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D2.1 Identification of Branded Pre-Packaged Medicinal Products

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Abstract (for dissemination)	This document describes the requirements for the identification of branded medicinal products for ePrescription / eDispensation. It outlines the data sets and standards, and proposes a solution for the capture and validation of branded medicinal product information, in line with ongoing projects across the European Medicines Regulatory network (EMRN).
Keywords	ePrescription, eDispensation, branded medicinal product, pharmaceutical products, database, data structure, European Medicines Regulatory Network

Statement of originality

This deliverable contains original unpublished work except where clearly indicated otherwise. Acknowledgement of previously published material and of the work of others has been made through appropriate citation, quotation or both.

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Executive Summary

Over the past number of years the concept of a definitive medicinal product database has been discussed and piloted within the European Medicines Regulatory Network. The issues and challenges of gathering and validating medicinal product information from both industry and regulatory stakeholders in a concise and acceptable manner have been well documented.

The intention of this document is to describe the current and future development of a single product database from a regulatory perspective excluding national requirements and restrictions such as reimbursement, substitution etc., that are addressed in other work packages.

As described in work package 1, deliverable D1.1 epSOS identification and description problems, one of the key issues highlighted was identification of branded pre-packaged medicinal products and the challenges of identifying a product in a cross border setting. In work package 1 the attributes to identify a product within a cross border setting have been analysed and documented. Key to the concept of openMedicine is a definitive source of medicinal product information that can be utilised by the health network.

With the development and adoption of the ISO IDMP standards by the European Medicines Regulatory Network (EMRN), there is an opportunity to bring together common terminologies and data structures to provide a single source of European medicinal product information.

Key to the successful implementation of the ISO IDMP is the adoption of common reference information for substances, units of measure and pharmaceutical dose forms for example.

These standards are available from different providers and are consumed to varying degrees by stakeholders within the medicines regulatory network. It is proposed through the EMRN that a single source to broker reference information will be identified which will enable a consistent and up to date set of reference data to be provided.

In advance of these standards the introduction of the Article 57(2) database together with the work underway at the European Medicines Agency (EMA) in the development and provision of standard terminologies and reference information has provided a basis for a European product database.

Within each member state product information is consumed by national health providers, and formulary management providers for prescribing and dispensing systems. With each of these stakeholders medicinal product information is grouped and supplemented with additional information for national requirements. In the follow up work on ISO IDMP, a core role is defined for Medicinal Product Dictionaries (ISO TS 19256:2016). These activities have not been scoped as part of this work package.

As part of this work package the proposed European Medicines Verification system foreseen under the Falsified Medicines Directive 2001/83/EC and its interaction with European medicines database has been reviewed and included in the conclusions.

This document provides an overview of the current environment, and proposed approach to the capture and validation of medical product information. It also describes the options to enable the delivery of the information to stakeholders and an implementation roadmap to provide a comprehensive set of medicinal product data in line with the current EU telematics roadmap.

1 Introduction

1.1 Scope of WP2

The scope of WP2 is to identify the minimum set of medical product information required to identify, prescribe or dispense branded pre-packaged medicinal products across European member states.

For clarity the term “branded pre-packaged medicinal products” includes all products authorised in accordance with European Regulation (EC) No 726/2004 and Directive 2001/83/EC of the community code relating to medicinal products for human use by a medicines regulator in a pre-packaged form and includes both innovator and generic products.

WP2 does not address the provision of data to external stakeholders such as national health providers of pharmacy and clinical systems, but will provide a proposed dataset that can be consumed by the various stakeholders.

1.2 Goal of D2.1

Deliverable D2.1 “Identification of Branded Pre-packaged Medicinal Products” has the goal to identify the following:

- Definition of the minimum data set for branded pre-packed medicinal products
- Standards associated with the defined data set
- Source and validation of data set
- Roadmap

1.3 Methodology adopted

Information included in this document has been gathered through a review of the deliverables from WP1, surveys from European Union member state medicines regulators, current standards documentation available, and the telematics work plan for the European Medicines Regulatory Network. [1]

[1] See http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000116.jsp&mid=WC0b01ac0580028c2b

2 Branded Pre-packaged Medicinal Products

2.1 Definition and Scope

For the purposes of this document a medical product includes products authorised by a competent authority of a member state or when an authorisation is granted by the entire Union under regulation (EC) no 726/2004.

Article 1 of Directive 2001/83/EC as amended by Directive 2004/27/EC defines a “medicinal product” as:

(a) “Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or

(b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis”

No common European definition exists for a brand name, but Article 1(20) of Directive 2001/83/EC defines the name of the medicinal product, as:

“The name, which may be either an invented name not liable to confusion with the common name, or a common or scientific name accompanied by a trade mark or the name of the marketing authorisation holder.”

And Article 1(21) of Directive 2001/83/EC defines the common name, as

“The international non-proprietary name recommended by the World Health Organization, or, if one does not exist, the usual common name.”

For the purposes of this document the “Brand Name” may be either:

a. The name of the medicinal product marketed in the member state under a name (not being a common name) which identifies the medicinal product to the extent that no other medicinal product is marketed in the member state under that name

b. A medicinal product marketed in the member state under a common name in conjunction with another name (which may be the name of the pharmaceutical company connected with the medicinal product) which identifies the medicinal product to the extent that no other medicinal product is marketed in the member state under those names.

2.2 Summary of the Regulatory Framework

Pharmaceutical legalisation for medicinal product authorisations for human use are set out under Directive 2001/83/EC and in Regulation (EC) no 726/2004 and provide the legal basis for authorisations with the EU.

In support of this legislation the Notice to Applicants documents outlined below provide an interpretation and application of EU pharmaceutical legislation for marketing authorisation holders.

- Volume 2A – Procedures for marketing authorisation
- Volume 2B – Presentation and content of the dossier
- Volume 2C - Regulatory guidelines

Volume 2A of the guidance describes the various methods that a medicinal product may be authorised for use with that member state either through a national authorisation, mutual recognition / decentralised procedure or a centralised procedure in each case a successful application results in the product being authorised in one or more member states and the product information being recorded in one or more regulatory systems.

2.2.1 Name of the medicinal product

For placing a product on the market through either the national authorisation, mutual recognition / decentralised procedure or a centralised procedure, the authorisation must contain the name of the medicinal product and each name is submitted by the applicant is assessed and approved.

The name may be the invented name, or a common or scientific name (when, available the International Non-Propriety name of the active substance) accompanied by a trade mark or the name of the marketing authorisation holder (1).

Under a centralised procedure once a name has been approved it is for all member states. There are exceptions to this when a name proposed is objected to under trade mark law and in these cases a different name may be approved for that member state.

For other procedure types the applicant may propose different names for each member state that the product will be made available on. For applications under the Mutual recognition procedure or decentralised procedure it is recommended that, where possible the same name is applied.

In principle, for all procedure types, the name of the product is checked against available databases both at a national and centralised level for uniqueness. However without a single database of product information to verify names against and rules in respect to naming conventions, the name of the product does not uniquely identify a product.

This document exposes the key aspects for that database and rules to be implemented in a way to support the required scenarios.

2.3 Identification of medicinal products

As per the use cases coverage described in D1.3, the foremost goal is to enable safe dispensation of a medicinal product by correctly identifying the product prescribed.

While a more detailed analysis of the possibilities is presented in D2.2, here we retain the key aspects:

- For the dispenser to have sufficient information, the prescription must be prepared in a "cross-border" way, either upfront or by adding information. To support any of these cases, we need to find the attributes that identify equivalent medication from one country to the other.

