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Introduction to ISO Identification of Medicinal Products, SPOR programme



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1. Executive summary

The International Organisation for Standardisation (ISO), Identification of Medicinal Products (IDMP) standards specify the use of standardised definitions for the identification and description of medicinal products for human use. The purpose of these standards is to facilitate the reliable exchange of medicinal product information in a robust and consistent manner, by providing a common product 'language' for stakeholders to use in their interactions. The use of these standards is a regulatory requirement as they are mandated by the EU legislation (Commission Implementing Regulation (EU) No 520/2012 [articles 25 and 26]).

ISO IDMP comprises five separate standards. These standards establish definitions and concepts and describe data elements and their structural relationships. They cover the following aspects to describe a medicinal product:

- Medicinal product name;
- Ingredient substances;
- Pharmaceutical product (route of administration, strength);
- Marketing Authorisation;
- Clinical particulars;
- Packaging;
- Manufacturing.

ISO IDMP covers the entire product lifecycle: products in development, investigational products, products under evaluation and authorised products.

ISO IDMP has multiple use cases within the regulatory context. For example:

- **Pharmacovigilance:** Adverse event reports are based on a harmonised set of product definitions, improving the quality of data used for signal management, and speeding up communication, decision-making and actions;
- **Regulatory submissions:** Submissions use a consistent standard to capture and manage data, allowing information on medicinal products to be shared and re-used across different procedures and among various regulators (subject to confidentiality restrictions);
- **Clinical trials:** Stakeholders can access Clinical Trial data using agreed and well-supported standards, improving the assessment and scientific evaluation of medicines as well as communication and transparency;
- **Good Manufacturing Practices (GMP) inspections:** Inspections on manufacturing sites are based on accessible information, which streamlines inspections particularly for urgent situations involving defects. Faster detection of falsified medicines can also be supported as a result of consistent data standards.

Implementation of the ISO IDMP standards is governed by the following specifications:

- **ISO IDMP Implementation Guides (Technical Specifications):** Define the technical details on how to implement the standards, such as specific fields, their formats, and business rules describing their use;

- **EU Implementation Guide:** Provides guidance on the interpretation of data fields specifically for the EU regulatory environment as well as guidance on the processes for submitting and updating data.
- **HL7 Messaging Specifications:** Define the messages that will be used to exchange IDMP information, which are based on HL7 (Health Level Seven) Standards;

The ISO IDMP standards will be implemented in phases, through a set of projects known as SPOR data management services (Substances, Products, Organisations, Referentials). They will establish ISO IDMP compliant business services for the central management of data in each of the four SPOR areas: The SPOR data management services are:

- Substance Management Services (SMS);
- Product Management Services (PMS);
- Organisations Management Services (OMS);
- Referentials Management Services (RMS).

The phased implementation of the ISO IDMP standards has been endorsed by the European Union Network Data Board (EUNDB) and the EU ISO IDMP Task Force (aka SPOR Task Force). The first two projects that EMA will deliver are RMS and OMS. They will lay the foundations for the subsequent delivery of SMS and PMS.

2. Background

2.1. Purpose of the ISO IDMP standards

ISO IDMP came from a need to standardise the definition of medicinal product information to facilitate the identification and exchange of such information in the context of pharmacovigilance activities (e.g. identifying medicines causing Adverse Events (AEs)). It was recognised that using a harmonised approach, to identifying and describing the medicinal product involved in an AE, was critical in ensuring accurate analysis and unambiguous communication across jurisdictions.

To ensure wide interoperability across global regulatory and healthcare communities, these standards were developed and published under the auspices of the ISO, with input from the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), Health Level Seven (HL7) and other international stakeholders and experts.

Whilst the initial driver for the development of these standards was pharmacovigilance, as the project evolved, the health arena recognised the need to expand the scope of the standards to support wider regulatory activities (e.g. clinical trials and inspections) and healthcare practises such as the prescription and dispensation of medicines.

With regard to stakeholder interactions, ISO IDMP standards describe that *"To meet the primary objectives of the regulation of medicines and pharmacovigilance, it is necessary to reliably exchange Medicinal Product information in a robust and consistent manner. The IDMP standards therefore support, at a minimum, the following interactions:*

- *regulator to regulator;*
- *pharmaceutical company to regulator;*
- *sponsor of clinical trial to regulator;*

- regulator to other stakeholder;
- regulator to worldwide-maintained data sources.”¹

2.2. ISO IDMP in the European Union

The use of ISO IDMP is a regulatory requirement according to the Commission Implementing Regulation (EU) No 520/2012 (articles 25 and 26) which mandates the use of ISO IDMP for the exchange of information on medicinal products across the European Union.

