Stakeholder consultation: (preliminary) main highlights

Data Standardisation Strategy Stakeholder Workshop
Virtual Meeting, 18 May 2021
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Data Analytics and Methods Taskforce

Starting question - What is a Data standard?

What Are International Standards

"An international standard provides rules, guidelines or characteristics for activities or for their results, aimed at achieving the optimum degree of order in a given context.

It can take many forms. Apart from product standards, other examples include: test methods, codes of practice, guideline standards and management systems standards."

Why Are They Important

1. Legal obligation to implement certain standards
2. Effective assimilation of new knowledge
3. Standardization of data exchange formats
4. Improved data provisioning between regulators and other parties
5. Harmonization efforts

Standard Development Organizations (SDOs)

SDO – a standard development organization that is active in developing and publishing international standards or implementation guides for standards.

Not always clear what is meant by "Data Standard"

Example responses received when asking the question, what data standards do you need?

"IT systems aren't connected hence this makes retrieving particular decision, updates or status of process difficult and time consuming. The IT system should have proper tracking ability to support efficient communication. "

"Using DICOM- imaging as part of inclusion criteria, currently it appears that the EMRN systems can not handle DICOM documents in submissions."

"A significant problem is that in most countries, either multiple standards exist for the same data element or, proprietary non-standard solutions are used."

"I use the eCTD documents a lot (mostly clinical overview and clinical summaries) but the data inside aren't structured in a way that you can search across products so you need to do a lot of CTRL F. "

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Example - Business case for ISO ICSR

In the past...

- Paper based process of (re-) entering data in one database to another via fax submission

- Intensive manual efforts

- Limited time and resources for analysis efforts

Nowadays...

+ More automated process, capable of processing >10,000 forms per day

+ Little manual efforts

+ More time and resources for analysis efforts

Data Standards development process – Example ISO ICSR

1 Business case
Electronic exchange of Adverse drug reaction data (CIOMS 1)

2 Determine data fields & data types

3 Agree Definitions & business rules

4 Create logical model

5 Create Messaging model

6 Agree messaging/ exchange format (JSON/ XML)

7 Create/ publish standard (SDO)

8 **Out of scope**
Implement/ Create physical model

Implementing Data Standards by the European medicines regulatory network (EMRN)

Legal obligation

Having the legal obligation to implement a Standard refers to when the regulatory agencies / industry are **obliged** to implement a certain Standard (e.g. Pharmacovigilance; ISO IDMP)

No obligation, but jurisdiction

For certain parties that have legal obligations, the EMRN can **require** to adhere to specific standards in the guidelines issued for example by marketing authorization holders, clinical trial sponsors (e.g. data exchange for clinical trial protocols)
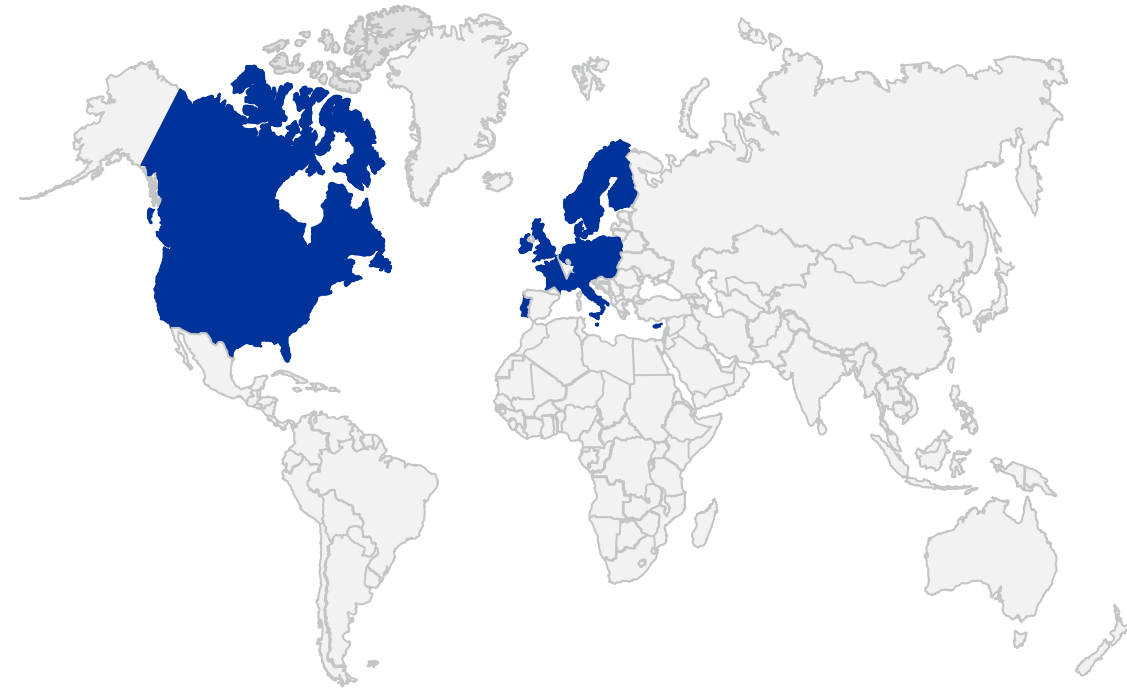
No obligation and no jurisdiction