- Across countries, medicinal products are identified differently, not only by not having a same identifier or name, but also by the fact that the identifiers refer to different concepts - products, clusters, etc.
- Unifying all of those concepts as a prerequisite would likely bring serious concerns in terms of patient safety, economic impact, fraud avoidance...

- To permit a roadmap to a solution, we explore the "anchor" concepts of identifying a medication in different levels. The main focus of this deliverable is the identification of a medicinal product, as defined in ISO IDMP.

- IDMP uses the concepts of Substance, Medicinal Product, Pharmaceutical Product, and Package, including levels within these concepts. This document recommends that in cross-border medication identification, these are the groups considered.

For example, identifying a substance is more "generic" and less restrictive than identifying the commercial product name. Given this different granularity, it is clear that a correspondence between attributes between these groups is not 1:1, but always 1:N. For example, there are typically several presentations of "paracetamol 500 mg coated tablets".

These levels are not the only ones existing: in some cases, the sets of attributes include the package size, etc. without including brand names. For this reason, it is important to start anchoring to a set of identification levels.

The concepts to be used are shown in figure 1:

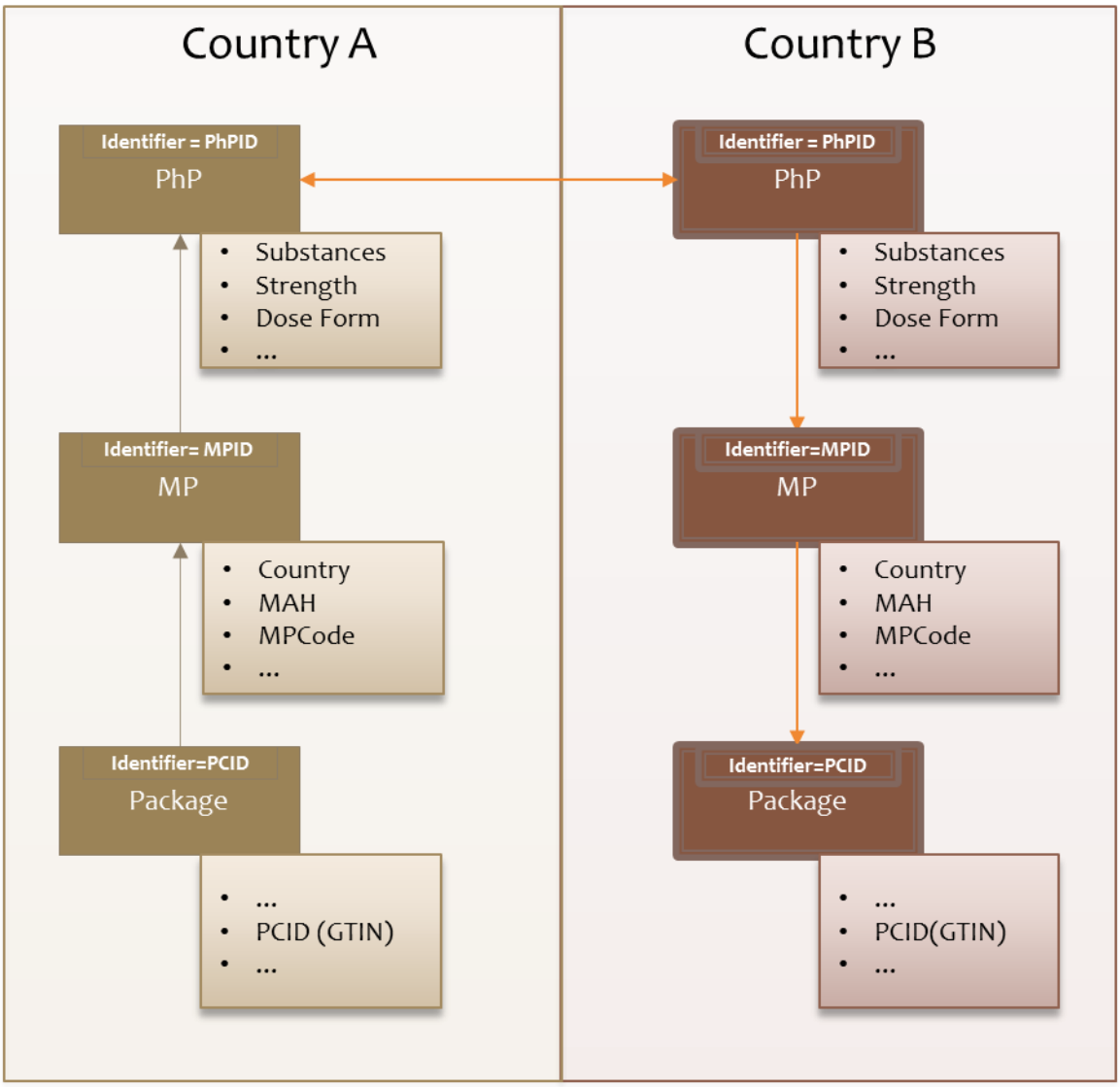


Figure 1 - Concept

This enables us to proceed and introduce the topic of defining the information needed to identify a product based on (and across) these levels, Section 2.4 – Sample Core Dataset exposes the product characteristics.

2.3.1 Using attributes to identify medicinal products

A few scenarios help identify what information may be required to identify products, and how that information is used.

Scenario 1: Common identifier(s):

The easiest case would be when the medication has one identifier that is commonly known by prescribing and dispensing systems: both prescriber and dispenser have the same understanding of the identifier, which means that there is no question about which product to dispense. This is not however, really expectable in cross-country dispensing, and may not even be possible to achieve. This scenario presents some dependencies - it may take considerable effort to ensure that all products have a common identifier at the prescribing side. In fact, in order to achieve this dependency, the other scenarios described below may need to be covered: matching identifiers that enable attribution of one common identifier, or even matching attributes to confirm the matching of the identifiers and adequacy of the common identifier.

A typical example of an implementation (or consequence) is that a prescription could be entered (or adapted) to refer to "internationally dispensable medication", where these "internationally dispensable item" had a common identification. How these attributes are filled is an implementation option. Since these attributes would be defined centrally and not locally, the concepts of Medicinal Product Dictionaries emerges, and ISO 19256 is relevant. Achieving these common identifiers is a possible recommendation of the openMedicine project but not the main focus.

Scenario 2: Matching identifier(s):

If (or while) the common identifier does not exist, then we can imagine that for one attribute (name, or package ID) there is a corresponding value of the same attribute on the other side. This means we must simply translate the attribute values.

Example: paracetamol 500 mg (code: ABC) in Spain corresponds to paracetamolo 500 mg (code: XYZ) in Italy.

Note that in this case we may not guarantee univocal equivalence: A product may have several equivalents.

This corresponding between equivalents is to be stored in a reference data repository. Achieving this correspondence, however, is something that requires manual verification or an automated matching.

Regardless of the process, the criteria for enabling the preparation of this correspondence (for example, determining that code ABC in Spain corresponds to code XYZ in Italy) requires the introduction of identifying attributes.

Scenario 3: Identifying attributes(s):

In some other cases, there is no common or equivalent identifier. One example is the active substance prescription to be dispensed in a country where the prescription is usually done by commercial name.