According to the regulation: *“The use of internationally agreed terminology, format and standards should facilitate the interoperability of systems used for the performance of pharmacovigilance activities and avoids the duplication of encoding activities concerning the same information. It should also allow for an easier information exchange between regulatory authorities on an international level”*²

The implementation of the ISO IDMP will be through a master data initiative. The approach to implementing the ISO IDMP standards is based on the four domains of master data in pharmaceutical regulatory processes: Substance, Product, Organisation and Referentials (SPOR) data.

3. Using ISO IDMP in the Regulatory Context

Using ISO IDMP within regulatory activities will bring benefits to regulators, industry and ultimately patients. It will do this by:

- Facilitating the identification and exchange of product and substance information globally, across regulators;
- Improving data integrity and reliability;
- Enabling reuse of data across different procedures and regulators;
- Reducing silos and improving interoperability across EU systems through the optimisation and simplification of data operating models and data management practices;
- Streamlining, optimising and simplifying regulatory processes to fulfil regulatory requirements more efficiently;
- Speeding up decision-making and improving communication with the stakeholders through easily accessible and highly reliable data.

The following sections describe how ISO IDMP can improve specific regulatory activities.

3.1. Pharmacovigilance

ISO IDMP can improve the accuracy of codification of Medicinal Products and Substance information reported in ICSRs (Individual Case Safety Reports) and SUSARs (Suspected Unexpected Serious Adverse Reactions). It does this by providing unambiguous product and substance definitions that can be referenced when reporting an AE. Specifically, ICSRs and SUSRs can include one of the identifications introduced by ISO IDMP.

This brings the following benefits/outcomes:

¹ Source: ISO 11615:2012(en) Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information

² Commission Implementing Regulation (EU) No 520/2012

- AE reports use consistent product IDs, and so can be easily shared across jurisdictions;
- Signal management can draw on a more accurate set of AE reports, that can be integrated globally to increase the breadth/scope of analysis;
- Decision-making and regulatory actions, such as Referrals, PSURs and Medical Literature Monitoring, can be sped up;
- Improvements in communication with stakeholders in relation to aspects of safety of medicines.

3.2. Regulatory Submissions

Product and substance information included in regulatory submissions can be provided in an ISO IDMP-compatible format. This means information on all medicinal products that has been submitted as part of an application is available in a standard and well-understood format.

This brings the following benefits/outcomes:

- Data submitted once can be re-used – for example, information provided as part of authorisation procedures can be used as the pharmacovigilance submission;
- Product and substance information can be shared across regulators.
- QPPV model: introduce potential regulatory optimisation to improve efficiency of processes.

3.3. Clinical Trials

As for other regulatory submissions, information on investigational products and substances can be provided in an ISO IDMP-compatible format as part of clinical trials (CTs).

This brings the following benefits/outcomes:

- Assessment and scientific evaluation of a medicine is improved by providing access to data in a standard format. For example, in the EU, new services can be developed by the integration of data from the EU CT database, EV SUSAR and Annual safety report repository;
- Allows proactive and reactive access to CT data thereby improving communication and transparency. For example, in the EU, a Clinical Trials Register will provide data to stakeholders in an ISO IDMP-compatible format.

3.4. GMP Inspections

ISO IDMP captures additional information on the manufacturing of medicinal products, in addition to other characteristics of the product.

This brings the following benefits/outcomes:

- Facilitates the retrieval of medicine information for the rapid and efficient handling of urgent situation (e.g. recalls) involving medicinal product defects;
- Supports and streamlines inspections on manufacturing sites based on accessible information;
- Allows sharing of information with international partners about alternative sources of supply when shortage of medicines occur;
- Supports in the context of anti-falsified medicines.

