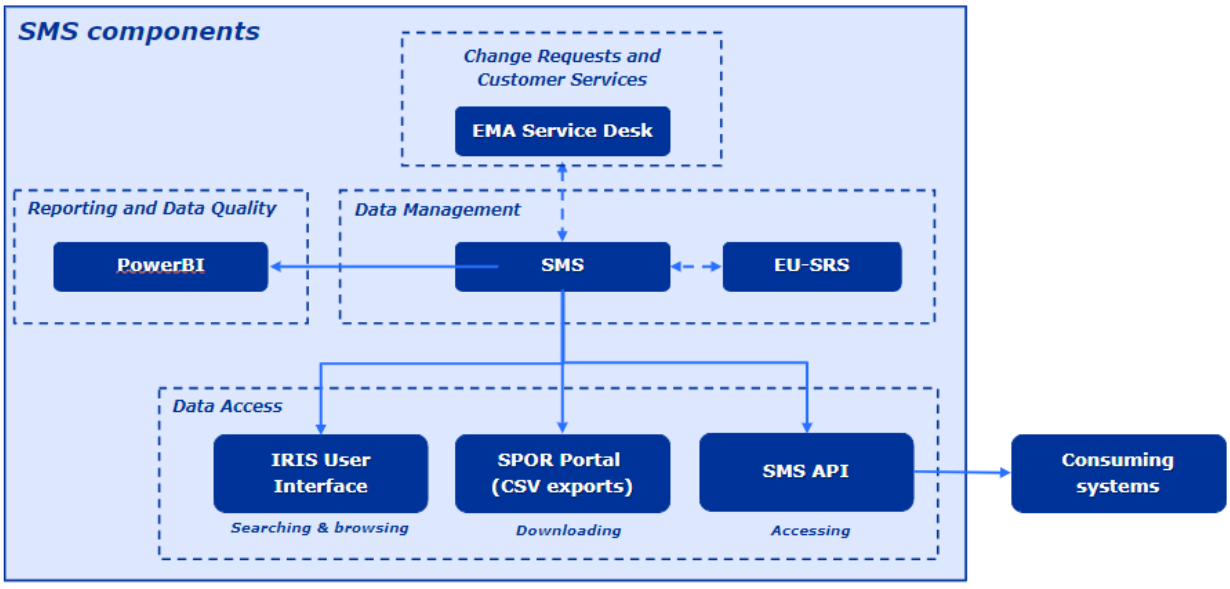
1. Introduction

Substances Management Service (SMS) is one of the four domains of Substance, Product, Organisation and Referential (SPOR) master data to be used in pharmaceutical regulatory processes. The SPOR services support the implementation of ISO IDMP standards in the European Union (EU) and European Economic Area (EEA). Although ISO IDMP standards relate to Human medicinal products, SMS manages both human and veterinary substance data.

SMS provides a central source of substance data that supports selection in regulatory processes and therefore enables to distinguish between two or more substances. It is managed by EMA data stewards for the benefit of the EU/EEA Network and Industry. EU-SRS is a complimentary system managed by the Substance Validation Group, with additional substance details, in accordance with ISO IDMP. It is currently accessible to NCAs only.

As illustrated in **Figure *1.*** SMS components, users can request changes in SMS (see Chapter *6. Change requests*) or ask questions about its processes (see *Chapter 7. Customer Service*) via the EMA Service Desk. SMS reports and data quality are analysed with PowerBI (see *Chapter 8.4 Data Quality monitoring*). SMS public data is accessible to external stakeholders via the IRIS User Interface (see *Chapter 4.1 SMS User Interface* and CSV exports in the SPOR Portal (see *Chapter 4.2 Downloading data*). SMS public data is also available the SMS Application Programming Interface (API) for Industry users, while NCAs have access to the full SMS data (see *Chapter 4.3 Application Programming Interface* . SMS data is also made available in several consuming systems such as XEVMPD, CTIS, UPD, etc. (see *Chapter 5. Consuming systems*).

Figure 1. SMS components



SMS currently supports the regulatory procedures and activities described in **Table 1**.

Table 1. Supported domain for regulatory procedures and activities

Regulatory Procedure	Domain
Innovation Task Force	Human & Veterinary
Scientific Advice	Human & Veterinary
PRIME	Human
Orphan Designation	Human
ATMP Classification & Certification	Human
Paediatric Investigation Plan	Human
Clinical Trial Application	Human
Eligibility for Centralised Procedure[1]	Human & Veterinary
Marketing Authorisation Application	Human & Veterinary
Maximum Residue Limits[1]	Veterinary
Article 58 - Medicines for use outside the EU	Human
Renewal & Variation	Human & Veterinary
Good Manufacturing Practices Certificates	Human & Veterinary
Art. 57/xEVMPD legal requirements	Human
Safety reporting	Human & Veterinary
Medicines Shortages	Human

[1]The application form for the regulatory procedure is free text, however, the information is then recorded in SIAMED, (the EMA product information and application tracking system for centrally authorised products) which consumes substance data from SMS.

2. SMS data and data fields

SMS data is managed in SMS IDD, which stands for "Informatica Data Director", a master data management tool. IDD is the back-end interface that enables specialised EMA data stewards to perform SPOR data management duties. Access to IDD is restricted to EMA users with the role "SMS data steward", which is authorised only after an appropriate extensive training.

External users do not have access to IDD and therefore cannot view, search or manage data in SPOR directly. However, external users can still access SMS data in several ways and can request data changes (i.e. creation or update of substance data) via the EMA Service Desk (see *Chapter 6. Change requests*). The accepted changes are then reflected in all systems using SMS data and in the SMS API, while the public data is also made available in the SMS exports from the SPOR portal and the SMS User Interface (UI) in IRIS. In the future, submissions of change requests are expected to be possible via a user interface, similarly to the OMS and RMS.

When SMS went live, substance data was imported into SMS IDD from xEVMPD, EUTCT and SIAMED. In addition, several data enrichment exercises were subsequently performed both based on internal EMA databases (e.g. Orphan Designation database, Scientific Advice Veterinary database) and external sources (e.g. INN and USAN). These resulted into a large dataset which is continuously undergoing cleansing and enrichment activities.

The most relevant data fields in SMS IDD are listed in **Table 2**, described by section.

Table 2. Relevant data fields in SMS IDD

Section	Data field	Conditionality	Content	Comments
Substance	SMS ID	System-generated		Unique for each substance record. SMS ID is also known as the EUTCT ID.
	Domain	Mandatory	RMS List "Domain"[2]	The choice between the "Human" or "Veterinary" domains trigger a different feedback loop to the concerned consuming systems. "Human" substances can be used in both human and veterinary products, while "Veterinary" substances can be exclusively used in veterinary products.[3] Further details are available in *Chapter 5. Consuming systems*.
	Data classification (Substance)	Mandatory	RMS List "Data Classification"[2]	SMS only uses the terms "Public" and "Restricted"
	Authorisation State	System-generated	RMS List "Substance Authorisation Status"[2]	All new substances are registered as "Authorised", which is known as "Approved" in xEVMPD, regardless of the approval status of the product. Legacy "Development" substances are kept for historical purposes only. Further details are available in *Annex 2: Frequently Asked Questions*.

[2] The respective RMS IDs and terms are listed in *Annex 4*.
[3] Substance registered with domain "Veterinary" are mainly vaccines for animal-exclusive diseases, monoclonal antibodies that target animal proteins and cell therapy substances made from animal cells for veterinary use.

	Substance Status	Mandatory	RMS List "Record Status" [2]	SMS only uses the terms "Current" and "Non-current". Users can only use "Current" records, while "Non-current" ones reflect the nullified substance records and cannot and shall not be used.
	Substance Name	System-generated	Automatically populated based on the preferred term set on Substance Name section	
	Comment	Optional	Free text	This field is mandatory when changing a substance to "non-current" (i.e. for substance nullification). It is used to flag duplicate or invalid substances.
	Substance Type	Mandatory	RMS List "Substance type"[2]	This data field has no regulatory impact.
	Molecular formula	Optional	Free text	
	Molecular weight	Optional	Numeric field (2 decimals)	
	InChIKey	Optional	Free text (27 characters)	International Chemical Identifier, which is an alphanumeric representation of the substance systematic name (mainly for chemicals). It can be generated from Opsin or other systematic name parsers.
	Last Update Date	System-generated		
Substance Name	Substance Name	Mandatory		Each substance must have at least one name, the preferred term.
	Language	Mandatory	RMS List "Language"[2]	The preferred term must be in English or Latin. Aliases (synonyms and translations) can be in any official EU/EEA language.
	Is Preferred	Mandatory	Binary	Only one preferred term can be set per record.
	Name Status	Mandatory	RMS List "Record Status"[2]	
	Data Classification (Name)	Mandatory	RMS List "Data Classification"[2]	Implications on confidentiality. Further details are available in *Chapter 3.1.General substance confidentiality principles*.
Substance Name Source	Source (Name Source)	Mandatory	RMS List "Source of Information"[2]	The source of information is required for all English and Latin terms.
Substance External Code	Source (External Code)	Optional	RMS List "Source of Information" – External codes (All with attribute "SMS Code")[2]	System-generated for EV Codes for Human substances. External codes (e.g. SVG flag, UNII, etc.) can be manually added.

	ID/Code Provided by Source	System-generated for EV Codes (Human) Optional for other codes	External code	
Substance Custom Attribute	Attribute Term	Optional	RMS List "SMS Custom Attribute" [2]	Active substance in valid EEA AMP Critical medicine
	Attribute Value	Optional	Free text	
Substance Relationship	Related substance	Optional	SMS ID	SMS ID of the related substance
	Substance Relationship Combination	Conditional	RMS List "Substance Relationship Combination"[2]	
Substance Current	Substance Current	Optional	SMS ID	SMS ID of the replacement substance

3. Substance confidentiality

3.1. General substance confidentiality principles

The confidentiality of substance data is managed in SMS IDD via the data fields "Data classification", both at substance and name level:

- **Data classification (substance)**: this data field allows the management, at substance record level, of the confidentiality of the molecular formula, molecular weight, InChIKey and enables the registration of restricted substance names in the Substance Name section;
- **Data classification (name)**: this data field allows the management, at substance name level, of the confidentiality of each individual name.

The data field "Data classification" can be set, both at substance and name level, as:

- **Public**: the concerned data is made publicly visible to all users (via consuming systems, substance exports in SPOR Portal and SMS API);
- **Restricted**: the concerned data is only made visible to EMA SMS Data Stewards, EMA IRIS users and NCA users (via the SMS API).

The tables below (**Table 3** and

Table *4*) further describe the management of the confidentiality of data via the two "Data Classification" data fields and the implemented action at system level as per the selected value (i.e. "Public" vs "Restricted"). Examples of public and restricted substances can be seen in

Figure 2. Example of Public (SMS ID: 100000128703) and Restricted (SMS ID: 300000032819) substances in the Substance export published in the SPOR Portal

Table 3. Data classification at substance level

Data Classification (substance)	Molecular formula	Molecular weight	InChIKey	Restricted names
Public	Published (if registered)	Published (if registered)	Published (if registered)	Not allowed for any name
Restricted	Not published	Not published	Not published	Allowed for aliases

Table 4. Data classification at name level

Data Classification (name)	Name
Public	Published
Restricted	Not published

Figure 2. Example of Public (SMS ID: 100000128703) and Restricted (SMS ID: 300000032819) substances in the Substance export published in the SPOR Portal

A	B	C	D	I	K	O	P	Q
#SMS_ID	Substance_Name	Is_Pref	Language	Molecular_Formula	Inchikey	External_Code_XEVMPD	External_Code_SVG	External_Code_UNI
100000128703	Olodaterol	TRUE	English	C21H26N2O5	COUYJEVMBVSIHV-SFHVURJKSA-N	SUB36104	1	VD2YSN1AFD
100000128703	BI 1744	FALSE	English	C21H26N2O5	COUYJEVMBVSIHV-SFHVURJKSA-N	SUB36104	1	VD2YSN1AFD
100000128703	Olodaterool	FALSE	Estonian	C21H26N2O5	COUYJEVMBVSIHV-SFHVURJKSA-N	SUB36104	1	VD2YSN1AFD
100000128703	OLODATEROL	FALSE	German	C21H26N2O5	COUYJEVMBVSIHV-SFHVURJKSA-N	SUB36104	1	VD2YSN1AFD
100000128703	OLODATEROL	FALSE	Hungarian	C21H26N2O5	COUYJEVMBVSIHV-SFHVURJKSA-N	SUB36104	1	VD2YSN1AFD
100000128703	Olodaterol	FALSE	Polish	C21H26N2O5	COUYJEVMBVSIHV-SFHVURJKSA-N	SUB36104	1	VD2YSN1AFD
300000032819	BI 1819479	TRUE	English			SUB222429	1	

It is important to be noted that even when the data classification is set as "Restricted", the following limited information **will always be made public**:

- SMS ID and associated EV code.
- preferred term and the respective name source.
- official names (e.g. INN, USAN) and the respective name source.

However, the restricted information will not be visible to industry users, including the requestor, and it will only be visible to EMA SMS data stewards, EMA IRIS users and NCA users accessing SMS data via the SMS API.

Depending on the concerned regulatory procedure, the applicant may designate a company code as the preferred term. In case a company code is requested as the substance preferred term, a systematic name or a common name describing the substance must still be provided. Any additional names will be registered as "restricted" and will not be displayed to the public nor published; this data will only be made visible to EMA SMS Data Stewards, EMA IRIS users and NCA users (via the SMS API and IRIS).

While these general substance confidentiality principles apply to both human and veterinary substance data, there are several particularities implied for each domain that will be further addressed and detailed in the next chapters.

3.2. Confidentiality for Human substances

The information in this chapter is provided for informational purpose only as it is currently under review by various relevant stakeholders, and it is therefore subject to change and further revision during 2025.

As per the general principles, each substance record shall have a public preferred term. However, when selecting the appropriate preferred term, it is essential to consider the regulatory procedure for which the substance record is required.

While for substances requested for use in PRIME, scientific advice or clinical trial applications it is possible for the company code to be set as the preferred term, with all the remaining names being registered as restricted, for Orphan Designations and Paediatric Investigation Plans the company code cannot be used as the substance preferred term. The use of a company code as the preferred term, in such instances, will block the regulatory procedure until a substance request for a preferred term update is submitted and processed. Instead, as required by the European Commission, a systematic name, for chemicals, or a common name, for other substance types, must be used.

In **Table 5**, information on setting the preferred term, taking into account the concerned regulatory purpose, is further detailed.

Table 5. Selection of the preferred term for human domain

Regulatory procedure	Company code allowed as preferred term?
PRIME	Yes, if no official name (e.g. INN, Ph. Eur.) is available
Scientific Advise	
Clinical Trials	
Marketing Authorisation Application	No, a systematic name, for chemicals, or a common name, for other substance types, must be used.
Orphan Designation	
Paediatric Investigation Plan	

3.3. Confidentiality for Veterinary substances

For veterinary substances, the impact of the concerned regulatory procedure on the selection of the preferred term is also essential. In **Table 6** further details are made available regarding the main regulatory procedures using veterinary substances and the possibilities of using a company code as the substance preferred term, with all the available names being registered as restricted.

Table 6. Selection of the preferred term for the veterinary domain

Regulatory procedure	Company code allowed as preferred term?
Scientific Advice	Yes, if all conditions apply simultaneously: • The substance is not used in any approved Veterinary medicinal product; • The substance does not have an official name (e.g. INN, USAN, Ph. Eur.). • The systematic name or common name is requested as "Restricted" and the company code is requested as "Public" by the Applicant in the Substance Request Form.
Marketing Authorisation Application (Centralised)	
Marketing Authorisation Application (MRP/DCP/National)	
Variation	No, a common name must be used.

4. Accessing substance data

SMS substance data can be accessed through several methods, depending on the user type. The concerned system will display the appropriate data, public or restricted, based on the user's authorisation level:

- SMS IDD - access is possible for EMA SMS data stewards who can view and manage all, both public and restricted, substance data.
- SMS User Interface (UI) in IRIS – access is possible for all users who can view limited public data; EMA IRIS users can view additional restricted information.
- SMS tab in the SPOR portal – access is possible for all users, who can download almost all public data.
- SMS Fast Healthcare Inte5roperability Resources Application Programming Interface (FHIR API) – access is possible for EMA and NCA users who can access public and restricted substance data, and to any other users who can only access public data.

Table 7. Substance data access

User	**SMS IDD** *Browse* *Search* *Edit* *Export*	**IRIS (SMS UI)** *Browse* *Search*	**EUTCT** *Browse* *Search*	**SPOR Portal** *Export*	**API** *Browse* *Search*
EMA	Public and restricted data	Public and restricted data	Public data	Public data	Public and restricted data
NCA	N.A.	Public data	Public data	Public data	Public and restricted data
Any other	N.A.	Public data	No access	Public data	Public data

4.1. SMS User Interface

The SMS User Interface (UI) is available to the public via IRIS, no login or credentials being required to access it. The SMS UI makes available to the public a set of public SMS substance data which is updated via the SMS API on a daily basis.