Another example is described in the previous scenario, when a correspondence must be established between two codes, based on some clear criteria (it must be objective, automated matching, since it is not feasible that regulators will do a manual match for all products).

To define which attributes can be used in finding an equivalent, it matters to define how these attributes are used in finding an equivalent. For this, the definition of equivalent is proposed:

(Computable) **Definition of equivalent products**:

*A medication B is correctly identified as equivalent to a medication A when in all **relevant** attributes of medication B, there is not one value that conflicts with the **relevant** attributes of medication A.*

*A set of medications BB is correctly identified as equivalent to a medication A when in all **relevant** values of all attributes of any medication in BB, there is not one value that conflicts with the **relevant** attributes of medication A.*

This means that the equivalence requires 2 steps: i. finding what the corresponding attributes are, and ii, finding the matching values.

In a practical example, if a physician prescribes "paracetamol 500 mg coated tablets", then any other formulation that is "paracetamol 500 mg coated tablets" (with or without lactose) is an equivalent.

If a physician prescribes paracetamol 500 mg coated tablets without lactose", then the equivalents are also limited to those that do not have lactose, if the composition containing lactose is one of the relevant attributes.

Note: Implementers must be aware that the level of detail in the prescription may have some assumptions, e.g. when a physician prescribes a medication without lactose, it is not possible to determine whether this is because it is a default choice, or because there is a clinical reason. The only safe approach is not to contradict the explicit or implicit decisions of the physician, or the implications in the prescribing country.

In the case of identifiers, the attribute comparison is on a 1:1 basis, i.e. we compare one identifier value with another value of the same identifier.

In the case of attribute sets, the match may be between groups of identifiers of different cardinality. For example, one product identifier {ProductID} may correspond to a unique set of attributes like {substance name; dosage; form; administration route…}.

D2.2 analyses these attributes in how they can be used to find an equivalent product.

In short, prescribing medication using common identifiers is one of the ways to resolve the problem addressed by openMedicine, Achieving and maintaining such common identifiers may require the use of attributes that identify a product in the data structure.

2.3.2 Classification of attributes according to sources

To avoid dependencies, it is important to consider the origin of the information needed to identify a specific product:

Some data elements are product characteristics, and are expected to be available in a repository that is maintained by an authority). For example, the composition of the medication, or the active substance, or the ID…

Note: maintaining these attributes up to date is a dependency for the implementers of such a repository.

Other data may be provided for each intended user of the medication. For example, the physician may indicate a posology and treatment duration (1 tablet TID for 2 weeks) which is used to determine the package size. Or the physician may add any constraints, in varying detail, that affect the product equivalence.

Some prescriptions may identify the package size.

Substitution indication is another example of an attribute that is available on the prescription, and that is important to determine the equivalent product.

Other information is not available in the prescription nor in the product data. For example: substitution rules. As per D1.1, substitution rules have an impact in the finding of an equivalent. Further analysing this question, we can state that …

…Prescription information, as well as other static or dynamic information (substitution rules and other restrictions) have an impact (extending or limiting) on the equivalence of products: For example, when a substitute is permitted in the prescription, this relieves the matching on one or several attributes when finding an equivalent (thus extending the permissible equivalents). When substitution is limited, this constrains the matching of the attributes.

These attributes from different sources introduce different requirements:

More importantly, this introduces the context in our previous definition of equivalent: A product may be equivalent not by definition, but within the scope of a given prescription, or between two countries, or at a given time.

If we consider that two tablets of paracetamol 500 mg from different manufacturers are equivalent, but the definition of equivalence above shows that depending on a specific prescription the equivalent range may be reduced (e.g. only if both don't contain lactose in the excipients) or extended (e.g. also capsules may be considered equivalent).

Therefore, the outcome of the equivalence of a prescribed product can be for a specific context.

The attributes are to be classified according to their origin and applicability context. This is addressed in D2.2.

2.4 Core Product Dataset

For each authorisation procedure a common set of product information is provided by the applicant as described in volume 2B – presentation and content of the dossier.

The dossier includes a structured application form that summarises the product information and together with the Summary of Product characteristics defines the Core Product Dataset (CPD) for the purposes of this document.

The table below describes a typical CPD extracted by the competent authority into their national regulatory systems for use in both Pre and Post authorisation activities. This sample data set along with other information relating to areas such a manufacturing process and regulatory information is generally captured within a competent authority system and is based where possible on standard terminologies for elements such as substance, routes of administration etc.

One exception in this data set is the Summary of product characteristics (SmPC), which is generally captured as either a MS word or PDF file.

Sample Core Product Dataset - Medicinal Product

Attribute Name	Medicinal Product Identifier (MPID)
Attribute Definition	Unique identifier allocated to a Medicinal Product supplementary to any existing authorisation number as ascribed by a Medicines Regulatory Agency in a jurisdiction
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.1

Attribute Name	Combined Pharmaceutical Dose form
Attribute Definition	Single term to describe two or more manufactured items that are intended to be combined in a specific way to produce a single pharmaceutical product, and that includes information on the manufactured dose form of each manufactured item and the administrable dose form of the pharmaceutical product
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.2

Attribute Name	Name
Attribute Definition	The full and complete Medicinal Product Name as approved by the Medicines Regulatory Agency in a jurisdiction shall be specified, as text
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.12.1

Attribute Name	Invented Name Part
Attribute Definition	The invented name (i.e. trade name) of the Medicinal Product without the trademark or any other similar designations reflected in the Medicinal Product Name can be specified as text, where applicable.
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.12.2

Attribute Name	Scientific Name Part
Attribute Definition	The scientific or common (i.e. generic) name of the Medicinal Product without any other descriptors can be specified as text, where applicable.
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.12.3

Attribute Name	Strength Name Part
Attribute Definition	The strength, if reflected in the Medicinal Product Name, shall be specified as text, where applicable.
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.12.4

Attribute Name	Pharmaceutical Dose Form Part
Attribute Definition	The pharmaceutical dose form, if reflected in the Medicinal Product Name, shall be specified as text, where applicable.
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.12.5

Attribute Name	Formulation Part
Attribute Definition	The formulation, if reflected in the Medicinal Product Name, shall be specified as text, where applicable
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.12.6

Attribute Name	Intended Use Part
Attribute Definition	The intended use, if reflected in the Medicinal Product Name, shall be specified as text, where applicable
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.12.7

Attribute Name	Target Population Part
Attribute Definition	The target population, if reflected in the Medicinal Product Name, shall be specified as text, where applicable
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.12.8

Attribute Name	Container or Pack Part
Attribute Definition	The container or pack, if reflected in the Medicinal Product Name, shall be specified as text, where applicable
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.12.9

Attribute Name	Device Name Part
Attribute Definition	The device, if reflected in the Medicinal Product Name, shall be specified as text, where applicable
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.12.10

Attribute Name	Trademark or Company Name Part
Attribute Definition	The trademark, if reflected in the Medicinal Product Name, shall be specified as text, where applicable
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.12.11

Attribute Name	Time/Period Part
Attribute Definition	The time/period, if reflected in the Medicinal Product Name, shall be specified as text, where applicable
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.12.12

Attribute Name	Flavour Part
Attribute Definition	The flavour, if reflected in the Medicinal Product Name, shall be specified as text, where applicable
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.12.13

Attribute Name	Language
Attribute Definition	The language of the Medicinal Product Name as applicable in the specified country and jurisdiction if appropriate shall be specified
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.12.16