4. Overview of ISO IDMP

4.1. Scope of the ISO IDMP

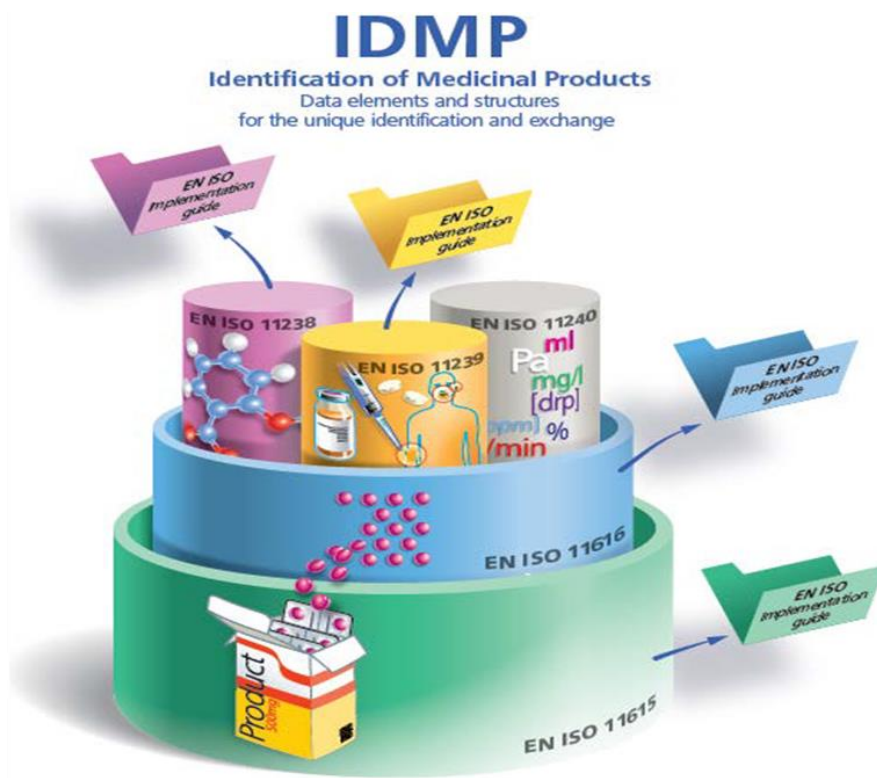
ISO IDMP is composed of five separate standards. An illustration of these standards, how they fit together and what each standard contains, is shown in Figure 1.

The specific standards are:

- **ISO 11238:** Data elements and structures for unique identification and exchange of regulated information on Substances;
- **ISO 11239:** Data elements and structures for unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation, routes of administration and packaging;
- **ISO 11240:** Data elements and structures for unique identification and exchange of units of measurement;
- **ISO 11616:** Data elements and structures for unique identification and exchange of regulated pharmaceutical Product information;
- **ISO 11615:** Data elements and structures for unique identification and exchange of regulated medicinal Product information.

ISO IDMP standards apply to Human medicinal products and investigational medicinal products.