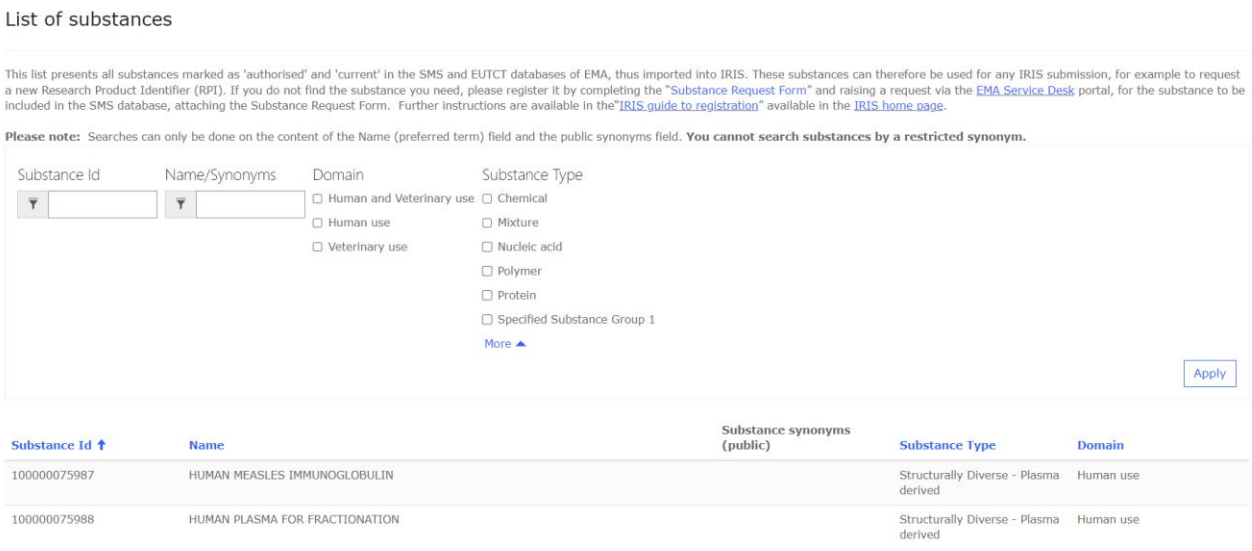
The following criteria is applied for the published SMS substance records:

- **Substance Authorisation State** in SMS IDD [RMS list ID 200000004906 "Substance Authorisation Status"] is set as "Authorised" (i.e. approved substance records) [RMS term ID 200000004972].
- **Substance Status** in SMS IDD [RMS list ID 200000005003 "Record Status"] is set as "Current" [RMS term ID 200000005004].

The following SMS data fields are currently available, as illustrated in **Figure *3.*** SMS User interface in IRIS:

- SMS ID.
- Preferred term.
- Public aliases (i.e. synonyms in English, with Data Classification at name level set as "Public").
- Substance type.
- Domain.

Figure 3. SMS User interface in IRIS



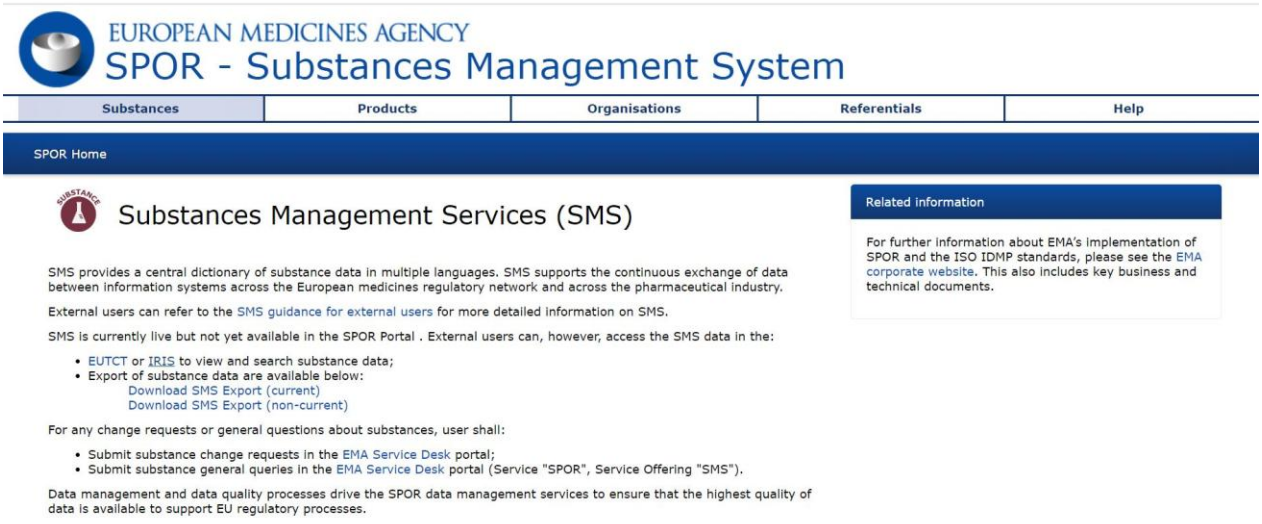
Additional data fields are expected to be added in the future:

- Translations.
- External codes (e.g. EV Code, SVG flag, UNII, etc.).
- Replacement substance ID (for identified duplicates).

4.2. Downloading data

In the SMS tab in the SPOR Portal, two comma-separated (.CSV) substance export files are made available. One file contains public information of all the substances with the status set as "Current" and the second one contains the public data of those records with the status set as "Non-current". These exports are refreshed every night and are available to all users, without the need for credentials.

Figure 4. The SMS tab in the SPOR Portal



Users can click on the appropriate link to download either the current or non-current .CSV export. In order to open the .CSV substance exports and access the substance data, the file should be opened and imported into a spreadsheet software. The following steps can be taken in Excel:

1. Click on the respective link to download the current or non-current export
2. Open Excel
3. Click "Blank workbook", "Data", "From Text/CSV"
4. Select the downloaded CSV file
5. Click load
6. Select column A, then change from "General" to "Number"
7. Remove the decimal cases by clicking twice on the button below

Both exports will reference the data fields described in **Table 8**.

Table 8. Data fields available in the public substance exports

Data field	Details
#SMS_ID	System-generated ID associated with a substance name
Substance_Name	Substance name, which can be the preferred term, a "Public" alias or a translation
Is_Preferred_Name	Information on the preferred name: the preferred term is indicated by the label "Yes"; the aliases and translations are marked with the label "No"
Language	Language of the concerned substance name as per the respective RMS list; the preferred term and aliases are in English or Latin, while the translations are in one of the official EU/EEA languages
Name_Source	Name of the source of information for the substance name as per the respective RMS list
Substance_Domain	Appropriate domain as per the respective RMS list (i.e. "Human" or "Veterinary")
Status	Status of the substance name as per the respective RMS list (i.e. "Current" or "Non-current"); each export only contains one status
Substance_Type	Substance type as per the respective RMS list
Molecular_Formula	Molecular formula, if applicable (only if the substance record is set as "Public")
Molecular_Weight	Molecular weight (field not yet populated; only applicable if the substance record is set as "Public")
InchIKey	InchIKey (field only populated for chemicals; Only applicable if the substance record is set as "Public")
Comment	Comment associated with the concerned term; it may reference the SMS ID/EV Code of an appropriate replacement substance for duplicate records. Additional information provided in *Chapter 8.3. Data Cleansing*
Created_Date	Date when the substance was created
Last_Updated_Date	Date when the substance was last updated
EV Code	Substance EV code from XEVMPD (only applicable to substances with domain "Human")
SVG flag	The label "1" indicates a valid substance, while the label "0" reflects an invalid/duplicated substance, empty data field not yet reviewed
UNII	Unique Ingredient Identifier from FDA
INN_number	International Nonproprietary Name number from WHO
EC_List/Number	European Commission list or number
Parent_Substance	SMS ID of the parent substance
Replacement_substance	Recommended replacement substance (only applicable for duplicates in the "Non-current" export)

4.3. Application Programming Interface

SMS exposes an Application Programming Interface (API) for system-to-system integration in order to query and retrieve substance data.

The SMS API is implemented using the Fast Healthcare Interoperability Resources (FHIR) standard. The API is currently on FHIR version 4.4.0 (R5 preview 2) and supports the SubstanceDefinition resource SubstanceDefinition - FHIR v4.4.0 (hl7.org).

The API is available for both NCAs and general users. However, general users will be able to view only public data fields. Endpoints 201 and 202 from the SPOR API Specification V2 R5 (europa.eu) are currently in scope.

Authentication to the API is using the OAuth2 standard Client credentials flow.

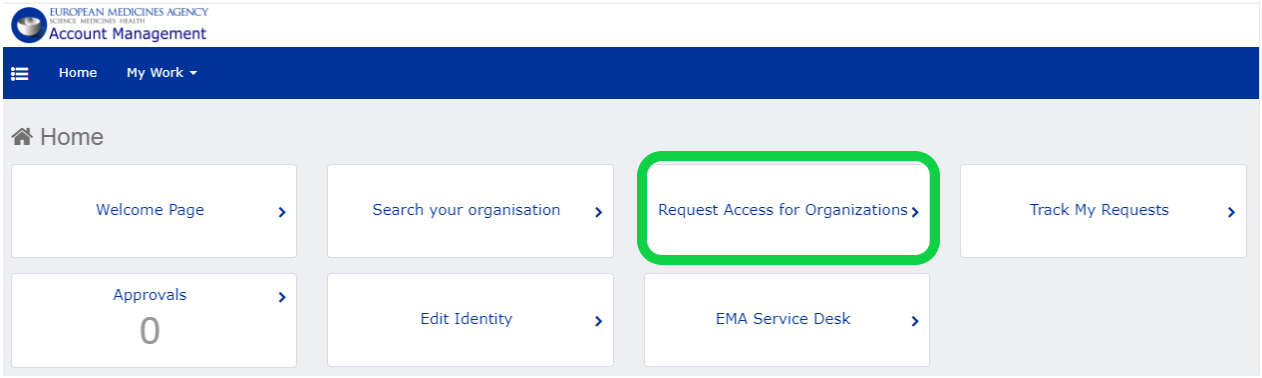
Table 9. API properties

API Property	Value
Base Path	https://spor.azure-api.net/sms/api/v3
Protocol	HTTPS
Authentication	OAuth2 Client Credentials flow
FHIR Version	4.4.0 (R5 Preview 2)

4.3.1. API registration process

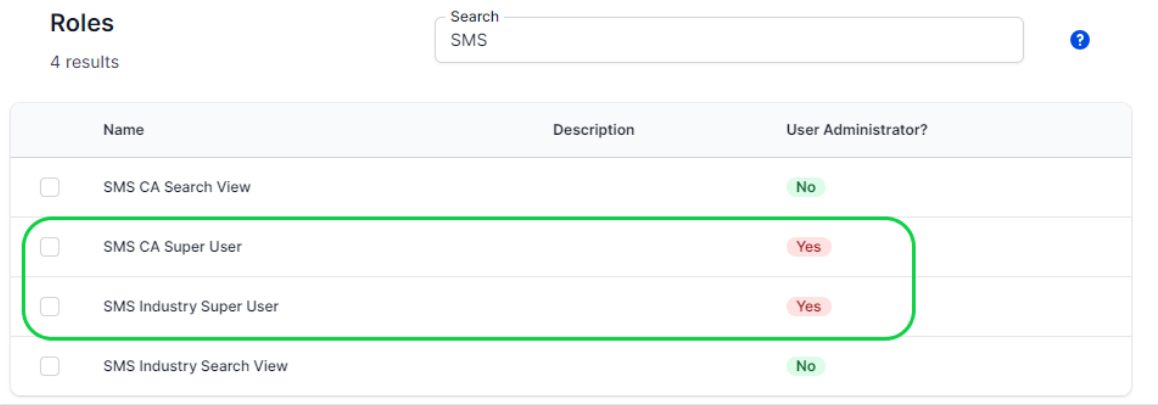
In order to generate client credentials, users should request their relevant SMS Super User role. Roles can be requested by registering on EMA Account Management portal. Once registered, users can login and request access in the context of the Organisation(s) they represent.

Figure 5. EAM portal link to Request access



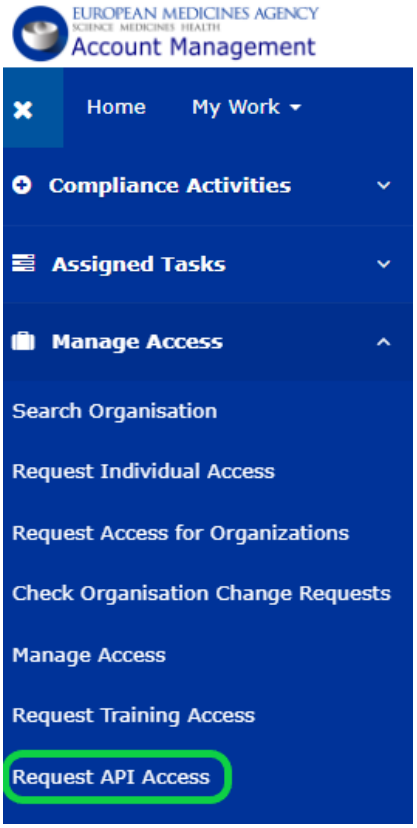
Once an Organisation is chosen, the user shall search for SMS roles (**Figure 6**) and select the relevant Super User role.

Figure 6. SMS Super User Roles



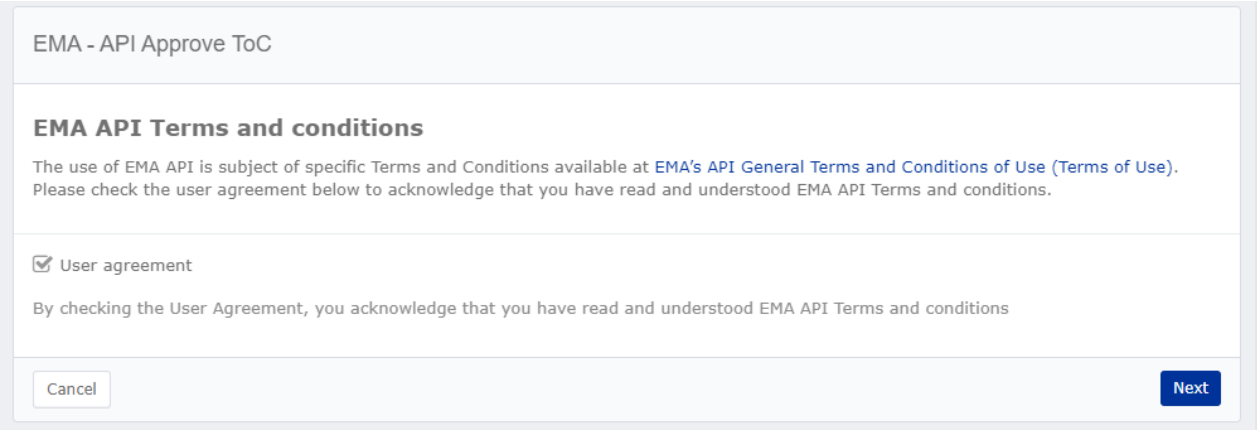
Once submitted, the request will be made available for approval by the system owner. Once the role is approved, the user will be able to request API Access from the side menu (**Figure *7***).

Figure 7. EAM Request API Access menu item



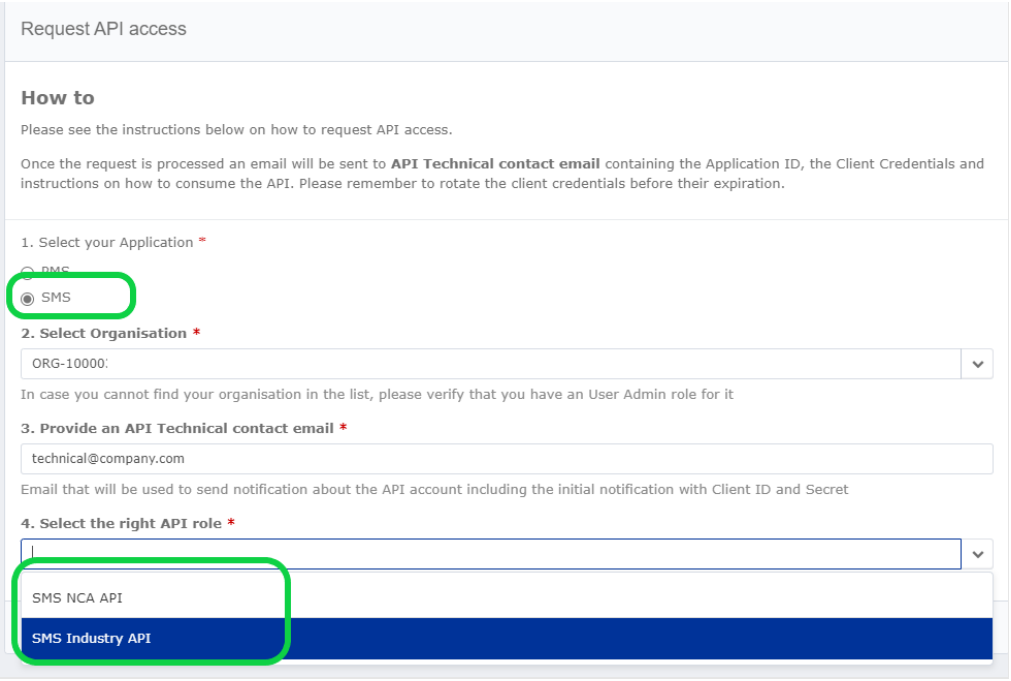
In order to proceed with the request for the API Access, the user shall first accept the API terms of use.