Attribute Name	Classification System
Attribute Definition	The Medicinal Product can be classified according to various classification systems, which may be jurisdictional or international. E.g. ATC Code, Legal Basis, Medicinal product type.
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.10

Attribute Name	Classification System Value
Attribute Definition	The individual value from the classification system that applies to the Medicinal Product shall be specified using a controlled term and a controlled term identifier
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.10

Attribute Name	Version Date
Attribute Definition	The date of the authorization or the latest update of the regulated product information (e.g. elements related to the Summary of Product Characteristics or Product Labelling, which serve as the reference for the unique Identification of Medicinal Products and their characteristics) shall be specified
Category	Medicinal Product
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section A.2.9.1

Sample Core Dataset - Pharmaceutical Product and Device

Attribute Name	Pharmaceutical product identifier (PHPID)
Attribute Definition	This class shall carry the relevant identifiers as defined by ISO 11616. This provides a uniform representation of the pharmaceutical product using the substance(s)/specified substance(s), their (reference) strength(s), the administrable dose form and, where applicable, the integral device
Category	Pharmaceutical Product and Device
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Standard ISO 11616:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15)

Attribute Name	Administrable Dose Form
Attribute Definition	This shall describe the administrable dose form in accordance with the regulated product information. This is after it has undergone any necessary reconstitution, where applicable. The administrable dose form shall be specified in accordance with ISO 11239 and the resulting terminology. The term and the term identifier shall be specified
Category	Pharmaceutical Product and Device
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Standard ISO 11616:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section E.2.1

Attribute Name	Unit of Presentation
Attribute Definition	The unit of presentation is a qualitative term describing the discrete unit in which a pharmaceutical product is presented to describe strength or quantity in cases where a quantitative unit of measurement is not appropriate. It is a term and a term identifier as defined in ISO 11239 and the resulting terminology
Category	Pharmaceutical Product and Device
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Standard ISO 11616:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section E.2.2

Attribute Name	Route of Administration
Attribute Definition	The route of administration is a concept that is used to describe the path by which the pharmaceutical product is taken into or makes contact with the body
Category	Pharmaceutical Product and Device
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Standard ISO 11616:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section E.2.4

Attribute Name	Device Type (combined medical device ATMP)
Attribute Definition	The type of device shall be specified using an appropriate controlled vocabulary. The controlled term and the controlled term identifier shall be specified
Category	Pharmaceutical Product and Device
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Standard ISO 11616:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section C.3.4.8.1

Attribute Name	Device Trade Name (combined medical device ATMP)
Attribute Definition	This can be used to specify the trade name of the device, where applicable, as text
Category	Pharmaceutical Product and Device
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Standard ISO 11616:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section C.3.4.8.2

Sample Core dataset - Substance

Attribute Name	Pharmaceutical Product Identifier (PhPID)
Attribute Definition	Unique identifier and uniform representation of the pharmaceutical product using the substance(s)/specified substance(s), their (reference) strength(s), the administrable dose form and, where applicable, the integral device
Category	Substance
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section E.2.6.1

Attribute Name	Ingredient Role
Attribute Definition	The role of the ingredient as part of the manufactured item/pharmaceutical product shall be specified using an appropriate controlled vocabulary. The controlled term and a term identifier shall be specified
Category	Substance
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section D.2.1

Attribute Name	Substance
Attribute Definition	Substance matter of defined composition that has discrete existence, whose origin may be biological, mineral or chemical (EN / ISO 11616). A substance can be specified for an ingredient in the role described. The substance shall be described in accordance with ISO 11238 and its resulting terminology. A term and a term identifier shall be used
Category	Substance
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP, Standard ISO 11616:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section D.2.2.1

Attribute Name	Specified Substance
Attribute Definition	When a specified substance is described, it shall be presented in accordance with ISO 11238 and its resulting terminology. A term and a term identifier shall be used
Category	Substance
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP, Standard ISO 11616:2012(E)

	ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section D.2.3.1

Attribute Name	Confidentiality Indicator
Attribute Definition	When a specified substance is described, it shall be presented in accordance with ISO 11238 and its resulting terminology. A term and a term identifier shall be used
Category	Substance
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP, Standard ISO 11616:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section D.2.3.3

Attribute Name	Strength Range (Presentation)
Attribute Definition	The strength range (presentation) shall be specified. It is defined as the quantity or range of quantities of the substance/specified substance present in the unit of presentation of or in the volume (or mass) of the single pharmaceutical product or manufactured item. When required for expression of strength, the unit of presentation shall be specified in accordance with ISO 11239 and its resulting terminology. The controlled term and a term identifier for the unit of presentation shall be specified in the associated manufactured item or pharmaceutical product. The representation of this information is further described above in 7.6.2.10.3 for manufactured item or 7.8.2.1.2 for pharmaceutical product. For strength expressed using standard units, the unit of measure symbol and the symbol identifier as defined in ISO 11240 and its resulting controlled vocabulary shall be specified.
Category	Substance
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section D.2.3.4.1

Attribute Name	Strength Range (Concentration)
Attribute Definition	The strength range (concentration) can be specified. It is defined as a quantity or range of quantities of the substance/specified substance present per unitary volume (or mass). When required for expression of strength, the unit of presentation shall be specified in accordance with ISO 11239 and its resulting terminology. The controlled term and a term identifier for the unit of presentation shall be specified in the associated manufactured item or pharmaceutical product. The representation of this information is further described in 7.6.2.10.3 for manufactured item or 7.8.2.1.2 for pharmaceutical product. For strength expressed using standard units, the unit of measure symbol and the symbol identifier as defined in ISO 11240 and its resulting controlled vocabulary shall be specified
Category	Substance
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , Section D.2.3.4.2

Attribute Name	Substance Name (ISO 11238 3.4 Naming **of** substances)
Attribute Definition	A least one substance name or company code shall be associated with each substance. If the name is an official name, the naming authority, language and jurisdiction in which the name is used shall be identified. This International Standard shall be neutral with respect to any given systematic or official nomenclature.
Category	Substance
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15)

Attribute Name	Substance ID (ISO 11238 3.5 Requirements for unique identifiers)
Attribute Definition	Each substance and specified substance shall have only one permanently associated unique identifier that shall not indicate the order of submission to the system. The unique identifier shall be non-semantic, random and fixed length with an internal integrity check. The unique identifiers shall be publicly available and their use royalty free. A unique identifier shall be assigned to approved and investigational substances, excipients and impurities, solvents, ions, fragments and moieties.
Category	Substance
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15)

Attribute Name	Substance Type (ISO 11238 3.6 Types of substances)
Attribute Definition	Substances shall be single substances, mixture substances or specified substances. If it is possible to represent a substance as a single substance or a mixture substance, the substance shall be represented as a single substance.
Category	Substance
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15)

Sample Core Dataset - Packaged Medicinal Product

Attribute Name	Package Identifier (PCID)
Attribute Definition	This is the unique identifier for the packaged Medicinal Product, constructed as described in section 6.3 of XXXX
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.1

Attribute Name	Package Description
Attribute Definition	A textual description of the packaged Medicinal Product shall be provided
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.2

Attribute Name	Package Item (Container) Type
Attribute Definition	The Package Item (Container) type shall be specified to describe the physical type of the container of the medicine in accordance with ISO 11239 and its resulting terminology. A term and a term identifier shall be specified
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.1

Attribute Name	Package Item (Container) Quantity
Attribute Definition	The quantity (or count number) of the package item shall be specified
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.2