Figure 1. Standards comprising ISO IDMP

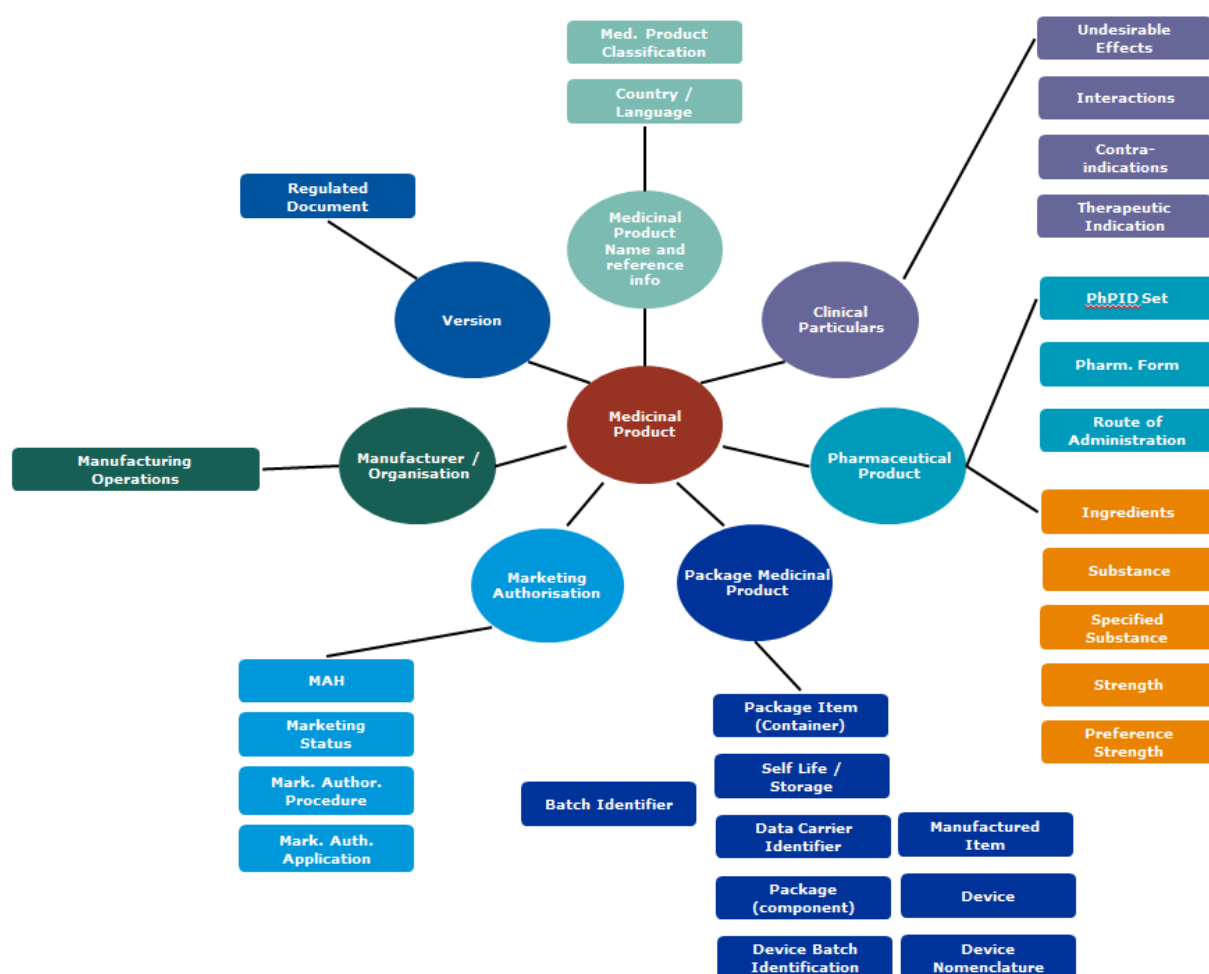


Source: ISO TC 215, Working Group 6 (Pharmacy and Medicines Business), December 2014

4.2. Identifying medicinal products via the ISO IDMP format

The ISO IDMP standards have been designed to cover many aspects of medicinal products, in order to support a broad range of regulatory contexts. An overview of the data elements contained in the ISO IDMP standard is shown (for illustration purposes only) in Figure 2.

Figure 2. Overview of ISO IDMP data elements - for illustration purposes only



Central to the IDMP model is the *Medicinal Product*. This covers all product characteristics that are necessary to describe and uniquely identify regulated products, and is composed of the following elements:

- **Medicinal Product Name;**
- **Pharmaceutical Product**, which describes the scientific properties of the medicine itself. This includes the *Ingredients*, which are one or more *Substances* (see below for further information on Substances), the pharmaceutical form, the route of administration and the strength;
- **Clinical Particulars** (e.g. indication, contraindications);

- **Packaged Medicinal Product**, which includes information on the products package, any included devices and the manufacturing batch;
- **Marketing Authorisation** details;
- **Manufacturer**; and
- **Version control system**.

The ISO IDMP standards allow the description of the active and inactive ingredients that constitute the medicinal products based on the substance terminology as defined in the ISO IDMP 11238 Standard. Whilst the substance terminology includes details of the ingredient characteristics, within the medicinal product the Substance IDs, the name of the substance itself and its strength are included. The above information allows the unambiguous identification of products by means of assigning a set of identifiers. These identifiers define the medicinal product at different level of granular information that are useful in various regulatory and healthcare professional contexts (e.g. Pharmacovigilance and e-Prescription). These levels of granular information and related identifiers are defined as follow:

- **Medicinal Product Identifier (MPID)**: Uniquely identifies a Medicinal Product, reflecting (but not replacing) any other authorisation numbers allocated by a regulator;
- **Packaged Medicinal Product Identifier (PCID)**: Uniquely identifies a Medicinal Product based on its packaging. This implies one MPID can be associated with more than one PCID, if the same Medicinal Product has more than one type of package;
- **Medicinal Product Batch Identifier (BAID)**: Uniquely identifies a Medicinal Product based on its packaging and the manufacturing batch. This implies one PCID can be associated with more than one BAID, if there are multiple batches for a given Packaged Medicinal Product;
- **Pharmaceutical Product Identifier (PhPID)**: Uniquely identifies medicinal product based on the generic composition, such as ingredients and route of administration, separate from any other details such as regulatory authorisation, organisation, packaging or naming. The PhPID can be specified at various levels of detail for a given Pharmaceutical Product.

5. Technical implementation of ISO IDMP

In addition to the ISO IDMP Standards, additional, more detailed specifications and guidance are required in order to implement ISO IDMP. These are outlined in Table 1.