Figure 8. API Terms and conditions screen



In the next screen, the user shall select SMS and the relevant Organisation for which they would like to request access. An e-mail address shall be provided in order to receive the client credentials details and further select the relevant API role.

Figure 9. Request API access screen



Finally, an e-mail with all the information necessary for OAuth2 Client credentials flow authentication will be sent to the provided e-mail address. The following information is included in the e-mail:

- Client ID.
- Client Secret.
- OAuth2 Token Endpoint.
- Scope.

Important: Please take note of the expiration date in the email and raise an EMA Service Desk request to renew the credentials before expiration.

Figure 10. Example of e-mail with OAuth2 information

Please find below the details of your registration with the SMS API.

OAuth2 Properties

Property	Value
Token URL	POST https://login.microsoftonline.co
Client Id	1a2ba6
Client Secret	d0M8Q~c
Scope	api://euema.onmicrosoft.
Expiration date	06/30/2027 03:44:32

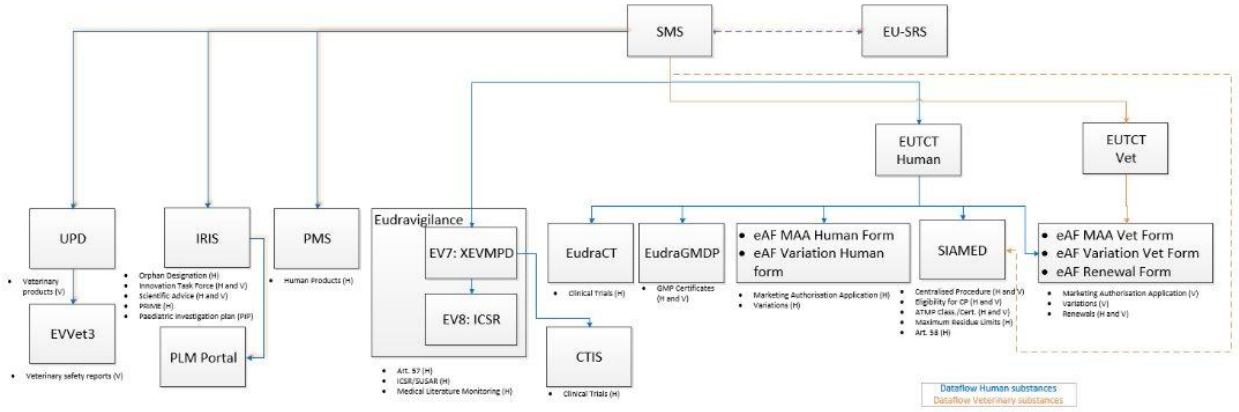
5. Consuming systems

5.1. Data flow

Substances created or updated in SMS are automatically synchronised with all the appropriate consuming systems, depending on the substance's domain (i.e. Human or Veterinary), as presented in **Figure 11**. Like it was mentioned in *Chapter 2. SMS data and data fields,* this data field has no regulatory impact, and it only impacts the consuming systems that will display the concerned substance.

Substances registered as "Human" are made available in all consuming systems (represented by blue arrows), while substances registered as "Veterinary" are only made available in certain systems (represented by orange arrows). Substance registered with domain "Veterinary" are mainly vaccines for animal-exclusive diseases, monoclonal antibodies that target animal proteins and cell therapy substances made from animal cells for veterinary use; all other substances are registered as "Human" in SMS.

Figure 11. Substance data flow



Once a *human substance record* is registered in SMS, the substance data is sent to the Extended EudraVigilance Medicinal Product Dictionary (xEVMPD) via a feedback loop. After several minutes, the substance record is automatically created in the xEVMPD, and an EV code is assigned to the new approved substance record. The substance EV Code is then provided to SMS, with the SMS record being automatically updated with the new external code. From the xEVMPD, substances can be used in the whole EudraVigilance module (particularly in pharmacovigilance activities) and in CTIS (for use in clinical trials).

In parallel, the new human substance record is also sent from SMS to EUTCT Human list, within seconds, where the public information can be browsed and viewed by any guest user. From EUTCT Human, the substance record is further made available in:

- EudraCT: for clinical trials.
- EudraGMDP: for GMP certificates.
- eAF forms:
  - Marketing Authorisation Application Human.
  - Marketing Authorisation Application Veterinary.
  - Variation Human.

- Variation Veterinary.
- Renewal.

- SIAMED: for EMA management of Centralised Procedure, Eligibility, ATMP Classification/Certification, Maximum Residue Limits and Art. 58 procedures (medicines for use in outside EU).

Both human and veterinary substance records are provided, via the SMS API, to the following systems:

- IRIS: for PRIME, Innovation Task Force, Orphan Designation, Innovation Task Force and Scientific Advice.
- UPD: for the registration of Veterinary Medicinal Products.
- EVVet3: for the pharmacovigilance of Veterinary Medicinal Products.

For *veterinary substance records*, the substance data is made available in EUTCT Veterinary list, for further use in the eAF for the "Marketing Authorisation Application - Veterinary", "Variation Veterinary" and "Renewal" forms. Since there is no automatic synchronisation of veterinary substances to SIAMED, they are kept aligned via a manual process (marked by dashed lines in the data flow).

SMS and EU-SRS are currently being aligned via data fixes/batches of data.

The presented data flow and principles also apply for substance updates, with the respective substance changes being synchronized with all the concerned consuming systems accordingly.

5.2. Systems details

SMS substance data is made available in multiple systems, various data fields being displayed depending on the particular needs and requirements of the concerned consuming system. This data is then maintained up to date in all systems, as it is synchronised at a specific interval. Detailed information on the consuming systems is further presented in **Table 10**.

Table 10. Consuming systems details

Consuming System	Substance Domain	Substances available	Data fields available	Synchronisation Frequency
IRIS	Human and Veterinary	Auth. State: Authorised Status: Current	• SMS ID • Preferred term • Public aliases • Domain • Substance type	Daily
UPD	Human and Veterinary	Auth. State: Authorised Status: Current	• Latest updated substance name (not necessary the Preferred term)	Daily
EudraVigilance/ xEVMPD	Human	Auth. State: Authorised (Approved) and Development (legacy data) Status: Current and Non-current (Nullified)	• EV Code • Authorisation state • Status • Preferred term (with Source) • Substance type • Molecular formula (if public) • Comments (if public) • Public aliases (with Source)	Within minutes

Consuming System	Substance Domain	Substances available	Data fields available	Synchronisation Frequency
			• Translations	
CTIS	Human	Auth. State: Authorised and Development Status: Current	• EV Code • Preferred term	Daily
EUTCT Human	Human	Auth. State: Authorised and Development Status: Current and Non-current	• SMS ID • Authorisation state • Status • Preferred term (with Source) • Public aliases (with Source) • Translations • Molecular formula (if public) • EV Code	Within seconds
EUTCT Veterinary	Veterinary			
EudraCT	Human	Auth. State: Authorised and Development Status: Current	• EV Code • Preferred term (with Source) • Public aliases • Translations • Authorisation state • Status	Within seconds
eAF MAA Human	Human	Auth. State: Authorised Status: Current	• Preferred term	Within seconds
eAF Variation Human				
eAF MAA Veterinary	Human and Veterinary			
eAF Variation Veterinary				
eAF Renewal				
SIAMED	Human and Veterinary	Auth. State: Authorised and Development Status: Current and Non-current	• SMS ID • Authorisation state • Status • Preferred term (with source) • Public aliases • Translations	Daily

6. Change requests

Once the creation or update of a substance record has been deemed necessary, a change request shall be submitted via the EMA Service Desk. In such cases, the following steps shall be followed for submitting a substance request:

1. *Check if the concerned substance data is already available.*
2. *Complete the Substance Request Form.*
3. *Prepare the required supporting documentation.*
4. *Submit the ticket via the EMA Service Desk.*
5. *Wait for the resolution of the request.*

1. Check if the concerned substance data is already available

Before creating a substance request, the applicant should first check if the substance is already available. The rationale for this step is that the concerned substance might already be registered, as needed or with a different preferred term, and can therefore be used by the applicant, even if the update of the substance record might still be required.

This can be done by searching in the concerned consuming system, in the SMS UI in IRIS or in the substance exports published in the SPOR Portal. Further information on accessing substance data and substance consuming systems is available in *Chapter 4. Accessing substance data* and *Chapter 5. Consuming systems,* respectively.

2. Complete the Substance Request Form

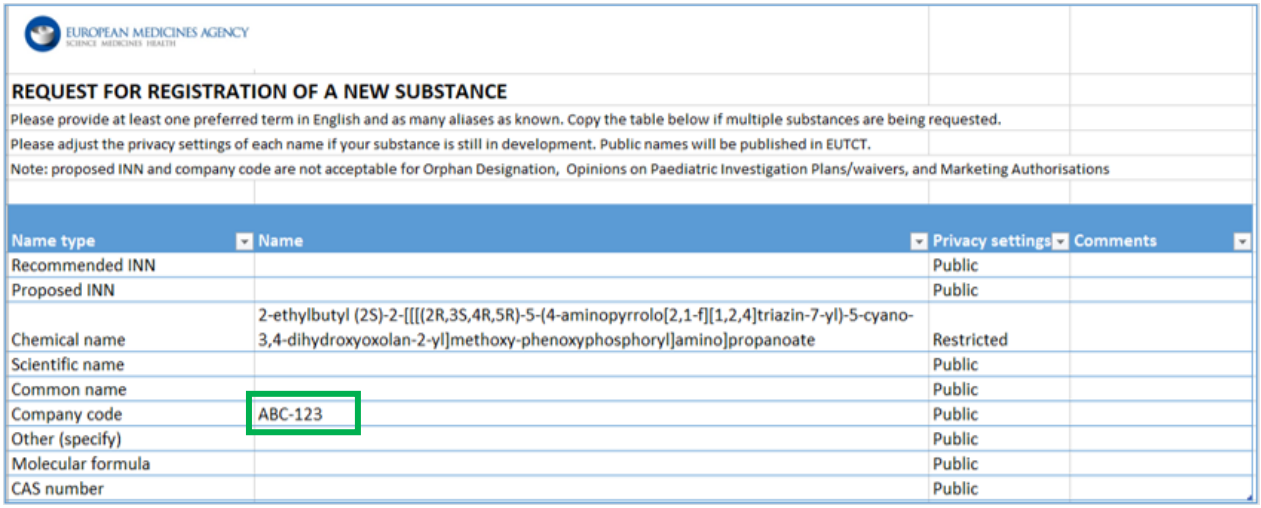
The applicant shall download and fill out the Substance Request Form. All available substance names shall be provided and, if needed, the "Privacy settings" can be set to "Restricted" individually. However, *at least one substance name must always be set as "Public" because every substance record shall have a public preferred term*, as detailed in *Chapter 3. Substance confidentiality*.

The choice for the substance preferred term will be decided by the SMS Data Stewards, based on the names provided, the concerned regulatory procedure and the naming rules defined in Annex 1 (to be published in 2024).

Some examples of completed Substance Request Forms can be found below, in the **Figures 10-13**. The preferred term is highlighted in each example and this represents the term which will be displayed to the public.

In **Figure 12**, the applicant has submitted a request for registration of a chemical for a clinical trial application and has provided the chemical name, set as restricted, and the company code, set as public. Since in the context of clinical trials, the company code can be registered as the preferred term, this term will be registered accordingly as the preferred term and the chemical name will be recorded as "Restricted".

Figure 12. Request for the registration of a Chemical for a Clinical Trial



EUROPEAN MEDICINES AGENCY

REQUEST FOR REGISTRATION OF A NEW SUBSTANCE

Please provide at least one preferred term in English and as many aliases as known. Copy the table below if multiple substances are being requested.

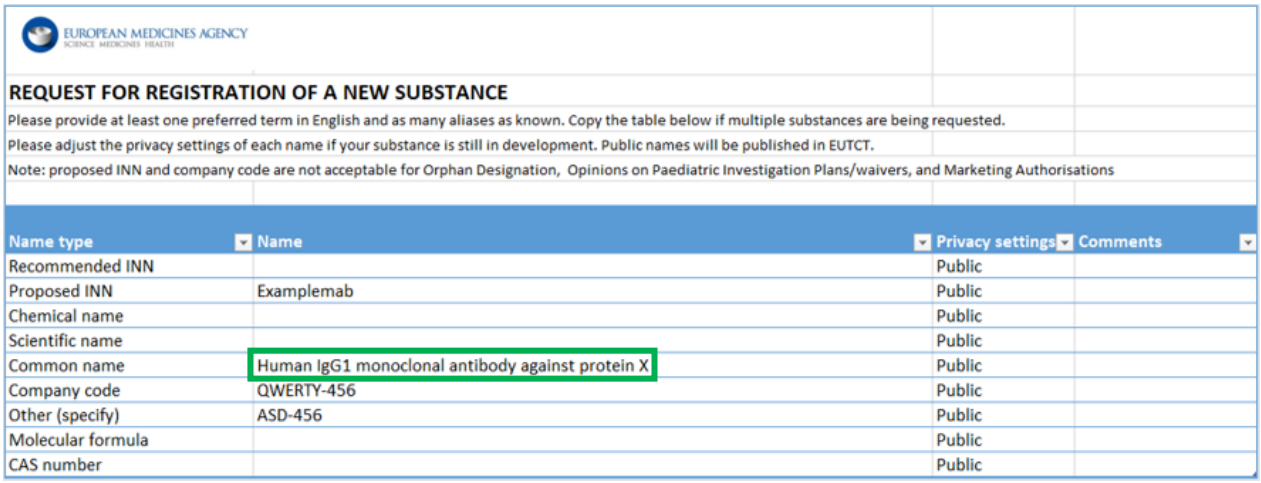
Please adjust the privacy settings of each name if your substance is still in development. Public names will be published in EUTCT.

Note: proposed INN and company code are not acceptable for Orphan Designation, Opinions on Paediatric Investigation Plans/waivers, and Marketing Authorisations

Name type	Name	Privacy settings	Comments
Recommended INN		Public	
Proposed INN		Public	
Chemical name	2-ethylbutyl (2S)-2-[[[(2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroxyoxolan-2-yl]methoxy-phenoxyphosphoryl]amino]propanoate	Restricted	
Scientific name		Public	
Common name		Public	
Company code	ABC-123	Public	
Other (specify)		Public	
Molecular formula		Public	
CAS number		Public	

In **Figure 13**, the applicant has submitted a request for registration of a protein for Orphan Designation/Paediatric Investigation Plan and has provided the proposed INN, common name, company code and another name, all set as public. In this context, the company code and the proposed INN cannot be registered as the preferred term and the common name will be registered accordingly as the preferred term, while all the other terms will be entered as public aliases.

Figure 13. Request for the registration of a Protein for Orphan Designation/Paediatric Investigation Plan



EUROPEAN MEDICINES AGENCY

REQUEST FOR REGISTRATION OF A NEW SUBSTANCE

Please provide at least one preferred term in English and as many aliases as known. Copy the table below if multiple substances are being requested.