When the EMRN has no jurisdiction over a party, no obligations can be enforced. In such cases the EMRN can **influence** e.g. get involved in the relevant fora to participate in the decision-making process (e.g. e-health records) for those standards

Data Standardisation Strategy | Survey Results

We have received 70 responses to the survey;

Category	Count
Clinical research organisation	5
EU Scientific Committee	4
EU/EEA Competent Authority	28
Healthcare Professionals	6
Learned Societies	2
Non-Commercial Sponsor of Clinical Trials	1
Other	8
Pharmaceutical Industry Association	8
Scientific/Academic Consortia	6
Standards Development Organisations	2
Non EU Regulatory Authority	1

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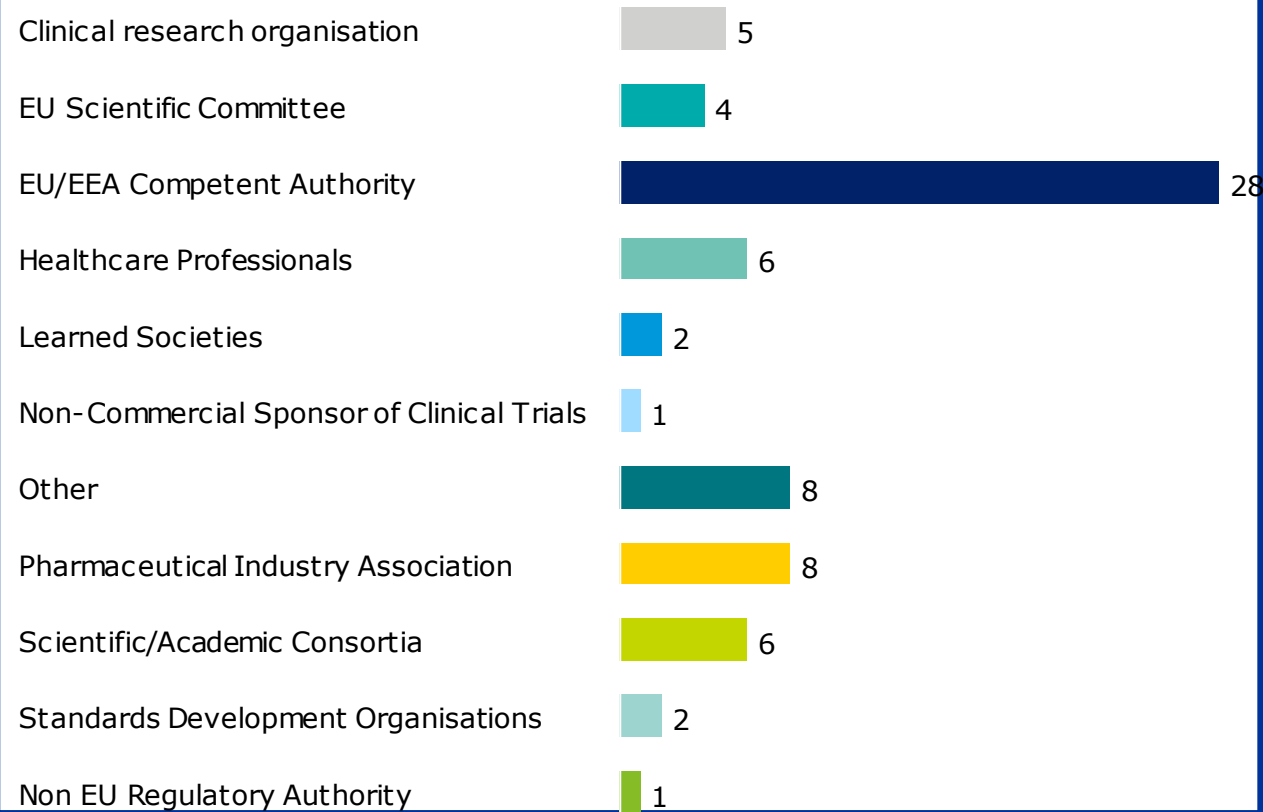
Data Standardisation Strategy | Themes