Table 1. Specifications and Guides

Specification/Guide	Description	Responsible organisation
ISO IDMP Standards	• Define the required data elements and their structure • Provide 'business-level' description of IDMP	ISO TC 215 Working Group 6
ISO IDMP Implementation Guides (Technical Standards)	• Define the technical details on how to implement the standards • Include field formats, business rules etc.	ISO TC 215 Working Group 6
HL7 Messaging Specifications	• Define the messages that will be used to exchange IDMP information • Based on existing HL7 'Common Product Model' standard (similar to FDA's SPL)	HL7 Working Group

Specification/Guide	Description	Responsible organisation
Regional Implementation Guides	• Interpretation of fields specifically for the regional regulatory environment • Guidance on processes of submitting and updating data	Regional regulators

5.1. ISO IDMP Implementation Guides

While the ISO IDMP standards themselves define what information is required, they do not specify exactly how this information should be captured. The Implementation Guides define actual data elements, what data types they should be (free text, date, controlled vocabulary), and business rules governing how they should be populated.

5.2. HL7 Messaging Specifications

In addition to defining the technical details of how ISO IDMP data should be captured, there is a further need to define how it can be exchanged. This is the purpose of the Health Level Seven (HL7) messaging specifications.

They define a messaging format that uses XML (eXtensible Markup Language), and is based on an existing HL7 standard called Common Product Model (CPM).

5.3. Regional Implementation Guides

Regional implementation guides define details of implementation that are specific to a jurisdiction. This includes both how specific fields should be interpreted as well as the processes mandated by the regulator to provide the data.

6. EU regional implementation: SPOR as the master data for the EU

6.1. ISO IDMP as an evolution of the current xEVMPD for Human medicines

The submission and maintenance of data regarding authorised human medicines in the EU and the European Economic Area (EAA) has been mandatory since July 2012. This is based on a format called xEVPRM (Extended EudraVigilance Product Report Message) which populates the xEVMPD (Extended Eudravigilance Medicinal Product Dictionary). As a consequence of the legal requirements set out in the legislation, the xEVPRM will be replaced by the ISO IDMP format.

ISO IDMP format is an extension of the current information available in the xEVMPD. In addition, some conceptual differences are introduced which will need to be taken into account whilst performing the data migration.

6.2. Master data approach and scope

The approach to implementing the ISO IDMP standards is based on the four domains of master data in pharmaceutical regulatory processes: Substance, Product, Organisations and Referentials (SPOR) data.

EMA will establish ISO IDMP compliant business services for the central management of data in each of the four SPOR areas. These include data management services for:

- **Substance data:** Harmonised data and definitions to uniquely identify the ingredients and materials that constitute a medicinal product;
- **Product data:** Harmonised data and definitions to uniquely identify a medicinal product based on regulated information (e.g. marketing authorisation, packaging and medicinal information);
- **Organisation data:** Data that comprises of organisation name and location address data for organisations such as MAH, sponsors, regulatory authority, manufacturers;
- **Referential data:** Lists of terms (controlled vocabularies) used to describe attributes of products e.g. lists of dosage forms, units of measurement, routes of administration.

6.3. Phased implementation of SPOR

The European Commission, the European Union Network Data Board (EUNDB) and the EU ISO IDMP Task Force have endorsed a phased implementation of the ISO IDMP standards. This approach will allow lessons learnt during each phase to be applied to subsequent phases, processes and systems to mature over time and stakeholders to gain an understanding prior to the full roll out.

The first phase of the implementation of SPOR focuses on delivery of RMS and OMS. These two services will lay data foundations for the subsequent delivery of PMS and SMS and will also continue to expand incrementally after the initial launch.

SPOR services will be enforced when they become mandatory in given regulatory business processes. The enforcement may vary between Human and Veterinary stakeholders according to the implementation timescales and integration with other solutions.

At OMS and RMS go-live, submission processes will continue as before and there will be no immediate process changes for stakeholders. Some changes in the current submission processes are being explored and consultation is taking place with stakeholders on these.

More information will be provided in due course to explain any applicable process changes and timings.

6.4. Veterinary

Although ISO IDMP standards relate to Human medicinal products, SPOR applies to both human and veterinary domains. Veterinary will use the same RMS and OMS services in terms of the data, format and processes. More information concerning SPOR for veterinary will be provided in due course.

6.5. Summary of high level benefits

Standardised data alone is not sufficient to achieve benefits. The benefits of SPOR will be realised incrementally as all phases of SPOR are completed; and as long as other opportunities for integration are implemented. The key benefits are:

- more efficient regulatory action and decision-making, thanks to improved data integrity and reliability;
- increased data quality and simplification of data management practices, since data will be reviewed, assessed and approved as part of the new data operating model;

- regulatory requirements can be met more effectively, by reducing data silos and improving interoperability across EU systems;
- operational savings and efficiencies can be achieved, as pharmaceutical companies only need to supply regulatory data once, which will be re-used across different procedures and regulators.

These operational benefits should have a positive impact on public health and safety.