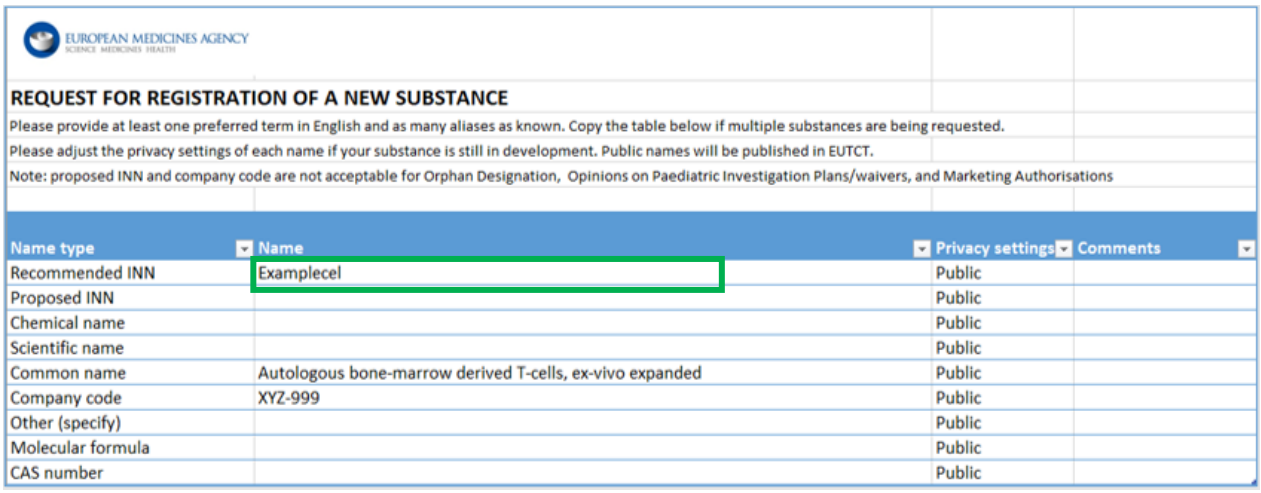
Please adjust the privacy settings of each name if your substance is still in development. Public names will be published in EUTCT.

Note: proposed INN and company code are not acceptable for Orphan Designation, Opinions on Paediatric Investigation Plans/waivers, and Marketing Authorisations

Name type	Name	Privacy settings	Comments
Recommended INN		Public	
Proposed INN	Examplemab	Public	
Chemical name		Public	
Scientific name		Public	
Common name	Human IgG1 monoclonal antibody against protein X	Public	
Company code	QWERTY-456	Public	
Other (specify)	ASD-456	Public	
Molecular formula		Public	
CAS number		Public	

In **Figure 14**, the applicant has submitted a request for registration of a cell therapy for Marketing Authorisation Application and has provided the recommended INN, common name and company code, all set as public. In this context, the recommended INN will be registered as the preferred term and all the other terms will be entered as public aliases.

Figure 14. Request for the registration of a Cell therapy for Marketing Authorisation Application



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

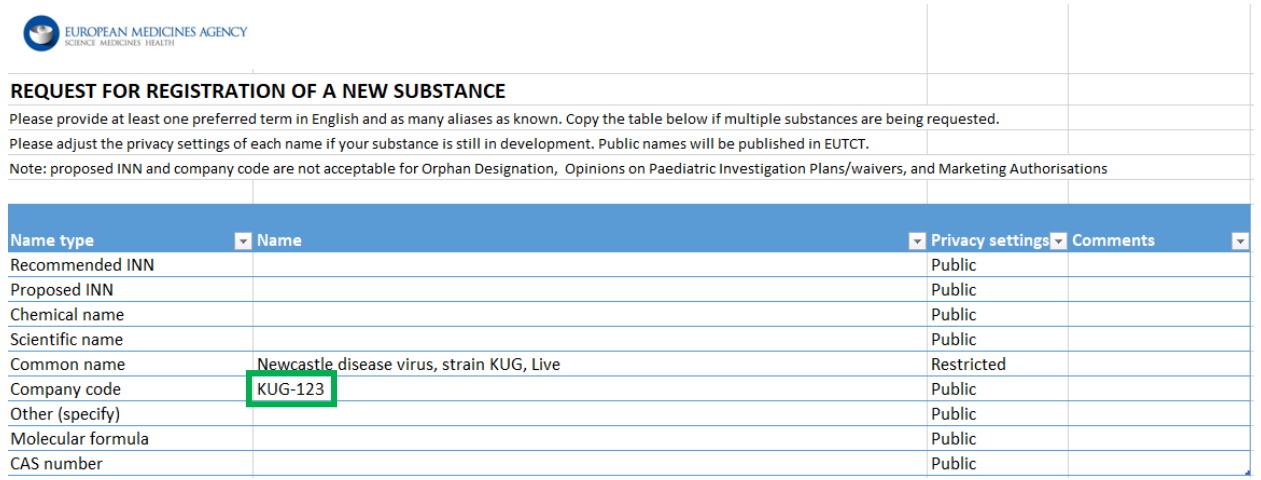
REQUEST FOR REGISTRATION OF A NEW SUBSTANCE

Please provide at least one preferred term in English and as many aliases as known. Copy the table below if multiple substances are being requested.
Please adjust the privacy settings of each name if your substance is still in development. Public names will be published in EUTCT.
Note: proposed INN and company code are not acceptable for Orphan Designation, Opinions on Paediatric Investigation Plans/waivers, and Marketing Authorisations

Name type	Name	Privacy settings	Comments
Recommended INN	Examplecel	Public	
Proposed INN		Public	
Chemical name		Public	
Scientific name		Public	
Common name	Autologous bone-marrow derived T-cells, ex-vivo expanded	Public	
Company code	XYZ-999	Public	
Other (specify)		Public	
Molecular formula		Public	
CAS number		Public	

In **Figure 15**, the applicant has submitted a request for registration of a veterinary vaccine for Scientific Advice and has provided the common name, set as restricted, and the company code, set as public. In this context, the company code will be registered as the preferred term and the common name will be registered accordingly as a restricted alias.

Figure 15. Request for the registration of a Veterinary vaccine for Scientific Advice



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

REQUEST FOR REGISTRATION OF A NEW SUBSTANCE

Please provide at least one preferred term in English and as many aliases as known. Copy the table below if multiple substances are being requested.
Please adjust the privacy settings of each name if your substance is still in development. Public names will be published in EUTCT.
Note: proposed INN and company code are not acceptable for Orphan Designation, Opinions on Paediatric Investigation Plans/waivers, and Marketing Authorisations

Name type	Name	Privacy settings	Comments
Recommended INN		Public	
Proposed INN		Public	
Chemical name		Public	
Scientific name		Public	
Common name	Newcastle disease virus, strain KUG, Live	Restricted	
Company code	KUG-123	Public	
Other (specify)		Public	
Molecular formula		Public	
CAS number		Public	

For bulk requests concerning translations, an excel file containing the substance SMS IDs/EV codes and the concerned translations can be provided instead of the Substance Request Form.

3. Prepare the required supporting documentation

For all substance requests, supporting documentation describing the substance structure/nomenclature must be provided. The only exceptions are when an official name (e.g. INN, USAN) or a UNII is available. In these cases, reference to the official name/UNII is deemed sufficient.

The documents listed below, including the draft versions of such documents, are some examples of accepted documentation:

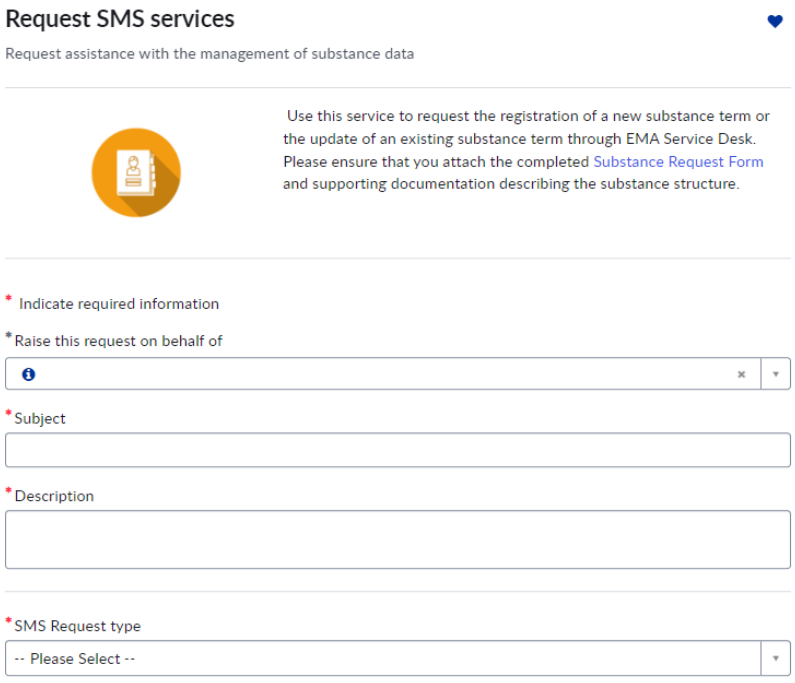
- Investigator's Brochure.
- Investigator's Medicinal Product Dossier.
- Summary of Product Characteristics.
- Package Leaflet.
- Section A.3. Medical Plausibility of Orphan Designation Application.

The provided supporting documentation will never be published and it will only be used in the context of the creation or update of a substance record. Documents are kept for at least 5 years, in accordance with the EMA Data Protection policy.

4. Submit the ticket via the EMA Service Desk

Access the form Request SMS Services in the EMA Service Desk (**Figure 16**) and fill out the mandatory fields, depending on the request type.

Figure 16. Request SMS Services form in the EMA Service Desk



For requests to create new substance record(s), the following fields are mandatory:

- **Subject**: enter a relevant subject (e.g. New substance(s) request).
- **Description**: provide a brief description of the requested substance(s).
- **SMS Request type**: select the most appropriate type that aligns with the regulatory procedure for the substance's subsequent use; please note that this will have an impact on the selection of the preferred term.
- **Attachments**: attach the filled-out Substance Request Form and appropriate supporting documentation.

For requests to update substance record(s) (e.g. to change the current preferred term, add one or more aliases, add one or more translations), the following fields should be filled-out:

- **Subject**: enter a relevant subject (e.g. Update substance(s) request).
- **Description**: provide the SMS ID(s) or EV Code(s) of the concerned substance record(s) and the new name(s)/translation(s);
- **SMS Request type**: select the most appropriate type that aligns with the regulatory procedure for the substance's subsequent use; please note that this will have an impact on the selection of the preferred term.
- **Attachments**: attach the filled-out Substance Request Form and appropriate supporting documentation.

5. Wait for the resolution of the request

After the request has been submitted, it will be further processed in accordance with the agreed Service-Level Agreements (SLAs), as described in **Table 11**. Applicants should therefore be mindful of the SLAs when planning a regulatory application submission.

Table 11. SMS change requests SLAs

Type of request	75% of requests	90% of requests	Expected outcome
Creation of substance, addition of an alias or change in preferred term (up to 20 terms/records)	Resolved within 5 working days	Resolved within 10 working days	The substance/alias is available for use, if the request is approved.
Addition of translation(s) (up to 20 terms/records)	Resolved within 10 working days	Resolved within 15 working days	The translation is available for use if the request is approved.
Creation of substance, addition of an alias, change in preferred term or addition of a translation(s) (over 20 terms/records)	No guaranteed SLA	No guaranteed SLA	The substances/aliases/translations are available for use if the request is approved.

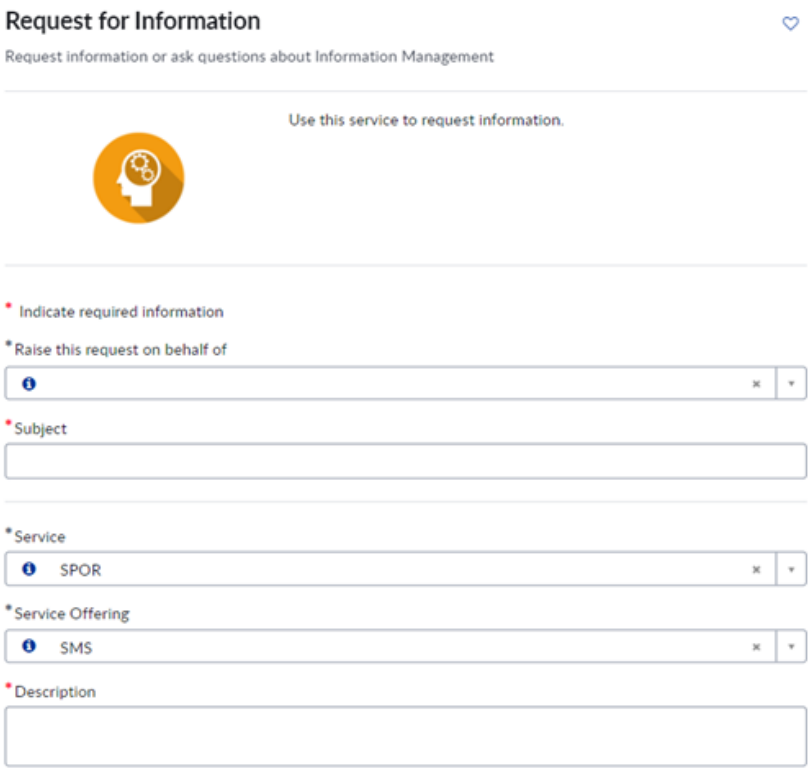
The requestor can withdraw the request at any time before the substance is registered in SMS. Once the substance is registered in SMS, it cannot be deleted, however, it can still be updated.

If additional clarifications or documentation is required during the request assessment, the SLA will be paused until the requestor replies. The requestor has 5 working days to provide a reply, otherwise the request will be closed. Any closed ticket can be reopened within 5 additional working days. If a new ticket is still required, reference to the original ticket should be provided.

7. Customer Service

Users can also submit substance related queries by accessing the Request for Information form in the EMA Service Desk (**Figure 17**) and setting the Service as "SPOR" and the Service Offering as "SMS".

Figure 17. Request for Information form in the EMA Service Desk



After the mandatory information is provided and the request for information concerning a substance related query has been submitted, it will be further processed in accordance with the agreed SLA, as described below, in **Table 12**.

Table 12. Request for Information SLAs

Type of request	75% of requests	90% of requests	Expected outcome
Request for information	Resolved within 22 working days	Resolved within 44 working days	The query is addressed

A list of frequently asked questions is available in *Annex 2: Frequently Asked Questions* to better support users with their queries on substances.

8. Data Stewardship

EMA SMS Data Stewards are continuously involved in data-centred activities, such as data mappings, data enrichments and data cleansing activities in cooperation with the SVG. These activities are essential for ensuring the quality, accuracy, and consistency of the data that is used by various stakeholders.

8.1. Data Mappings

Data mapping activities consist in matching substance data in EMA/NCA legacy systems to existing SMS substance data, resulting in the subsequent update or creation of relevant data in SMS. These exercises support data migrations and implementation of SMS in telematics systems.

The following substance data mappings have already been completed after SMS went live:

- Active and Withdrawn Orphan Designations for IRIS.
- Veterinary Scientific Advice for IRIS.
- Innovation Task Force for IRIS.
- PRIME for IRIS.
- Minor Use Minor Species (MUMS) for IRIS.
- EVVet substances for SMS.
- Veterinary active substances from 27 NCAs for UPD.
- xEVMPD development substances for SMS.
- Relevant Veterinary substances shared with European Food and Safety Authority (EFSA)
- Relevant Human substances shared with European Chemicals Agency (ECHA)

As an outcome of the substance mapping exercises, substance records might be created or updated (e.g. new aliases added), based on supporting documentation from the related regulatory procedures and information from the public domain.

New data mappings can be performed when needed to integrate a new system with SMS or to support new activities with other international organisations.

8.2. Data Enrichments

Data enrichment activities consist in proactively adding new and relevant information to existing SMS data, according to public reference information. These exercises improve data accuracy, reliability and value, ultimately increasing the data quality in SMS and, by facilitating substance identification and subsequently preventing the submission of change requests, they minimise the burden on industry, NCA and EMA users.

There are currently 8 data enrichment exercises regularly performed by the SMS team, listed in **Table *13*.** Data enrichment exercises

Table 13. Data enrichment exercises

Enrichment	Trigger	Frequency	Data fields impacted	Outcome
Proposed INN (pINN)	Publication of a new pINN list by WHO	Twice a year	• Substance names • External code: UNII	Substances created or updated
Recommended INN (rINN)	Publication of a new rINN list by WHO	Twice a year	• Data Classification • Substance names • External code: UNII	Substances created or updated
United States Adopted Name (USAN)	Publication of a new batch of USANs by USAN Council	Ad-hoc	• Substance names	Substances created or updated
Unique Ingredient Identifier (UNII)	Refresh of UNII exports by FDA	Ad-hoc	• External code: UNII	Substances updated
European Pharmacopoeia (Ph. Eur.)	Publication of a new Ph. Eur. supplement by the European Directorate for the Quality of Medicines & HealthCare (EDQM)	Three times a year	• Substance names	Substances created or updated
Custom Attribute: Critical Medicines	Publication of a new version of the Union List of Critical Medicines by the European Commission	Yearly	• Custom Attribute: Critical Medicine	Substances updated
Custom Attribute: Active substance in EEA human medicinal products	Internal process	Quarterly	• Custom Attribute: Active substance in valid EEA human AMP	Substances updated
Custom Attribute: Excipient/Adjuvant in EEA human medicinal products	Internal process	Quarterly	• Custom Attribute: Excipient/Adjuvant in valid EEA human AMP	Substances updated

8.3. Data Cleansing

Data cleansing activities consist of proactively reviewing SMS data to identify and eliminate duplicates, as well as to verify and to standardise SMS data against established public reference information.