Attribute Name	Material
Attribute Definition	The material(s) of the package item shall be described in accordance with ISO 11238 and its resulting terminology. A term and a term identifier shall be specified
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.3

Attribute Name	Alternate Material
Attribute Definition	The alternate material(s) of the package item shall be described in accordance with ISO 11238 and its resulting terminology. A term and a term identifier shall be specified
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.4

Attribute Name	Component Type
Attribute Definition	The type of component whose material is being described should be specified, using an appropriate controlled vocabulary. The controlled term and the controlled term identifier shall be specified
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.6.1

Attribute Name	Component Material
Attribute Definition	The material(s) of the component can be specified. Materials shall be described in accordance with ISO 11238 and its resulting terminology. A controlled term and a controlled term identifier shall be specified
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.6.2

Attribute Name	Component Alternate Material
Attribute Definition	Alternative materials for the component can be specified. Materials shall be described in accordance with ISO 11238 and its resulting terminology. A controlled term and a controlled term identifier shall be specified
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.6.3

Attribute Name	Manufactured Dose Form
Attribute Definition	This describes the pharmaceutical dose form of the manufactured item, where applicable, before transformation into the pharmaceutical product. The manufactured dose form shall be specified in accordance with ISO 11239 and its resulting terminology. A term and a term identifier shall be used.
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.9.1

Attribute Name	Unit of Presentation
Attribute Definition	The unit of presentation is a qualitative term describing the discrete unit in which a pharmaceutical product is presented to describe strength or quantity in cases where a quantitative unit of measurement is not appropriate. It is a term and a term identifier as defined in ISO 11239 and the resulting terminology
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.9.2

Attribute Name	Manufactured Item Quantity
Attribute Definition	The quantity (or count number) of the manufactured item shall be described. It shall be specified as a value and units, and the units shall be specified as a symbol and a symbol identifier as defined in ISO 11240 and the resulting terminology.
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.9.3

Attribute Name	Other Characteristics Code System
Attribute Definition	The code system being used to describe the type of characteristic shall be specified using an appropriate identification system
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.11.1

Attribute Name	Other Characteristics Code Value
Attribute Definition	The individual value from the Characteristics code system that applies shall be specified using a controlled term and controlled term identifier
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.11.2

Attribute Name	Device Type
Attribute Definition	The type of device shall be specified using an appropriate controlled vocabulary. The controlled term and the controlled term identifier shall be specified
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.8.1

Attribute Name	Device Trade Name
Attribute Definition	This can be used to specify the trade name of the device, where applicable, as text
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.8.2

Attribute Name	Device Listing Number
Attribute Definition	This can be used to specify the listing number of the device, where applicable, in text
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.8.3

Attribute Name	Model Number
Attribute Definition	This can be used to specify the device model or reference number, where applicable, in text
Category	Packaged Medicinal Product
Standards	ISO IDMP, Standard ISO11238:2012(E) ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section C.3.4.8.3

Sample Core Dataset - Clinical Particulars

Attribute Name	Indication Text
Attribute Definition	The authorised therapeutic indication(s) shall be described in text
Category	Clinical Particulars
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section F.2.1.1

Attribute Name	Indication as "Disease/ Symptom/ Procedure"
Attribute Definition	The underlying disease, symptom or procedure that is the indication for treatment shall be specified as it is referenced in the regulated product information using an appropriate controlled reference terminology. The controlled term and the controlled term identifier shall be specified
Category	Clinical Particulars
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section F.2.1.2

Attribute Name	Co-Morbidity
Attribute Definition	If there is any co-morbidity (concurrent condition) or co-infection described as part of the indication as it is referenced in the regulated product information, it can be specified here using an appropriate controlled reference terminology. The controlled term and the controlled term identifier shall be specified
Category	Clinical Particulars
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section F.2.1.4

Attribute Name	Intended Effect
Attribute Definition	The intended effect, aim or strategy to be achieved by the indication can be specified as it is referenced in the regulated product information using an appropriate controlled vocabulary. The controlled term and the controlled term identifier shall be specified
Category	Clinical Particulars
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section F.2.1.5

Sample Core Dataset - Authorisation

Attribute Name	Marketing Authorisation Number
Attribute Definition	The number as assigned to a Medicinal Product by the Regulatory Medicines Agency of a country or jurisdiction shall be specified in text.
Category	Authorisation
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section B.2.1

Attribute Name	Country
Attribute Definition	The country in which the marketing authorization has been granted shall be provided. Where a marketing authorization spans more than one country, all the applicable countries/jurisdictions shall be described
Category	Authorisation
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section B.2.2

Attribute Name	Legal Status of Supply
Attribute Definition	The legal status of supply of the Medicinal Product as classified by the Regulatory Medicines Agency shall be specified (e.g. subject to medical prescription or not). The legal status of supply shall be described using an appropriate controlled vocabulary. The controlled term and the controlled term identifier shall be specified
Category	Authorisation
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section B.2.3

Attribute Name	Authorisation Status
Attribute Definition	The status of the marketing authorization changes throughout the lifecycle of a Medicinal Product depending on the regulatory process applicable in a jurisdiction. This shall be specified using an appropriate controlled vocabulary. The controlled term and the controlled term identifier shall be specified
Category	Authorisation
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section B.2.4

Attribute Name	Authorisation Status Date
Attribute Definition	The date at which the given status has become applicable shall be specified. A complete point in time date consisting of day, month and year shall be specified
Category	Authorisation
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section B.2.5

Attribute Name	Date of First Authorisation
Attribute Definition	The date that the product was first authorised
Category	Authorisation
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section B.2.8

Attribute Name	Procedure Identifier/Number (e.g. MRP number
Attribute Definition	The unique identifier for the specific instance of a procedure undertaken shall be provided in text
Category	Authorisation
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section B.2.11.2

Attribute Name	Marketing Authorisation Holder Identifier
Attribute Definition	The unique identifier of the organization shall be provided. An international coding system for unique organization identifiers can be used
Category	Authorisation
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section B.2.9, G.2.1

Attribute Name	Marketing Authorisation Holder Name
Attribute Definition	The name of the organization shall be provided in text
Category	Authorisation
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section B.2.9, G.2.1.1

Attribute Name	Marketing Status
Attribute Definition	indicates the marketing status of the product
Category	Authorisation
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section B.2.12.6 , B.2.12.7

Attribute Name	Marketing Date (Start / Stop)
Attribute Definition	The date when the Medicinal Product is placed on the market by the Marketing Authorization Holder (or where applicable, the manufacturer/distributor) in a country and/or jurisdiction shall be provided, as shall the date when the Medicinal Product is “no longer available on that market”. Complete point in time dates consisting of day, month and year shall be specified
Category	Authorisation
Standards	ISO IDMP, Standard ISO11615:2012(E) ISO IDMP Implementation Guide ISO/DTS 20443 (2015-07-15) , section B.2.12.4

Attribute Name	**Summary of Product Characteristics (SmPC)**
Attribute Definition	The SmPC is a legal document approved as part of the marketing authorisation of each medicine and contains the basis of information for healthcare professionals on how to use the medicine. Regulated Document
Category	Authorisation
Standards	Volume 2c Notice to Applicants

This information is updated on an ongoing basis throughout the lifecycle of the product by way of a variation application to the product information submitted by the marketing authorisation holder. The information is reviewed and approved by the competent authority, who updates the master product record in the competent authority national system (refer to medicinal product dictionary standard, ISO TS 19256) and an updated authorisation is sent to the marketing authorisation holder.