Data cleansing improves the data quality and, by preventing the submission of change requests, minimises the burden on industry users.

The Substance Validation Group (SVG) is a European group of experts involved in the cleansing of the legacy substance data, as prioritised by the Network. As of September 2025, the following substance types/groups have now been cleansed:

- Veterinary active substances used in veterinary authorised products (all substance types)
- Chemicals
- Proteins
    - Proteins used in approved medicinal products
    - All insulins (Proteins and Specified Substance Group 1)
- Polymers most used in approved medicinal products
- Proprietary mixtures of excipients from Colorcon® (Specified Substance Group 1)
- Solutions (Specified Substances Group 1)
- Substances with pharmacopoeia references (Specified Substances Group 3)
- Herbals

An overview of the cleansing status of all substance types, as of September 2025, can be found in the **Table *14***.

Table 14. Cleansing status by substance type, as of January 2026

Substance type	% cleansed	Comments
Chemical	100%	
Structurally Diverse - Herbal	99%	
Specified Substance Group 3	98%	
Structurally Diverse - Vaccine	54%	Veterinary vaccines cleansed, Human vaccines ongoing
Polymer	34%	
Mixture	28%	
Specified Substance Group 1	17%	Includes flavours, proprietary mixtures of excipients, solutions, homeopathics, herbal extracts
Structurally Diverse - Plasma derived	12%	
Structurally Diverse - Other	11%	Includes gene therapy and animals
Protein	11%	
Nucleic acid	4%	
Structurally Diverse - Allergen	2%	
Structurally Diverse - Cell therapy	1%	
Overall	**51%**	

This represents 100% of active substances used in veterinary authorised medicinal products and 79% of substances used in human authorised medicinal products.

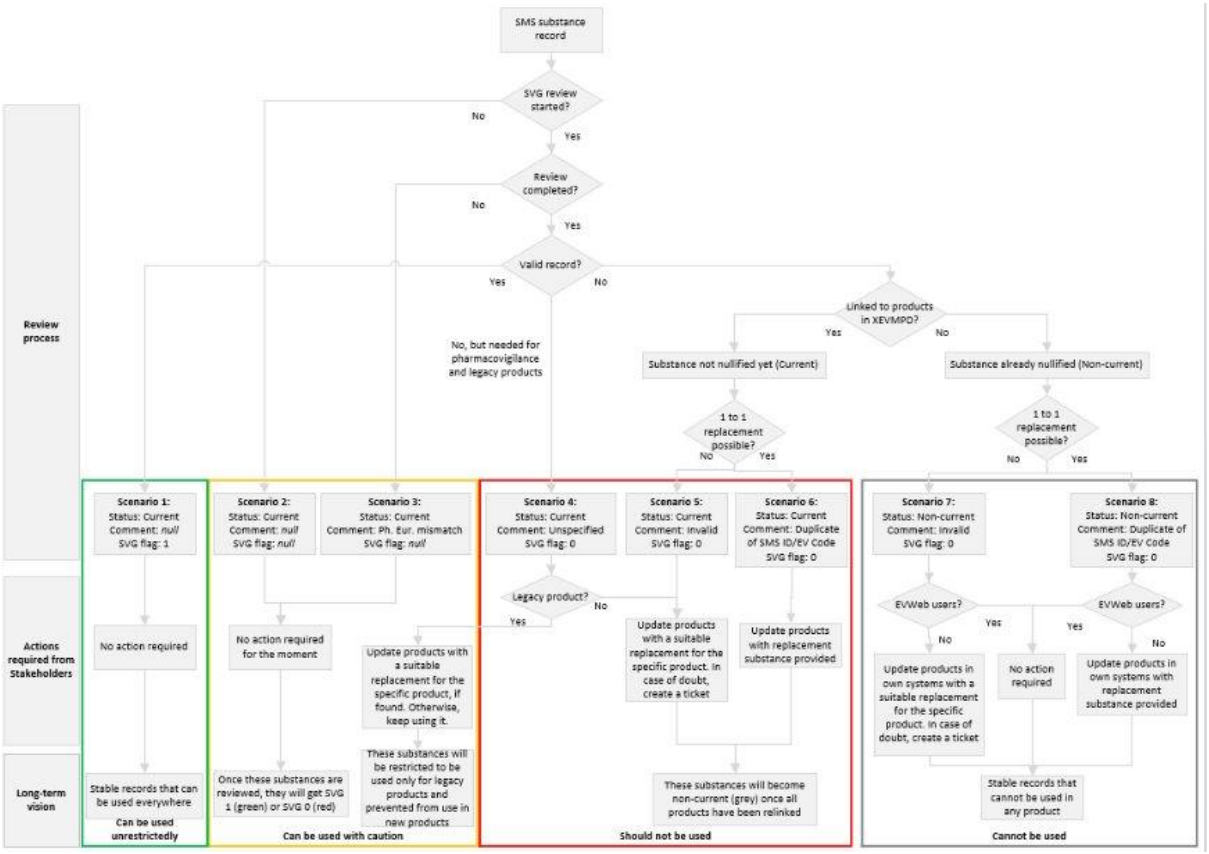
The most relevant data fields to highlight the substance cleansing status are described in **Table 15**:

Table 15. SMS data fields relevant for cleansing outcomes

Data field	Value	Meaning
Substance Status	Current	Record that can be used
	Non-current	Record that cannot be used
Comments	Ph. Eur. mismatch	Record cannot be cleansed due to a mismatch in Ph. Eur.
	Unspecified	Record is very general and should be avoided
	Duplicate of *SMS ID*/EV *Code*	Record is a duplicate of another record and should not be used
	Invalid	Record is not a substance
SVG flag	1	Record deemed valid by SVG
	0	Record deemed not valid by SVG
	Null	Record not yet reviewed by SVG
Substance (Current)	SMS ID of the replacement substance	Only added in case of Duplicates

Depending on the substance cleansing status and the respective products linked, there are currently 8 identified scenarios, with different combinations of the data fields above. The different scenarios expected actions from stakeholders and long-term vision are illustrated in **Figure *18.*** Request for Information form in the EMA Service Desk and further explained below.

Figure 18. Request for Information form in the EMA Service Desk



Scenario 1

These are substance records that have been fully reviewed and were deemed valid. These records have status "Current", SVG flag 1 and no comments nor replacement substance. These records are not expected to have major changes in the future, with the exception of regular updates as part of the substance lifecycle (e.g. addition of an INN, an UNII, translations, etc.). They do not require any action from stakeholders and can be used without restrictions in any products or regulatory procedures.

Scenario 2

These are substance records that have not yet been reviewed. They have status "Current" and no comments, SVG flag or replacement substance. These substances will be reviewed in the future taking into account the priorities defined by the Network. Once reviewed, they will then become a scenario 1 if deemed valid or any other scenario if deemed not valid. For the moment no action is required on them from stakeholders, and they can be used with caution in products or regulatory procedures. However, the status/SVG flag might change in the future and an action might then become required.

Scenario 3

These are substance records that the review has started but could not be completed since a mismatch between the European Pharmacopoeia monograph title (usually pointing to an anhydrous substance) and definition (usually pointing to a hydrated substance) was detected, which makes the substance record ambiguous. They have status "Current", Comment "Ph. Eur. mismatch" but no SVG flag or replacement

substance. There is ongoing discussion between the Substance Validation Group and EDQM to review these monographs. For the moment, no action is required from stakeholders, and they can be used with caution in products or regulatory procedures. Once the monographs are reviewed, these substances will be fully cleansed and will follow the same outcome as from scenario 2.

Scenario 4

These are substance records that have been fully reviewed and were deemed not valid, since they refer to very general substances. However, these records are still needed to support pharmacovigilance activities and to be used in legacy products (e.g. veterinary products that were approved without a strain in the SmPC). These records have status "Current", SVG flag 0, Comment "Unspecified" but no replacement substance. When possible, stakeholders should try to refer to a more specific substance in their legacy products. However, if that is not possible, these records can still be used.

For new products these records should not be used, and a more specific substance should be used instead. For these cases, if no suitable replacement is found, then users should create a ticket in EMA Service Desk asking for advice. In the future, it is expected that these substances will be technically blocked from being used in new products and their use will be restricted to only legacy products (i.e. already approved with these Unspecified substances).

Scenario 5

These are substance records that have been fully reviewed and were deemed not valid, since they are invalid according to the SMS business rules. However, since they are linked to product records in XEVMPD, they cannot yet be nullified. They have status "Current", SVG flag 0, Comment "Invalid" but the data field "Substance (Current)" is null, since the replacement SMS ID will depend on a case-by-case situation. Stakeholders should not use these records in any products or regulatory products and, instead, refer to a suitable replacement substance for their specific products. If no suitable replacement is found, then users should create a ticket in EMA Service Desk asking for advice. Once all products in XEVMPD have been relinked, these substances will be made non-current, and they will no longer be able to be used (i.e. scenario 7).

Scenario 6

These are substance records that have been fully reviewed and were deemed not valid, since they are duplicates of another substance. However, since they are linked to product records in XEVMPD, they cannot yet be nullified. They have status "Current", SVG flag 0, Comment "Duplicate of *SMS ID of replacement substance */*EV Code of replacement substance*" and the data field "Substance (Current)" is also populated with the SMS ID of replacement substance. Stakeholders should not use these records in any products or regulatory products and, instead, refer to the replacement substance provided in the "Comments" and "Substance (Current)" data fields. Once all products in XEVMPD have been relinked, these substances will be made non-current, and they will no longer be able to be used (i.e. scenario 8).

Scenario 7

These are substance records that have been fully reviewed and were deemed not valid, since they are invalid according to the SMS business rules. They were not linked to any product in XEVMPD, so these substances were already nullified. They now have status "Non-current", no SVG flag, Comment "Invalid"

but the data field "Substance (Current)" is null, since the replacement SMS ID will depend on a case-by-case situation. These substances can no longer be used in any product or regulatory procedures. Non-EVWeb (i.e. RIM or UPD) users should ensure that their own systems no longer refer to these substances and, instead, refer to a suitable replacement substance for their specific products. If no suitable replacement is found, then users should create a ticket in EMA Service Desk asking for advice. The non-current status is permanent and cannot be reverted back to current.

Scenario 8

These are substance records that have been fully reviewed and were deemed not valid, since they are duplicates of another substance. They were not linked to any product in XEVMPD, so these substances were already nullified. They now have status "Non-current", no SVG flag Comment "Duplicate of *SMS ID of replacement substance */*EV Code of replacement substance*" and the data field "Substance (Current)" is also populated with the SMS ID of replacement substance. These substances can no longer be used in any product or regulatory procedures. Non-EVWeb (i.e. RIM or UPD) users should ensure that their own systems no longer refer to these substances and, instead, refer to the respective replacement substance. The non-current status is permanent and cannot be reverted back to current.

8.3.1. Cleansing follow-up actions

8.3.1.1. SVG flag 0 and comment "Duplicate"

Known duplicated substance records have SVG flag 0, so they are no longer available in eAF and UPD (for new products). However, they are still available in XEVMPD and can technically be used in the creation or update of product records. It is not technically possible to flag these substances in XEVMPD in the product view, so it is not easy for MAH to identify them and correct them. In order to minimise the burden on MAHs, EMA is preparing a data fix to relink the impacted products in XEVMPD/PMS during 2025. Before the data fix, EMA will publish an export of impacted product and substance EV codes. EMA will then nullify the duplicated substances, and they will no longer be usable in any consuming system. MAH that are Gateway users should update their systems with the replacement substances provided ahead of the data fix to prevent negative acknowledgements. If desired, MAH can optionally update their products in XEVMPD before the data fix.

8.3.1.2. Pending changes in Preferred Terms

The SVG has identified substances that have an incorrect PT in SMS. The substance name that should be the preferred term is highlighted with the name source "Substance Validation Group". However, changing PTs has an impact on ICSR recoding, so these updates have not been implemented yet. There is a technical development ongoing to prevent disruptions in the ICSR recoding. After this is completed, the respective substance preferred terms will be updated in SMS.

8.3.1.3. SVG flag 0 and comment "Invalid" or "Unspecified"

Known "Invalid" or "Unspecified" substance records have SVG flag 0, so they are no longer available in eAF and UPD (for new products). However, they are still available in XEVMPD and can technically be used in the creation or update of product records. These are complex scenarios that require a product-by-product analysis and will be only addressed in late 2025, after the duplicates are addressed.

8.4. Data Quality monitoring

Data quality encompasses the overall condition and usability of data assets within an organisation. The following data quality dimensions are monitored and maintained in SMS:

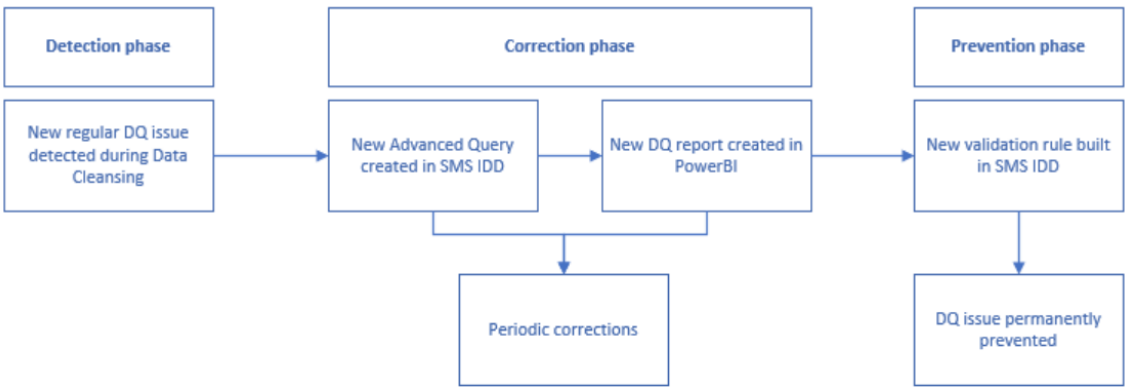
- Uniqueness
- Accuracy
- Completeness
- Consistency
- Conformity
- Currency

Uniqueness refers to the quality of data being distinct and devoid of duplicates. In SMS, each record should represent a unique substance. Accuracy denotes the correctness of data. In SMS, each record should reflect the actual values the substance it represents. Completeness measures the extent to which all required data elements are present in a dataset. In SMS, each record should have all the required values populated, in accordance with the business rules of each substance type and domain. Consistency refers to the coherence and uniformity of data across different data fields. In SMS, it means that values from different sections are consistent with each other. Conformity relates to the adherence of data to predefined standards. In SMS, it means that the concerned data fields are populated according to the defined business rules. Currency pertains to the timeliness and relevance of data in relation to the present moment. In SMS, it means that the concerned data fields are still up to date.

In order to prevent data quality issues, SMS IDD has built-in validation rules covering the data quality dimensions mentioned above. In addition, there are data quality profiles available in SMS IDD and in PowerBI to monitor quality issues that can't be prevented (yet) by validation rules. There are then defined processes to correct the identified issues in a timely manner.

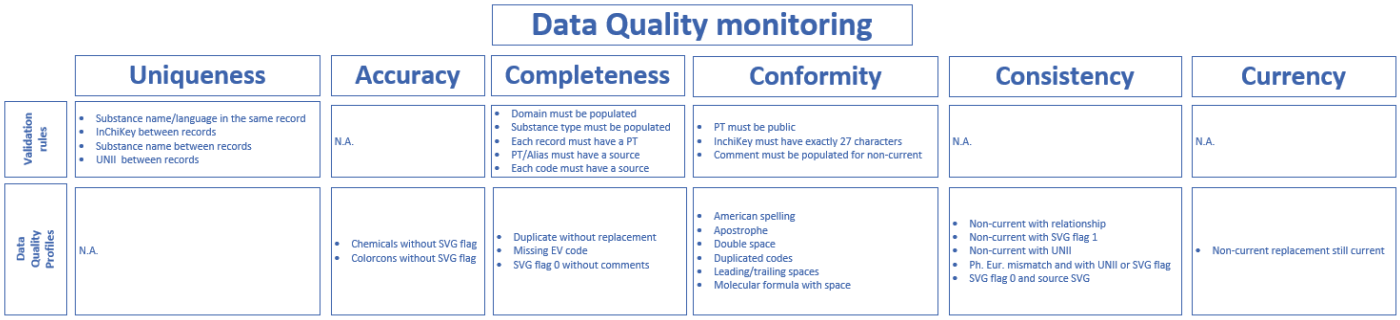
As illustrated in **Figure *19.*** Development of data quality profiles and validation rules, when regular DQ issues are identified during data cleansing exercises, a new advanced query is developed in SMS IDD and a corrective process is developed and implemented on a daily, weekly or monthly basis. Later, the same report will be built in PowerBI to allow an easier monitoring and correction. Finally, if possible, a new validation rule is built in SMS IDD directly to prevent the data quality issue from happening again.