A subset of this data would provide a mechanism to identify a product across product ranges based on a combination search of active substance, pharmaceutical form , strength, unit of measure and then refining the results with for example with a combination of excipient, route of administration or packaging data. This type of search relies on the data set complying with a common set of reference data e.g. substance, units of measure etc. for all products within the data set at a national level.

3 Models for Product Data Provision

The following section outlines two basic models available for the capture, validation and distribution of medicinal product information.

A competent authority model with product information provided by the competent authority either locally or through a centralised hub or a centralised industry model with information provided by marketing authorisation holder to a centralised system.

3.1 Competent Authority Model

At present there are 34 competent authorities responsible for the authorisation of medicinal products for human use within the European Union, under either a national, mutual recognition or centralised procedure as described in the Volume 2a of the notice to applicants.

Each competent authority captures information for medicinal products in regulatory systems based on their requirements for pre and post authorisation activities. These product data sets once approved are often published on competent authority websites, provided to other agencies responsible for health or to software providers of pharmacy / clinical software systems for updating of product data within these systems. The method of data provision and format of this data to these stakeholders can vary depending on the requirement and can range from structured XML feeds to Excel / CSV files containing the data.

Each competent authority has, over time developed regulatory systems and databases to support their national operations and each system although similar in content can be structured differently and use multiple versions for standard terminologies.

A competent authority model for a European Medicines database could be delivered in one of the following approaches:

1. Data is stored and accessed at the national competent authority and can be accessed using web services to interrogate the data.

2. Data is provided to a central system by the national competent authority on a regular basis and interrogated using a web interface or a web service.

Provisioning of product data can be provided by each competent authority using one or more of the available formats e.g. XML, XLS, CSV, but unless this information can be cross referenced using standard terms and common structures it becomes a silo of data for the competent authority even in a shared data environment.

Harmonisation and synchronization of the core product data, supporting standard vocabularies and the messaging standard across the EMRN would be critical for either option to operate effectively and would be required across all member states prior to going live with either solution. For these two options to operate effectivity each stakeholder would be required to adopt a common messaging system (e.g. HL7) to allow the transfer and integration of data between national systems or to a centralised system.

With the development and implementation of the ISO IDMP standards across the EMRN, many competent authorities have started work to update their national regulatory systems to comply with these new standards. Implementation of the standards will require updating of the core product information record and the adoption of common standard terminologies to be used with the system.

In a recent survey responded to by 20 competent authorities the majority of information described in section 2.3 was available in a structured format and aligned with current standards for reference information.

Although the reference terminologies used to identify the attributes of the product are available, the level of compliance with the most current set of reference information may differ depending on the current version and process for updating this type information through the regulatory process at a national level. This inconsistency of reference data would not provide the required level of accuracy in identification of products in a cross border setting and each competent authority would need to ensure that they were compliant with the latest version of reference data for the system to operate effectively.

For data stored and accessed at the competent authority, each national system would be required to be able to provide information in line with agreed standard for data structure and terminologies.

A significant investment in both the scientific and IT areas would be needed to adjust the product information to make it consistent across the network and to develop and maintain the IT infrastructure necessary.

The system itself would require connectivity to each national product database available on a 24 x 7 basis and in line with a defined messaging protocol to enable the required level of access.

3.2 Centralised (Industry) Model

The model of European Medicines Database provided by industry is already in operation through the European Medicines Agency using Art 57(2) of regulation (EU) no 1235/2010.

This regulation requires each marketing authorisation holder to submit electronically, information for all products authorised for human use and to keep the information up to date based on any new or varied marketing authorisations granted, through any procedure type.

Although initially conceived for use in pharmacovigilance activities the dataset required under Art 57(2) is comparable to the dataset described in section 2.3 and based on the gap analysis carried out in the deliverable D1.1. EpSOS identification and description problems, the dataset can provide a level of data that can be used to identify products across member states held with the database.

The main differences identified in the gap analysis carried out between epSOS and Art (57)2 across the main elements of the dataset are:

1. Different versions of the controlled terminologies in operation.
2. Upper case vs lower case term sets.
3. Use of free text to describe data elements
4. Non-standard terminology used to describe a substance

The set of controlled terminologies used for pharmaceutical forms, routes of administration and ATC codes etc. are based on the list provided by EDQM and WHO. A free text section has been included in the system to capture packaging information on the product. This information is not structured and does not comply with any agreed standard.

The substance terminologies list was initially derived from the list of substances available within EMA systems and after, an exercise to remove any duplicates, the list of substances were published for use by MAH's when submitting data to the system. This substance list is not linked to a single validated source of substance information and as new substances are added through Art (57), the substance list is updated.

With over 450,000 products of an estimated 600,000 products recorded in the system a significant number of MAH's are compiling with the legislation. Some marketing authorisation holders with a small number of products are still not yet providing the data to the system

At present the submission, validation and management of data is an industry / EMA activity and there is currently no interaction with the competent authority to validate the data or to follow up with the non-compliant marketing authorisation holders.

3.3 Data Validation

Within the current Art (57) 2 database compliance with the legalisation by the marketing authorisation holders is the key quality control for the system to operate. Two areas of data quality are still being addressed by EMA in relation to the Art (57) 2 data, completeness of the data and the quality of the information.

In a recent study of Art (57) 2 data for completeness, a comparison of five competent authority data sets to the Art (57) 2 data set based on the authorisation number of the products was carried out. The comparison found that 91% of the products in the competent authority database were found in the Art (57)2 database and that the majority of missing products were from marketing authorisation holders with small numbers of products. For datasets that are missing from the Art (57)2 database, competent authorities are contacting the relevant MAH's and requesting that they provide the required data to the Art (57)2 database.

The technical compliance to data standards published by EMA for data provision to the Art (57)2 database by the MAH would appear to be quite high. Data sets are technically verified against the business rules defined by EMA and erroneous data such as non-complaint controlled terms, e.g. pharmaceutical forms and substances not complying with the agreed term set or non-conforming records are rejected by the system and the MAH is requested to re-submit.

The quality and accuracy of the information provided by MAH in comparison to the information that the competent authorities hold for medical products has not been verified. As part of a review of the Irish competent authority data and a sample set of Art (57)2 product data a selection of information t was checked and, the quality of information contained was quite good for the majority of the key elements. In general the active substances of products, matched across both data sets while slight differences in the recording of the excipients for the product were found. Other information such as product names matched in the majority of products. Terminologies' also matched well when compared, with differences found due to the versions of the terminology sets.

The summary of product characteristics was not checked as part of this exercise as this was unstructured data with a pdf document. This level of validation could only be carried out using automated tools and by comparing the MAH submitted data to the data authorised by the competent authority, and would only be available to the structured dataset (i.e. excluding the SmPC) using the agreed standard terminologies.

Art 25 and 26 of the commission implementing Regulation (EU) no 520/2012 requires the use of common standards, formats and terminologies in the EU for the identification and exchange of information on medicines. It is planned to replace with current Art 57(2) database with the new formats, standards and terminologies defined by the ISO IDMP standards and as agreed within the EMRN.

4 Conclusion

Both of the models (competent authority and industry model) proposed have the ability to provide the required product information for cross border prescribing. Each relies heavily on the use of standard terminologies, data structures and adoption of these by all stakeholders to enable them to operate effectively.

For both models the quality of information is the key requirement and based on the current process, availability for managing data and the legislation basis available, it is proposed that a hybrid model be adopted gathering and validating information from both industry and competent authorities into a single European medical Product data (EPMD) repository.

For this system to deliver a qualified set of medicinal product information three key areas need to be addressed.

4.1 Adoption of standard terminologies and ISO IDMP data standards

The long term goal is the implementation of the ISO IDMP standards, in particular ISO - 11615 which defines the standard for the data elements and structures for unique identification and exchange of regulated medicinal product information, that have been agreed by both the EMRN and industry stakeholders.

To achieve this a phased implementation is planned over the next three years and based on a recent survey of regulators it is estimated that these standards will be in place for the majority of competent authorities by 2018, for which planning is currently underway. This timeline is probably optimistic.

The first step in this implementation is the identification and adoption of standard terminologies which will comply with the agreed standards:

- EN/ISO 11238:2012(E), Health Informatics, Identification of Medicinal Products (IDMP) standard Data elements and structures for unique identification and exchange of regulated information on substances
- EN/ISO 11239:2012(E), Health Informatics, Identification of Medicinal Products (IDMP) standard Data elements and structures for unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation, routes of administration and packaging
- EN/ISO 11240:2012(E), Health Informatics, Identification of Medicinal Products (IDMP) standard Data elements and structures for unique identification and exchange of units of measurement.

For each terminology it has been agreed that a single broker would be identified for the regulatory network to consolidate and distribute the approved terminologies. The broker would work in conjunction with terminology providers such as EDQM, WHO and GINAS to manage these on behalf of the network.

Of particular relevance to the openMedicine project is the Global Ingredient Archival System (GINAS) that has been adopted by the EMRN as a provider of substance information. The GINAS will provide a common identifier of the substances used in medicinal products, utilis-

ing a consistent definition of substances globally that is consistent with the ISO 11238 standard. At this time it is still unclear who will manage the global identifiers for substances.

It is currently proposed that the broker for terminologies will be EMA as they have set up a controlled term management service called EUTCT that currently provides 64 controlled terms lists, consolidated from the various terminology providers. The broker will manage all updates and change requests to terminologies and ensure that they are available for use in the various regulatory systems.

In parallel with this work, competent authorities and industry stakeholders are developing new data structures in line with the ISO 11615 and ISO 11616 standards, this work is being coordinated through the EU Network data board (EUNDB) and the ISO IDMP Task Force that is a joint industry / regulator group organised by the EMA

- EN/ISO 11615:2012(E), Health Informatics, Identification of Medicinal Products (IDMP) standard Data elements and structures for unique identification and exchange of regulated medicinal product information
- EN/ISO 11616:2012(E), Health Informatics, Identification of Medicinal Products (IDMP) standard Data elements and structures for unique identification and exchange of regulated pharmaceutical product information

The groups are currently reviewing the standards and the requirements for managing information and the operating model for the management of key terms such as MPID and PHPID which will be an integral part of identity a medicinal product within the new ISO IDMP data structure. It is currently planned that the first iteration of the ISO IDMP model will be available in 2018.

4.2 Data Capture & Validation

Under Art (57) 2 of Regulation (EC) 726/2004/EU, marketing authorisation holders are required to provide medical product information to EMA and this has been in operation since July 2012. The process for submitting information by marketing authorisation holders is through a standard xml schema and are automatically processed and stored within a proprietary database. As a part of the EMA telematics strategy and implementation roadmap 2015 – 2017, it is planned that the article 57 database will be modified to comply with the ISO IDMP standards.

Currently, data captured by the system is not validated by the competent authority that authorised the product for the market. It is proposed that a validation step be incorporated within the process to allow a check of the data submitted by the MAH be carried out by the competent authority. With the large volume of updates on product data through article 57 submissions, manual checking is not being considered as a viable option but an automatic check between member states systems and the article 57 database is under review.

This approach has already been discussed within the EMRN as a potential way forward to ensure the accuracy of the data within the system. To enable this type of validation process, both the data structures and terminologies will need to be aligned across the EMRN.

4.3 Publication and provision of data

As part of the EU telematics Strategy and Implementation roadmap 2015-2017, it is proposed to develop a European medicines web portal that will provide a source of medical product information that could also be used for cross border prescribing.

With an estimated product database in excess of 600,000 products across all 28 member states the EU medicines web portal would need to provide the data consumer with a number of methods to access data to options are:

1. Web portal could provide an online search capability to allow a data consumer to search and report on products using any combination of criteria that the system provides to the user. The results of a search can be presented to the user online or through a file download and will display details of the medicinal products meeting the search criteria that are authorised and marketed for the selected member states.

2. The web portal could provide a data consumer access to a web service that would automatically query the product database based on criteria specified by the user. This information provided in a greed data standard could be then included within national formularies or systems. By allowing the data consumer to define the requested product data based on member state(s), it will reduce the number of products that they will be required to manage within their national system. This type of select and download would allow the data consumer to focus on products data sets that they would normally use within their systems but still allow a more general search of the product dataset through the web portal if required.

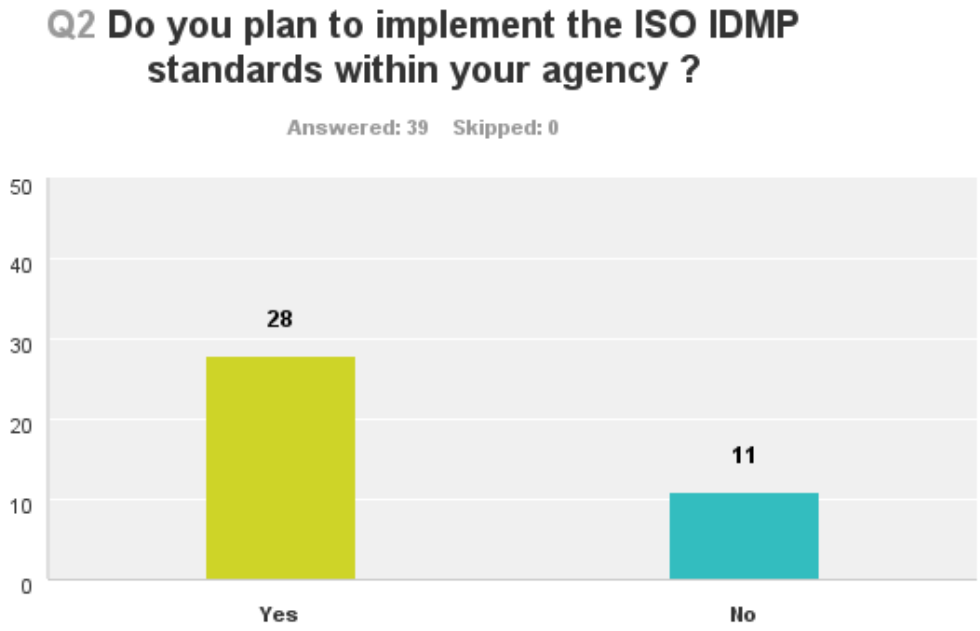
3. The availability of relevant data as discussed here for use in specific jurisdictions can be handled through the locally available medicinal product dictionaries, using EN/ISO TS 19256 as guidance. This CEN / ISO technical specification guides the creation and maintenance of local / national dictionaries or databases of medicinal products based on ISO IDMP series, and augmented with local data elements.