Figure 19. Development of data quality profiles and validation rules



In **Figure *20.*** Validation rules and Data Quality Profiles it is possible to see the current validation rules in SMS and the data quality profiles. When a new issue is detected in a data quality profile, it tiggers a corrective action in SMS to address it.

Figure 20. Validation rules and Data Quality Profiles



9. Document versions

A major version is considered when a new chapter is published or an existing chapter is radically changed, while a minor version is considered when an already existing chapter is updated.

Version	Date	Main changes
3.2	23 January 2026	Chapter 8.3 – Data cleansing statistics updated Annex 1 – Business rules revised
3.1	2 October 2025	Chapter 4.3. - Application Programming Interface revised Annex 1 – Business rules revised
3.0	3 April 2025	Chapter 8.2 - Data enrichments revised Annex 1 – Business rules published
2.0	25 November 2024	Chapter 4.3 - Application Programming Interface revised Chapter 8.3 - Data Cleansing revised Chapter 8.4 - Data quality monitoring published Annex 5 - Data fields to FHIR mappings published
1.0	1 December 2023	First version

Annex 1: Business rules per substance type

1. General naming rules

A substance record may reference different name types which, based on concerned regulatory procedure, will impact the selection of the preferred term and influence the confidentiality selection:

- **Systematic (chemical) names** follow a set of rules that are defined by an international body, such as the International Union of Pure and Applied Chemistry (IUPAC). Systematic names are based on the structure and composition of the chemical, and they uniquely identify one chemical. This name type can be either public or restricted and can therefore be set either as the preferred term or as an alias.
- **Common names** are names that are widely used, but do not follow the systematic naming convention. This name type can be either public or restricted and can therefore be set either as the preferred term or as an alias.
- **Official names** are names that are referenced in an official public source (e.g. Ph. Eur., INN, USAN, JAN). This name type will always be public and can therefore be set as the preferred term (for recommended INNs) or as an alias (for proposed INNs, USAN, etc.).
- **Company or laboratory codes** are combinations of letters and numbers given by companies developing a substance and are used to identify the substance while it is in development. This name type can be either public or restricted and can therefore be set either as the preferred term or as an alias.

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

1. Pharmacopoeia Europea name[4]
2. (Modified) Recommended International Non-Proprietary Name
3. Other official name type with EU/EEA jurisdiction (e.g. INCI)
4. Common name mentioned in the SmPC or package leaflef
5. Systematic/scientific name
6. Company code

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

- Proposed INN
- United States Approved Name
- United States Pharmacopoeia
- Japanese Approved Name
- Official name in other jurisdictions (e.g. BAN, AAN)

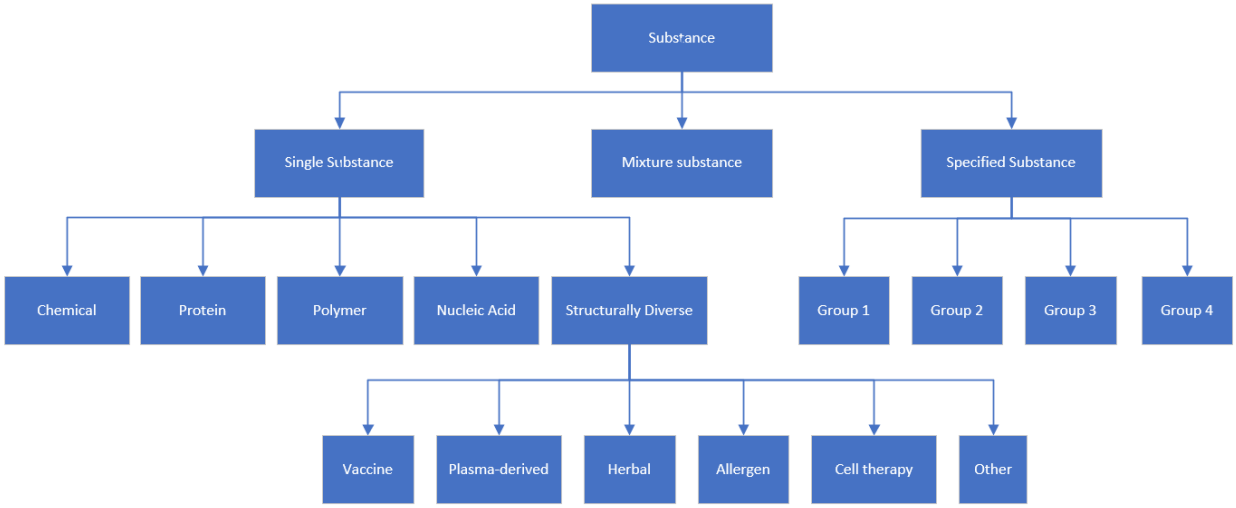
If a salt/solvate is requested, the active moiety (free base or free acid or anhydrous substance) will also be registered for the purposes of grouping/hierarchy, if missing. If only a company code is provided (e.g. ABC-123) for a substance with a sodium salt, then "ABC-123" will be used for the free base and "ABC-123 sodium" will be used for the salt. If different company codes are provided, then they will be used accordingly. Similarly, when a radioactive substance is requested, the unlabelled substances will also be registered, if missing.

[4] Some older Ph. Eur. monographs have a mismatch between the name and its definition, leading to ambiguous substance records. These situations are exceptions and are between discussed between the SVG and EDQM. Further information is provided in chapter 8.3 Data Cleansing – Section 3.

2. Substance type-specific naming rules

The substance type is defined by SMS data stewards, and it is only used for data management purposes in SMS and has no impact in any regulatory procedure. Like mentioned in chapter 2, the substance types in SMS are a controlled vocabulary list from RMS and are listed in **Figure 21.** Substance type values in SMS.

Figure 21. Substance type values in SMS



The business rules described below have been reviewed by the SVG and are considered stable. However, minor adjustments are still possible.

2.1. Chemicals

Chemicals are single substances with a discrete molecular structure.

Key principles

- Systematic name must always be provided, unless an official name or UNII or CAS is provided
- Molecular formula, molecular weight and InChIKey will be generated based on systematic name
- UNII will be added as an external code, if available at the time of registration

Examples

SMS ID	**100000174650**
Preferred term	Nirogacestat
Alias	PF-03084014
Molecular formula	C27H41F2N5O
Molecular weight	489.65
InChiKey	VFCRKLWBYMDAED-REWPJTCUSA-N
UNII	QZ62892OFJ

SMS ID	**100000124142**
Preferred term	Rilpivirine hydrochloride
Alias	TMC278 hydrochloride
Molecular formula	C22H18N6.ClH
Molecular weight	402.88
InChiKey	KZVVGZKAVZUACK-BJILWQEISA-N
UNII	212WAX8KDD

SMS ID	**100000174986**
Preferred term	BI 113823
Alias	*Restricted*
Molecular formula	*Restricted*
Molecular weight	*Restricted*
InChiKey	*Restricted*
UNII	Not available

2.2. Veterinary vaccines

Key principles

All new veterinary vaccines must be registered with a strain unless they belong to one of the identified exceptions:

1. Vaccines for Scientific Advice
2. Recombinant protein vaccines

Some existing vaccine records without strain are kept as current but can only be used for already approved veterinary products. They have the comment "Unspecified" and SVG flag 0 and are not visible in the eAF and not usable in UPD for new products. When required for a variation in the eAF, the SVG flag 0 is temporarily removed and added later on again.

Additionally, certain microorganisms have a different set of rules:

3. Influenza vaccines
4. Vector vaccines
5. Infectious bursal disease virus (intermediate strains)

2.2.1. General rules

- Preferred term syntax: <Microorganism>, <taxonomic levels>, <strain>, <vaccine status> or <antigen>
- Alias(es) syntax: <Microorganism>, <taxonomic levels>, <strain>, <vaccine status> or <antigen>

Name part	Conformance	Details
Microorganism	Mandatory	Microorganism preferred term, as defined by the SVG
Taxonomic levels	Conditional	Taxonomic levels (e.g. serotype, serogroup, serovar) applicable for the given microorganism, as defined by the SVG
Strain	Mandatory*	Strain used in the given vaccine
Vaccine status or Antigen	Mandatory	"Live" or "Inactivated" or "Antigen" used. Live attenuated vaccines are registered as "Live".

*with the exceptions mentioned below

Examples

SMS ID	300000040441
Preferred term	Bovine viral diarrhoea virus, strain BK-1/B-1, Live
Alias	BVDV-1, strain BK-1/B-1, Live
Alias	Pestivirus A, strain BK-1/B-1, Live

SMS ID	300000040172
Preferred term	Infectious bursal disease virus, strain 89/03, Inactivated
Alias	IBDV, strain 89/03, Inactivated
Alias	Gumboro virus, strain 89/03, Inactivated

2.2.2. Vaccines for Scientific Advice

Preferred term syntax: Usually just a company code

Alias(es) syntax: <Microorganism>, <taxonomic levels>, <strain>, <vaccine status or antigen>

Name part	Conformance	Details
Microorganism	Mandatory	Microorganism preferred term,
Taxonomic levels	Conditional	Taxonomic levels mandatory for the given microorganism, as defined by the SVG
Strain	Optional	Strain used in the given vaccine, if already known*
Vaccine status or Antigen	Mandatory	Live or Inactivated or Antigen used in the given vaccine

If the strain is not present, then the substance should be registered with the following data fields populated:

- Comments: Unspecified
- SVG flag: 0

Once/if information on strain becomes available, the substance preferred term/aliases will be updated in accordance with the general rules and the comment/SVG flag 0 will be removed.

Examples

SMS ID	300000018122
Preferred term	PB-133
Alias	*Restricted*
Comments	Unspecified
SVG flag	0

SMS ID	300000039789
Preferred term	FEC-1
Alias	*Restricted*
Comments	*Null*
SVG flag	1

2.2.3. Recombinant protein vaccines

Preferred term syntax: <Microorganism>, <taxonomic levels>, <antigen> (recombinant)

Name part	Conformance	Details
Microorganism	Mandatory	Microorganism taxonomic name
Taxonomic levels	Conditional	Taxonomic levels (e.g. serotype, serogroup, serovar) applicable for the given microorganism, as defined by the SVG
Antigen	Mandatory	Antigen used in the given vaccine
(recombinant)	Mandatory	The word recombinant added in brackets without comma in the end

Examples

SMS ID	300000017891
Preferred term	Bovine viral diarrhoea virus 1, protein E2 (recombinant)

SMS ID	300000037079
Preferred term	Rabbit haemorrhagic disease virus, type 2, capsid protein (recombinant)

2.2.4. Influenza vaccines

Preferred term syntax: Influenza A virus, <subtype>, <lineage*>, <sublineage*>, <strain>, <vaccine status>
Alias syntax: Not applicable
*if applicable

Name part	Conformance	Details
Microorganism	Mandatory	Influenza A virus
Subtype	Mandatory	
Lineage	Conditional	Only applicable to H3N8. Not yet in use in SMS
Sublineage	Conditional	Only applicable to H3N8. Not yet in use in SMS
Strain	Mandatory	
Vaccine status	Mandatory	Live or Inactivated

Examples

SMS ID	300000023551
Preferred term	Influenza A virus, subtype H5N2, strain A/duck/Potsdam/1402/86, Inactivated

SMS ID	300000018465
Preferred term	Influenza A virus, subtype H7N7, strain A/equine/Newmarket/77, Inactivated

2.2.5. Vector vaccines

Preferred term syntax: <Vector>, <Strain*> <(gene(s) deleted*)>, expressing <gene(s) inserted> of <Inserted microorganism> <(Strain*)>, <Status*>
*if applicable

Name part	Conformance	Details
Vector	Mandatory	Microorganism preferred term
Vector strain	Optional	
Vector deleted genes	Optional	
Expressing	Mandatory	
Gene of expressed microorganism	Mandatory	
Expressed microorganism	Mandatory	Microorganism preferred term
Expressed microorganism strain	Optional	
Vaccine status	Mandatory	Live or Inactivated

Examples

SMS ID	300000058484
Preferred term	Turkey herpesvirus, strain rHVT-IBD-H5 (cell-associated), expressing VP2 protein of infectious bursal disease and haemagglutinin gene of avian influenza virus subtype H5, Live

SMS ID	300000009186
Preferred term	300000009186 - Canarypox virus, strain vCP65, expressing glycoprotein G gene of Rabies virus, Live

2.2.6. Infectious bursal disease virus (intermediate strains)

Preferred term syntax: <Microorganism>, <taxonomic levels>, <strain (intermediate/ intermediate plus)>, <vaccine status>

Name part	Conformance	Details
Microorganism	Mandatory	Microorganism taxonomic name
Taxonomic levels	Conditional	Taxonomic levels (e.g. serotype, serogroup, serovar) applicable for the given microorganism, as defined by the SVG
Strain (intermediate) or (intermediate plus)	Mandatory	The word intermediate/ intermediate plus added in brackets without comma in the end
Vaccine status	Mandatory	Mandatory

Examples

SMS ID	300000025039
Preferred term	Infectious bursal disease virus, strain VMG 91 (intermediate), Live

SMS ID	300000018586
Preferred term	Infectious bursal disease virus, strain Winterfield 2512 (intermediate plus), Live

2.3. Specified Substances Group 1 (SSG1)

SSG1 include several different groups of substances, which are listed below:

- Records related to Ph. Eur.:
  - Substances with certain physical properties defined in Ph. Eur
  - Solutions or dispersions with a defined concentration defined in Ph. Eur.
- Proprietary mixtures of excipients
- Coatings
- Flavours
- Veterinary vaccines with different antigens from different strains
- Homoeopathic substances
- Herbal extracts
- Isophane insulins

2.3.1. SSG1 related to Ph. Eur.

This section summaries all the agreed rules on Specified Substances Group 1 (SSG1) related to European Pharmacopoeia (Ph. Eur.) monographs. The rules are described for the following subgroups:

- Property
- Solutions

The rules in this section do not apply to the following substance types:

- Radiolabelled chemicals
- Proteins
- Structurally Diverse - Plasma derived
- Herbals
- Herbals extracts
- Homeopathics

These substance types will have separate rules, which will be published at a later date.

2.3.1.1. Property

Business rules

This category refers to SSG1 records that include additional properties in the substance name. Most of the properties are not considered relevant and will not be kept. The only two properties that can be kept, if a respective Ph. Eur. monograph is present, are:

- "Form"
- "Intermix"

In the cases above, a separate SSG1 record will be kept. In all the remaining cases, a SSG1 will not be created and, instead, users should refer to the respective parent substance.

Property	**Business rules**	**SMS Implementation**
Form Intermix	To be kept if a Ph. Eur. monograph is available	• Preferred term aligned with Ph. Eur. monograph title • SVG flag 1
Amorphous Capsules Concentrate Crystalline Injection	Never to be kept	• Comment "Duplicate of SMS ID/EV Code" of the parent substance • SVG flag 0 • Parent substance added as replacement

Liposomal		
Micronised		
Nanonised		
Powder		
Sterile		
Synthetic		
Tablet		

Maintenance

All the relevant SSG1 related to the proprieties above are already available in SMS. New SSG1 under this rule will be created by SMS data steward in data enrichments exercises, upon publication of new Ph. Eur. monograph relevant by EDQM and follow-up discussions with the SVG. No change requests for new SSG1 in this scenario are expected.

Substance names with the properties not considered relevant will not be registered as aliases or translations of the parent substance.

Examples

Substance name	**Relevant property?**	**Ph. Eur. monograph**	**SMS record**
Vitamin A concentrate (oily form), synthetic	Yes	Vitamin A concentrate (oily form), synthetic	100000131318 - Vitamin A concentrate (oily form), synthetic
Acetylene intermix (1 per cent) in nitrogen	Yes	Acetylene intermix (1 per cent) in nitrogen	300000058768 - Acetylene intermix (1 per cent) in nitrogen
ADIPIC ACID, MICRONISED	No	N.A.	100000077961 - Adipic acid
PACLITAXEL, LIPOSOMAL	No	N.A.	100000085474 - Paclitaxel

2.3.1.2. Solutions

Business rules
A SSG1 will be kept for a solution, if under one the following conditions:

- An individual monograph (i.e. 4 digits) for the solution is present in the European Pharmacopoeia;
- A monograph for the solution is present in an EEA national pharmacopoeia;
- It is a SVG identified exception and is listed in this guidance document

If under one of the scenarios above, a SSG1 record for the solution will be kept in SMS:

Scenario	**Preferred term**	**Alias 1**	**Alias 2**
Ph. Eur. monograph for SSG1 solution	Title of the monograph	Concentration range as defined in Ph. Eur.	Concentration range in an alternative unit of measure as defined in Ph. Eur. (if available)
Other EEA national monographs for SSG1 solution	Title of the monograph	Concentration range as defined in the national monograph	Concentration range in an alternative unit of measure as defined in national monograph (if available)
SVG exception	Parent substance + solution	N. A.	N. A.

Substance names with a specific concentration will not be added as aliases or translations of the replacement records.

Maintenance

Scenario	**Change requests for new SSG1 accepted?**	**Explanation**
Ph. Eur. monograph for SSG1 solution	No	As of Ph. Eur. 11.8, all the relevant SSG1 solutions are already available in SMS. New SSG1 records will be created by SMS data steward in data enrichments exercises, upon publication of new relevant Ph. Eur. monographs by EDQM and follow-up discussions with the SVG.
Other EEA national monographs for SSG1 solution	Yes, with monograph attached	Any change request will be discussed with the SVG and a new SSG1 solution might be created.
SVG exception	No	All required SSG1 solutions are already available in SMS. In the absence of a record with a specific concentration, the general solution SSG1 (if available) or the parent substance should be instead.

Examples

Scenario	SMS ID	SMS PT	Reference	Outcome in SMS
Ph. Eur. monograph for SSG1 solution	100000076353	Ethanol (96 per cent)	Ph. Eur: 1317: Ethanol (96 per cent) Concentration range: 92.6-95.2% m/m (95.1-96.9% V/V)	The record 100000076353 - Ethanol (96 per cent) will be kept with SVG flag 1. Translations of this substance name can be added in SMS.
Ph. Eur. monograph for SSG1 solution	100000134653	ETHANOL 94% (M/M)		The ethanol concentration within the range specified in the Ph. Eur. monograph. These two records will have SVG flag 0 and, eventually, will be nullified. The substance names "ETHANOL 94% (M/M)", "Ethanol 96.6 % (V/V)" and their respective translations in other EU languages will not be kept in SMS
Ph. Eur. monograph for SSG1 solution	300000001482	Ethanol 96.6 % (V/V)		
Other EEA national monographs for SSG1 solution	300000061034	Potassium lactate solution	German Pharmacopoeia: Potassium lactate solution Concentration range: 49-51% m/m	The record 300000061034 - Potassium lactate solution will be kept with SVG flag 1. Translations of this substance name can be added in SMS
SVG exception	100000077713	Ammonia solution	SVG	This record is kept with SVG flag 1, since it is a SVG listed exception.
SVG exception	300000023303	Ammonia solution 28%	None	This record is considered a duplicate of the general record 100000077713 - Ammonia solution. "Ammonia solution 28%" and their respective translations in other EU languages will not be kept in SMS
Not applicable	100000163031	GLYCEROL 96%	0497 - Glycerol (85 per cent) Concentration range: 83.5-88.5 per cent *m/m*	Outside of scope of Ph. Eur. specification. The SMS ID is replaced by general record: 100000092821 – Glycerol "GLYCEROL 96%" and its respective translations in other EU languages will not be kept in SMS.
Not applicable	100000135488	BENZYL ALCOHOL (1%)	None	No monograph available. The SMSID is replaced by substance record: 100000086395 - Benzyl alcohol "Benzyl alcohol (1%)" and its respective translations in other EU languages will not be kept in SMS.

All the relevant SSG1 solutions that will be maintained in SMS are listed on the table below.

Parent record	Concentration range	Reference	SMS ID	Preferred term
Acetic acid	99.0-100.5% m/m	Ph. Eur.: 0590 - Acetic acid, glacial	100000076667	Acetic acid, glacial
Acetic acid	Any not mentioned above	SVG	100000162503	Acetic acid solution
Aluminium acetate tartrate	1.3-1.45% m/m Al, 5.3-6.3% m/m acetate	German Pharmacopoeia	100000168525	Aluminium acetate tartrate solution
Ammonia	25.0-30.0 % m/m	Ph. Eur.: 0877 - Ammonia solution, concentrated	100000076694	Ammonia solution, concentrated
Ammonia	Any not mentioned above	SVG	100000077713	Ammonia solution
Benzalkonium chloride	475-525 g/L	Ph. Eur.: 0371 - Benzalkonium chloride solution	100000076913	Benzalkonium chloride solution
Chlorhexidine digluconate	190-210 g/L	Ph. Eur.: 0658 - Chlorhexidine digluconate solution	100000091053	Chlorhexidine digluconate solution
Ethanol	92.6-95.2% m/m (95.1-96.9% V/V)	Ph. Eur.: 1317 - Ethanol (96 per cent)	100000076353	Ethanol (96 per cent)
Ethanol	Any not mentioned above	SVG	100000140938	Ethanol, diluted
Formaldehyde	34.5-38.0% m/m	Ph. Eur.: 0826 - Formaldehyde solution (35 per cent)	100000080149	Formaldehyde solution (35 per cent)
Glucose	>70.0% V/V	Ph. Eur.: 1330 - Glucose, Liquid	100000080176	Glucose, liquid
Glycerol	83.5-88.5% m/m	Ph. Eur.: 0497 - Glycerol (85 per cent)	100000078195	Glycerol (85 per cent)
Glyceryl trinitrate	1-10% m/m	Ph. Eur.: 1331 - Glyceryl trinitrate solution	100000092262	Glyceryl trinitrate solution
Hydrochloric acid	35.0-39.0% m/m	Ph. Eur.: 0002 - Hydrochloric acid, concentrated	100000075989	Hydrochloric acid, concentrated
Hydrochloric acid	9.5-10.5% m/m	Ph. Eur.: 0003 - Hydrochloric acid, dilute	100000075990	Hydrochloric acid, dilute
Hydrochloric acid	Any not mentioned above	SVG	100000078724	Hydrochloric acid
Hydrogen peroxide solution	2.5-3.5% m/m	Ph. Eur.: 0395 - Hydrogen peroxide solution (3 per cent)	100000075991	Hydrogen peroxide solution (3 per cent)
Hydrogen peroxide solution	29-31% m/m	Ph. Eur.: 0396 - Hydrogen peroxide solution (30 per cent)	100000075992	Hydrogen peroxide solution (30 per cent)
Hydrogen peroxide solution	Any not mentioned above	SVG	300000061030	Hydrogen peroxide solution
Iodine	2.4-2.7% m/m iodine, 2.4-2.7% m/m potassium iodide	German Pharmacopoeia	100000077357	Alcoholic iodine solution
Lactulose	Lactulose solution > 620 g/L	Ph. Eur.: 0924 - Lactulose, liquid	100000091963	Lactulose, liquid
Maltitol	>50% m/m	Ph. Eur.: 1236 - Maltitol, liquid	100000080123	Maltitol, liquid
Methacrylic acid - ethyl acrylate copolymer (1:1)	No range available	Ph. Eur.: 1129 - Methacrylic acid - ethyl acrylate copolymer (1:1) dispersion 30 per cent	100000079565	Methacrylic acid - ethyl acrylate copolymer (1:1) dispersion 30 per cent

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Nitric acid	68.0-70.0% m/m		100000080017	Nitric acid
Nitric acid	Any not mentioned above	SVG	300000061031	Nitric acid solution
Oxygen	>96.0% V/V	Ph. Eur.: 3098 - Oxygen (98 per cent)	300000060787	Oxygen (98 per cent)
Oxygen	90.0-96.0% V/V	Ph. Eur.: 2455 - Oxygen (93 per cent)	300000060786	Oxygen (93 per cent)
Phosphoric acid	84.0-90.0% m/m	Ph. Eur.: 0004 - Phosphoric acid, concentrated	100000090950	Phosphoric acid, concentrated
Phosphoric acid	9.5-10.5% m/m	Ph. Eur.: 0005 - Phosphoric acid, dilute	100000079606	Phosphoric acid, dilute
Poly(vinyl acetate)	25.0-30.0%	Ph. Eur.: 2152 - Poly(vinyl acetate) dispersion 30 per cent	100000166436	Poly(vinyl acetate) dispersion 30 per cent
Polyacrylate	28.5-31.5%	Ph. Eur.: 0733 - Polyacrylate dispersion 30 per cent	100000079840	Polyacrylate dispersion 30 per cent
Potassium hydroxide	Any concentration	SVG	300000061033	Potassium hydroxide solution
Potassium lactate	49-51% m/m	German Pharmacopoeia	300000061034	Potassium lactate solution
Propylene glycol	Any concentration	SVG	300000061108	Propylene glycol solution
Sodium (S)-lactate	>50% m/m	Ph. Eur.: 2033 - Sodium (S)-lactate solution	100000127143	Sodium (S)-lactate solution
Sodium chloride	Any concentration	SVG	100000138605	Sodium chloride solution
Sodium hydroxide	Any concentration	SVG	100000078045	Sodium hydroxide solution
Sodium lactate	>50% m/m	Ph. Eur.: 1151 - Sodium lactate solution	100000092018	Sodium lactate solution
Sorbitol	68.0-72.0% m/m (crystallising)	Ph. Eur.: 0436 - Sorbitol, liquid (crystallising)	100000079562	Sorbitol, liquid (crystallising)
Sorbitol	68.0-72.0% m/m (non-crystallising)	Ph. Eur.: 0437 - Sorbitol, liquid (non-crystallising)	100000079582	Sorbitol, liquid (non-crystallising)
Sorbitol	68.0-85.0% m/m	Ph. Eur.: 2048 - Sorbitol, liquid, partially dehydrated	100000133229	Sorbitol, liquid, partially dehydrated
Sucrose	66.0-67.5 m/m	Ph. Eur.: 2797 - Sucrose, liquid	100000093359	Sucrose, liquid
Sulfuric acid	Any concentration	SVG	100000128795	Sulfuric acid solution
*Any other**	*Any concentration*	*N.A.*	*N.A.*	*N.A.*

*Additional SSG1 solutions records related to an EEA national pharmacopoeia can be registered upon request.

2.3.2. Proprietary mixtures of excipients

The most common manufacturer of propriety mixtures of excipients is Colorcon®. The most common excipients from this manufacturer are listed below:

· Opadry®
· Opalux®
· Opacode®
· Opaspray®
· Opatint®
· Pigment blend®
· Lake blend®
· Acryl-EZE®

Name part	Conformance	Details
Type	Mandatory	Brand name, as listed above (e.g. Opadry®), as per Colorcon® specifications
Subtype	Conditional	Subtype, if applicable, as per Colorcon® specifications
Code	Mandatory	Code, as per Colorcon® specifications
Colour	Mandatory	Colour, as per Colorcon® specifications

SMS ID	100000086588
Preferred term	Opadry II Y-30-18037 white

SMS ID	100000130702
Preferred term	Pigment blend PB-22877 yellow

2.4. Structurally Diverse - Herbal

Key principles

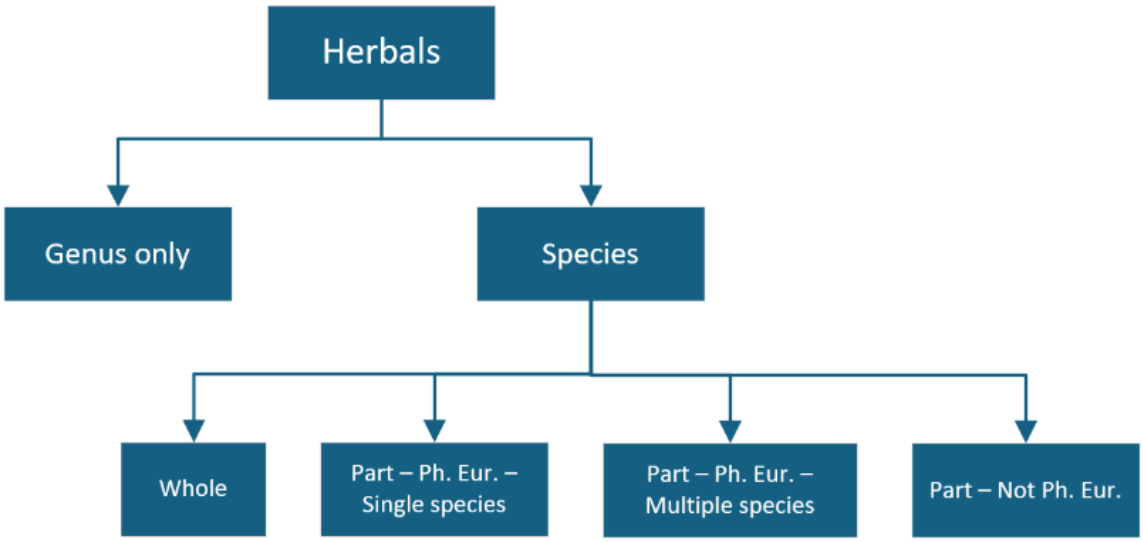
In accordance with Directive 2004/24/EC, herbal substances are "all mainly whole, fragmented or cut plants, plant parts, algae, fungi, lichen in an unprocessed, usually dried form, but sometimes fresh".

For the purposes of SMS maintenance, herbal substances are divided in five subgroups, each with different business rules:

- Genus-only
- Whole
- Part – Ph. Eur. – Single Species
- Part – Ph. Eur. – Multiple Species*
- Part – Not Ph. Eur.

These records are registered in SMS with the substance type "Structurally Diverse – Herbal" if only one species is present. If multiple species are/can be present*, then the substance type would be considered a "Mixture".

The business rules described in this section do not apply to herbal extracts and homeopathic substances.



Reference sources for SMS Preferred term of herbal substances:
1. European Pharmacopoeia (if Ph. Eur. monograph available)
2. Taxonomic Databases (if Ph. Eur. monograph not available):
   - Plants: Plants of the World Online (Kew Gardens)
   - Fungi: Index Fungorum
   - Algae: AlgaeBase

2.4.1. Genus-only records

Context
Only to be created if both conditions below apply simultaneously:
- Request for pharmacovigilance purposes
- Reported substance name does not include species nor is it possible to infer it

Business rules

Data field	Rules
Preferred term	<Taxonomic name of the Genus (without Author) in accordance with the respective taxonomic database>
Alias	N.A.
Substance type	Structurally Diverse – Herbal
Comments	Unspecified
UNII	N.A.
SVG flag	SVG flag 0

Examples

SMS ID	100000153626
Preferred term	Carlina (Source: Plants of the World Online)
Alias	N.A.
Substance type	Structurally Diverse – Herbal
Comments	Unspecified
UNII	N.A.
SVG flag	SVG flag 0

SMS ID	100000138865
Preferred term	Alternaria (Source: Index Fungorum)
Alias	N.A.

SMS ID	100000138865
Substance type	Structurally Diverse – Herbal
Comments	Unspecified
UNII	N.A.
SVG flag	SVG flag 0

2.4.2. Whole

Context
Only to be created if all conditions below apply simultaneously:
- Request for pharmacovigilance purposes
- Reported substance name includes species
- Reported substance name does not include part

Business rules

Data field	Rules
Preferred term	<Taxonomic name of the Species (with Author*) in accordance with the respective taxonomic database>, whole
Alias	Common name, if available
Substance type	Structurally Diverse – Herbal
Comments	Unspecified
UNII	To be added, if available
SVG flag	SVG flag 0

*Some plant varieties do not include author in Kew Gardens. In that case, the taxonomic name will be exceptionally registered without author.
Examples

SMS ID	100000090721
Preferred term	Artemisia vulgaris L., whole
Alias	Mugwort, whole
Substance type	Structurally Diverse – Herbal
Comments	Unspecified
UNII	JDR81QW9ZQ
SVG flag	SVG flag 0

SMS ID	300000057904
Preferred term	Angelica dahurica var. formosana (H.Boissieu) Yen, whole
Alias	Baizhi, whole
Substance type	Structurally Diverse – Herbal
Comments	Unspecified
UNII	247A107296
SVG flag	SVG flag 0

SMS ID	100000093281
Preferred term	Aspergillus fumigatus Fresen, whole
Alias	N.A.
Substance type	Structurally Diverse – Herbal
Comments	Unspecified
UNII	X88DF51T48
SVG flag	SVG flag 0

2.4.3. Part - Ph. Eur. – Single species

Context
- To be created upon publication of a new herbal Ph. Eur. herbal monograph for a single species

Business rules

Data field	Rules
Preferred term	<Ph. Eur. monograph title in English>
Alias	<Ph. Eur. monograph title in Latin>

Data field	Rules
Alias	<Taxonomic name of the Species (with Author) in accordance with the respective taxonomic database>, <part>
Alias	Common name, if available
Substance type	Structurally Diverse – Herbal
Comments	*Null*
UNII	To be added, if available
SVG flag	SVG flag 1

Examples

SMS ID	
Preferred term	Arnica flower
Alias	Arnicae flos
Alias	Arnica montana L., flower
Substance type	Structurally Diverse – Herbal
Comments	Null
UNII	OZ0E5Y15PZ
SVG flag	SVG flag 1

SMS ID	100000076326
Preferred term	Iceland moss
Alias	Lichen islandicus
Alias	Cetraria islandica (L.) Ach., thallus
Substance type	Structurally Diverse – Herbal
Comments	Null
UNII	N.A.
SVG flag	SVG flag 1

2.4.4. Part - Ph. Eur. – Multiple species

Context

- To be created upon publication of a new herbal Ph. Eur. herbal monograph for multiple species

Business rules

Data field	Rules
Preferred term	<Ph. Eur. monograph title in English>
Alias	<Ph. Eur. monograph title in Latin>
Alias	<Taxonomic name of the Species 1 (with Author) in accordance with the respective taxonomic database> and/or <Taxonomic name of the Species 2 (with Author)> and/or <Taxonomic name of the Species 3 (with Author)> and/or <Taxonomic name of the Species 4 (with Author)>, <part>
Alias	Common name, if available
Substance type	Mixture
Comments	*Null*
UNII	To be added, if available
SVG flag	SVG flag 1

Examples

SMS ID	100000176006
Preferred term	Pelargonium root
Alias	Pelargonii radix
Alias	Pelargonium sidoides DC. and/or Pelargonium reniforme (Andrews) Curtis, root
Substance type	Mixture
Comments	Null
UNII	Not available
SVG flag	SVG flag 1

SMS ID	100000077047
Preferred term	Kelp
Alias	Fucus vel Ascophyllum
Alias	Fucus vesiculosus Linnaeus and/or Fucus serratus Linnaeus and/or Ascophyllum nodosum (Linnaeus) Le Jolis, thallus
Substance type	Mixture
Comments	Null
UNII	Not available
SVG flag	SVG flag 1

2.4.5. Part – Not Ph. Eur.

Context

- Can be created for any request type

Business rules

Preferred term	<Taxonomic name of the Species (with Author) in accordance with the respective taxonomic database>, <part>
Alias	Common name, if available
Substance type	Structurally Diverse – Herbal
Comments	*Null*
UNII	To be added, if available
SVG flag	SVG flag 1

Examples

SMS ID	100000158141
Preferred term	Corylus americana Walter, leaf
Alias	Hazelnut, leaf
Substance type	Structurally Diverse – Herbal
Comments	Null
UNII	KT0L68561O
SVG flag	SVG flag 1

SMS ID	100000176945
Preferred term	Tremella fuciformis Berk., fruiting body
Substance type	Structurally Diverse – Herbal
Comments	Null
UNII	GG8N28393G
SVG flag	SVG flag 1

SMS ID	300000057682
Preferred term	Fucus vesiculosus Linnaeus, thallus
Substance type	Structurally Diverse – Herbal
Comments	Null
UNII	Not available
SVG flag	SVG flag 1

The business rules described below have not yet been reviewed by the SVG and are subject to considerable changes in the future. However, they can serve as guidance in the interim.