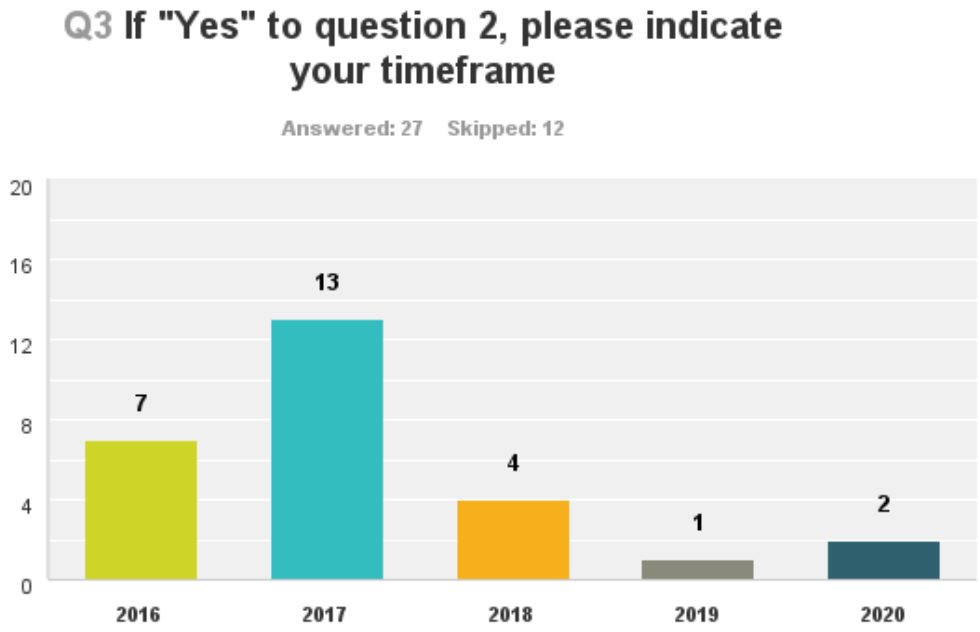
5 Appendixes

5.1 Appendix 1: Acronyms & Definitions

Acronym	Description
COPE	
EC	European Commission
eDis	eDispensation
EMA	European Medicines Agency
EMRN	European Medicines Regulatory Network
EMVO	European Medicines Verification Organization
EU	European Union
ePr	ePrescription
FMD	Falsified Medicines Directive
GINAS	Global Ingredient Archival System
MPD	Medicinal Product Dictionary
MS	Member State
PS	Patient Summary
SLA	Service Level Agreement

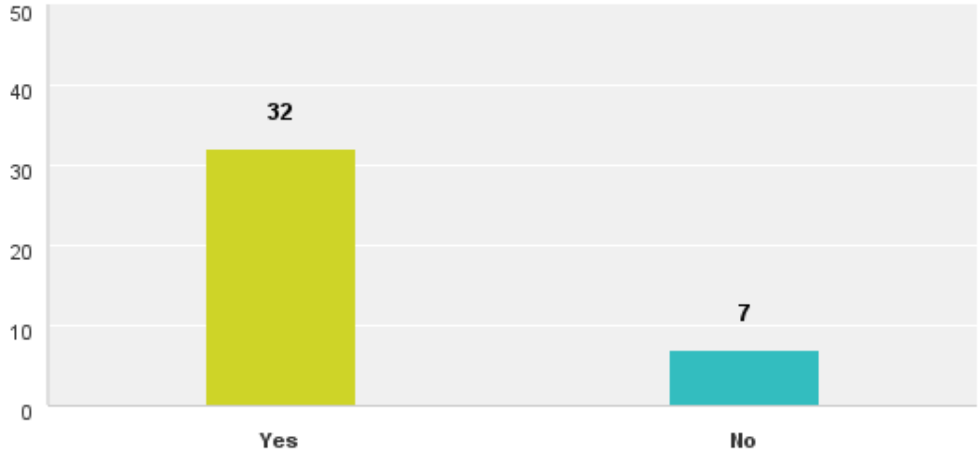
5.2 Appendix 2: ISO IDMP & SPOR Survey Results





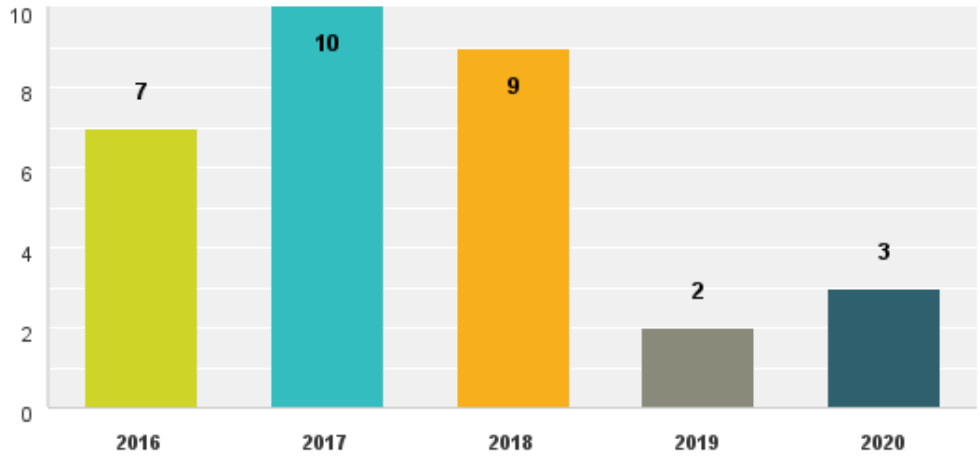
Q4 Development of Substance, Product, Organisation and Referential (SPOR) Is currently underway by the EU network data board, when available will you be consuming this information in you national systems?

Answered: 39 Skipped: 0



Q5 If "Yes" to question 4 please indicate your timeframe

Answered: 31 Skipped: 8



5.3 Appendix 3: References to legislation standards, guidelines

- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (Official Journal ('OJ') L 311, 28/11/2001 p. 67 – 128).
- Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use (OJ L136, 30/4/2004 p. 34 – 57).
- Notice to Applicants – Volume 2a Procedures for marketing authorisations
- ISO 11615 Identification of medicinal products – data elements and structures for the unique identification and exchange of regulated medicinal products.
- ISO 11616 Identification of medicinal products – data elements and structures for the unique identification and exchange of regulated pharmaceutical product information.
- ISO 11238 Identification of medicinal products – data elements and structures for the unique identification and exchange of regulated information on substances.
- ISO 11239 Identification of medicinal products – data elements and structures for the unique identification and exchange of regulated information on products Pharmaceutical dose forms, units of presentation, routes of administration and packaging..
- ISO 11240 Identification of medicinal products – data elements and structures for the unique identification of units of measurement.
- Pr/EN/ISO/DTS/20443 Implementation guide for EN/ISO 11615– data elements and structures for the unique identification and exchange of regulated medicinal products
- Pr/EN/ISO/DTS/20451 Implementation guide for EN/ISO 11615– data elements and structures for the unique identification and exchange of regulated pharmaceutical product information
- Pr/EN/ISO/DTS/19844 Implementation guide for EN/ISO 11238– data elements and structures for the unique identification and exchange of regulated information on substances
- Guidelines on ePrescriptions dataset from electronic exchange under cross-border Directive 2011/24/EU Release 1
- Guideline of Summary of product Characteristics (SmPC) Revision 2
- Presentations and documentation from the EMA EU Network Data Board

5.4 Appendix 4: Implementation roadmap