2.5. Proteins

Proteins are single substances with a structure based on a sequence of amino acids. Small proteins (peptides) can also be scientifically described as a chemical. According to the SMS business rules, any peptide with more than 3 amino acids will be registered as a protein. Proteins modified with a polymer or a chemical will also be registered as a protein.

2.5.1. Peptide

Peptides can be registered as proteins or chemicals. Peptide with three or less amino acids are to be considered chemicals, while peptides with four or more are to be considered proteins.

- Amino acid sequence must be provided

2.5.2. Antibody

The following data elements must be provided:

- Source of the immunoglobulin (e.g. Human, Humanised, etc.)
- Immunoglobulin type (e.g. IgG1, IgG4, etc.)
- Immunoglobulin modifications (if applicable)
- Target(s)

In case of antibody-drug conjugates, information on the payload (usually a chemical) must also be provided. The payload might also be registered as a separate substance record, taking into account the business rules for the concerned substance type.

2.5.3. Fusion protein

Individual protein components must be provided

2.6. Polymers

Polymers are substances with a multiple repeating unit. Substances composed of a chemical covalently linked to a polymer will be registered as a polymer.

2.7. Nucleic acid

Nucleic acids are single substances with a structure based on a sequence of nucleotides.

2.8. Mixture

Mixtures are combinations of related single substances that are extracted/synthesised together without defined proportions.

2.9. Human vaccines

These are substance records with multiple unknown molecular entities, that are used to stimulate the body's immune response against one or more microorganisms. Vaccines based on a protein antigen are also registered as Structurally Diverse – Vaccine.

2.10. Structurally Diverse - Plasma derived

These are substance records with multiple unknown molecular entities that are derived from plasma. They mainly include immunoglobulins for passive immunity.

2.11. Structurally Diverse - Cell therapy

These are substance records with multiple unknown molecular entities, composed of multiple cells.
The following data elements must be provided:

- Organism source (e.g. Autologous, Allogenic, etc.)
- Tissue source (e.g. adipose-derived)
- Cells
- Relevant modifications

2.12. Structurally Diverse - Other

All remaining structurally diverse substances (i.e. that do not fit any of the types listed above). For the moment this also includes gene therapy substance but, in the future they will have a separate substance type.
The following data elements must be provided:

- Microorganism
- Serotype (if applicable)
- Gene encoded

2.13. Specified Substances Group 2 (SSG2):

SSG2 substances are not currently in use in SMS.

2.14. Specified Substances Group 3 (SSG3):

SSG3 substances are not currently in use in SMS.

2.15. Specified Substances Group 4 (SSG4):

SSG4 substances are not currently in use in SMS.

Annex 2: Frequently Asked Questions

I didn't request the registration of my substance, but it is already available. Who has registered it?

Substances can be requested by any user. The concerned substance might have been requested by a partner company or a Contract Research Organisation (CRO) acting on behalf of a Sponsor. The substance might have also been reported in an ICSR and was registered based on publicly available information. Additionally, the substance might have been registered as part of a data mapping based on a legacy regulatory procedure or a data enrichment exercise based on INN, USAN or FDA public data. Due to personal data regulations, we are unable to disclose the user who has originally requested the substance registration.

Why is a substance registered as "approved" if it is still in clinical development?

Since SMS went live in July 2019, all substances have been registered by EMA SMS data stewards with the authorisation state "Authorised"; this substance data is subsequently made available in the xEVMPD list of "Approved" substances. This has no relationship with the approval status of the respective medicinal product.

Can I delete my substance from SMS?

The requestor can withdraw the request for the creation of a substance record at any time before the substance is registered in SMS. Once the substance is registered in SMS, it cannot be deleted, however, it can still be updated. Substances are kept in SMS even if development has stopped, since the substance can be linked to ICSRs/SUSARs or be used in the future by a different sponsor.

Why has the preferred term been published as public if I set all the data as restricted?

The substance preferred term is always registered as "public". This is a technical validation rule in SMS, and it ensures that the requestor/sponsor can find its substance.

Why can't the company code be registered as the preferred term?

Company codes cannot be used as the substance preferred term for the purposes of Orphan Designation, Paediatric Investigation plan. This is a requirement from the European Commission. Additionally, company codes can also not be used as the preferred term for Marketing Authorisation Application for Human medicinal products.

Why has my substance been published as "public" since I have requested it to be registered as "restricted"?

The substance has been registered as "public" since it is considered to be in the public domain, most likely due to the fact that an official name (e.g. INN, USAN) has been published.

Why is the substance unavailable after requesting its registration?

Depending on the concerned system, the SMS substance data is made available in different systems after a determined period of time, as described in **Table 10**. If the referenced period has passed and the substance is still unavailable in the concerned system, then the user shall contact the EMA via the EMA Service Desk.

Why has my substance been updated as "public" after its initial registration as "restricted"?

The substance has been initially registered as "restricted" according to the information provided by the applicant and information available in the public domain. As part of regular data enrichments (see section 8.2), substance records are reviewed periodically and might be updated based on new information made available in the public domain. Therefore, even if a substance record is initially registered as "restricted" it might be later updated and made "public", once new information is published, or the substance record is required for another regulatory procedure which requires an update to be performed.

Annex 3: Glossary

Acronym	Name
API	Application Programming Interface
Art. 57	Article 57 of Regulation (EU) 726/2004, which requires marketing authorisation holders to electronically submit to the Agency information on all medicinal products for human use authorised in the EU
CAP	Centrally Authorised Product
CR	Change Request
CTIS	Clinical Trials Information System
DMP	Development Medicinal Product
DCP	De-centralised Procedure
DQ	Data Quality
eAF	Electronic Application Form
EU-SRS	European Substance Reference System
EDQM	European Directorate for the Quality of Medicines & HealthCare
EUTCT	European Union Telematics Controlled Terms
FHIR	Fast Healthcare Interoperability Resources
ICSR	Individual Case Safety Report
IDMP	The ISO IDMP standards specify the use of standardised definitions for the identification and description of medicinal products for human use
INN	International Nonproprietary Names
InChIKey	International Chemical Identifier in "key" format
IRIS	A secure online platform for handling product-related scientific and regulatory procedures with EMA (iris.ema.europa.eu)
KUG	Key User Group
KPI	Key Performance Indicator
MAA	Marketing Authorisation Application
MAH	Marketing Authorisation Holder
MRP	Mutual Recognition Procedure
NAP	Nationally Authorised Product
NCA	National Competent Authority
OD	Orphan Designation
OMS	Organisation Management Service
Ph. Eur.	European Pharmacopoeia
pINN	Proposed International Non-proprietary Name
PIP	Paediatric Investigation Plan
PMS	Product (Data) Management Service
PT	Preferred Term
rINN	Recommended International Non-proprietary Name
RMS	Referential Management Service
SIAMED	An Information System for the management of regulatory procedure for centrally authorised products
SLA	Service Level Agreement
SPOR	Substance, Product, Organisation and Referential
SmPC	Summary of product characteristics
SMS	Substance Management Service
SVG	Substance Validation Group
UNII	Unique Ingredient Identifier
USAN	United States Adopted Name
WHO	World Health Organisation
xEVMPD	eXtended EudraVigilance Medicinal Product Dictionary

Annex 4: RMS Lists/IDs used in SMS

RMS List ID	RMS List name	RMS terms used	SMS Data field
100000000004	Domain	100000000012 - Human use 100000000013 - Veterinary use	Domain
200000004983	Data Classification	200000004985 - Public 200000004986 - Restricted	Data Classification (Substance) Data Classification (Name)
200000004906	Substance Authorisation Status	200000004972 - Authorised 200000004975 - Development	Authorisation State
200000005003	Record Status	200000005004 - Current 200000005006 - Non-current	Substance Status Name Status
100000075826	Substance Type	100000075670 - Chemical 200000005023 - Mixture 200000005035 - Nucleic acid 200000005022 - Polymer 200000005020 - Protein 200000005031 - Specified Substance Group 1 200000005032 - Specified Substance Group 2 200000005033 - Specified Substance Group 3 200000005034 - Specified Substance Group 4 200000005026 - Structurally Diverse - Allergen 200000005029 - Structurally Diverse - Cell therapy 200000005025 - Structurally Diverse - Herbal 200000005030 - Structurally Diverse - Other 200000005024 - Structurally Diverse - Plasma derived 200000005027 - Structurally Diverse - Vaccine	Substance Type
100000072057	Language	100000072142 - Bulgarian 100000072258 - Croatian 100000072167 - Czech 100000072168 - Danish 100000072169 - Dutch 100000072147 - English 100000072172 - Estonian 100000072149 - Finnish 100000072175 - French 100000072178 - German 100000072181 - Greek, Modern (1453-) 100000072187 - Hungarian 100000072156 - Icelandic 100000072179 - Irish 100000072194 - Italian 100000072226 - Latin 100000072205 - Latvian 100000072206 - Lithuanian 100000072236 - Maltese 100000072243 - Norwegian 100000072217 - Polish 100000072251 - Portuguese 100000072254 - Romanian 100000072259 - Slovak 100000072260 - Slovenian 100000072264 - Spanish 100000072288 - Swedish	Language

100000000009	Source of Information	Substance names (All with attribute "SMS Name"): 200000025184 - ADISINSIGHT 200000032270 - Anthroposophic Pharmaceutical Codex 100000075734 - BAN 100000115264 - BRITISH HERBAL PHARMACOPOEIA 100000075723 - BRITISH PHARMACOPOEIA 100000152989 - CHEBI 100000075787 - CHEMICAL ABSTRACT SERVICE 100000125793 - CHEMICALBOOK 100000124125 - CHEMIDPLUS 200000005827 - CHINA FOOD AND DRUG ADMINISTRATION 100000125797 - CHINESE PHARMACOPOEIA 100000133971 - COLORCON 100000125798 - COMMUNITY HERBAL MONOGRAPHS 100000125799 - COMMUNITY REGISTER OF THE EUROPEAN COMMISSION 100000075712 - COMPANY SPECIFICATION 100000170926 - COSING 100000167113 - CZECH PHARMACOPOEIA 100000075697 - DEUTSCHES ARZNEIBUCH 100000075824 - EMEA RECOMMENDATIONS FOR INFLUENZA VACCINATIONS PLANS 100000159429 - ENCYCLOPEDIA OF LIFE (EOL) 100000170925 - EUROPEAN CHEMICALS AGENCY (ECHA) 200000005829 - EUROPEAN FOOD SAFETY AUTHORITY (EFSA) 100000075790 - EUROPEAN PHARMACOPOEIA 100000134409 - FDA INACTIVE INGREDIENTS DATABASE 100000151869 - FDA SUBSTANCE REGISTRATION SYSTEM 100000075745 - FRENCH PHARMACOPOEIA 100000075820 - GLOBAL DIVERSITY INFORMATION FACILITY 100000134592 - GREEK PHARMACOPOEIA 100000144867 - HAB 100000075692 - HANDBOOK OF PHARMACEUTICAL EXCIPIENT 100000127906 - HOMEOPATHIC PHARMACOPOEIA OF THE UNITED STATES 200000005828 - INDEX FUNGORUM 100000075715 - INN 100000075699 - INNM 100000125815 - INTERNATIONAL CODE OF NOMENCLATURE OF BACTERIA (ICNB) 100000125816 - INTERNATIONAL CODE OF VIRUS CLASSIFICATION AND NOMENCLATURE 100000125813 - INTERNATIONAL CODE OF ZOOLOGICAL NOMENCLATURE (ICZN) 100000133377 - INTERNATIONAL NUMBERING SYSTEM (INS) FOR FOOD ADDITIVES 100000075807 - INVESTIGATOR'S BROCHURE 100000075748 - ITALIAN PHARMACOPOEIA 100000124117 - ITIS (INTEGRATED TAXONOMIC INFORMATION SYSTEM) 100000075688 - JAN 100000075690 - JAPANESE PHARMACOPOEIA 100000125807 - KEW GARDEN- IPLANTS DATABASE 100000124119 - MARTINDALE 100000133378 - PHARMACOPOEIA HELVETICA	Source (Name Source) Source (External Code)

		100000075797 - POLISH PHARMACOPOEIA 100000130608 - PORTUGUESE PHARMACOPOEIA 200000005826 - PROTEIN DATA BANK (PDB) 100000153275 - PUBCHEM 100000075742 - SPC 200000025197 - Substance Validation Group 100000075717 - THE MERCK INDEX 100000125810 - THE PLANT LIST 100000075736 - USAN 100000075738 - USP 100000075726 – WHO <u>External codes (All with attribute "SMS Code"):</u> 100000075787 - CHEMICAL ABSTRACT SERVICE 200000032418 - EC/List number 100000075665 - Extended EudraVigilance Medicinal Product Dictionary 100000075715 - INN 100000146035 - SIAMED - EMA CP management system 200000025197 - Substance Validation Group 200000018817 - Unique Ingredient Identifier 100000075736 - USAN	

Annex 5: Data fields to FHIR mappings

Section	Data field	FHIR Path
Substance	SMS ID	SubstanceDefinition.id
	Domain	SubstanceDefinition.domain
	Data classification (Substance)	SubstanceDefinition.extension url="https://ema.europa.eu/fhir/dataClassification"
	Authorisation State	N/A
	Substance Status	SubstanceDefinition.status
	Substance Name	SubstanceDefinition.name
	Comment	SubstanceDefinition.note
	Substance Type	SubstanceDefinition.type
	Molecular formula	SubstanceDefinition.structure.molecularFormula
	Molecular weight	SubstanceDefinition.structure.molecularWeight
	InChIKey	SubstanceDefinition.structure.representation.representation
	Last Update Date	SubstanceDefinition.meta.lastUpdated
Substance Name	Substance Name	SubstanceDefinition.name.name
	Language	SubstanceDefinition.name.language
	Is Preferred	SubstanceDefinition.name.preferred
	Name Status	SubstanceDefinition.name.status
	Data Classification (Name)	SubstanceDefinition.name.extension url="https://ema.europa.eu/fhir/dataClassification"
Substance Name Source	Source (Name Source)	SubstanceDefinition.name.source

Substance External Code	Source (External Code)	SubstanceDefinition.code.code.coding.system
	ID/Code Provided by Source	SubstanceDefinition.code.code.coding.code
Substance Custom Attribute	Attribute Term	SubstanceDefinition.property.code
	Attribute Value	SubstanceDefinition.property.amountString
Substance Relationship	Related substance	SubstanceDefinition.relationship.substanceDefinitionReference
	Substance Relationship Combination	SubstanceDefinition.relationship.type
Substance Current	Substance Current	SubstanceDefinition.extension url="https://ema.europa.eu/fhir/currentSubstance"