Use case received have been grouped as Themes

The following Themes have been identified so far

Use cases

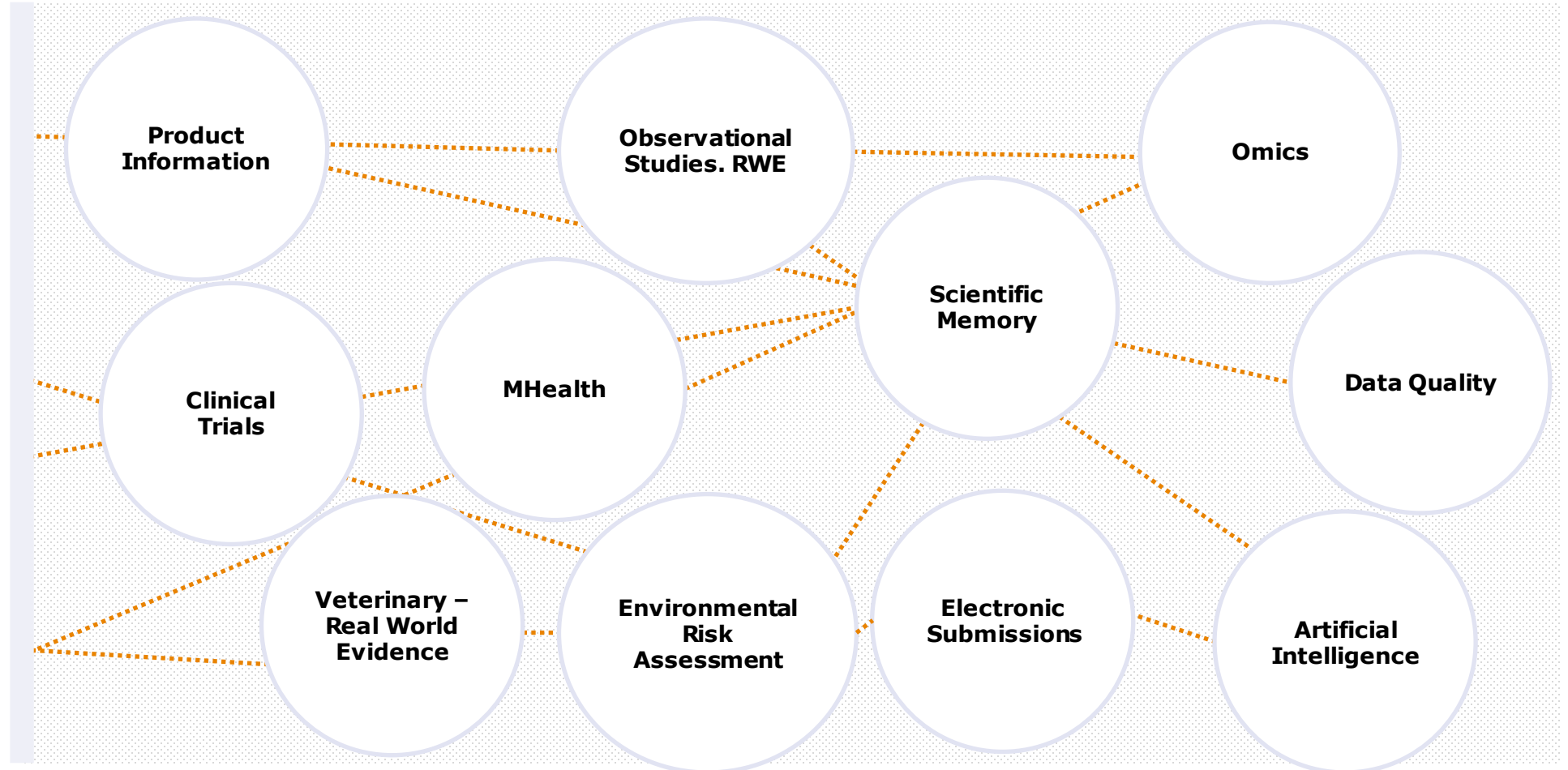The next set of slides provide the consolidated uses cases received so far through the survey and interviews conducted.

Data Standardisation Strategy | Product Information

ePI

Theme	Use cases

Product Information
 	
The ePI project is working on developing a standard for the publication of product information
	o Structured text in the SmPC, PIL and product label
	
	o Structured information on:
	  ▪ side effects of medicines to support easy identification of known and unknown side effects
	  ▪ clinical particulars, such as indications and contra-indications to facilitate clinical decision support systems used by prescribers
	
	o Support parallel distribution of medicines by simplifying the process of approving changes to the product information in the repackaged medicinal product
	
	o Support the move to online repositories of the latest product information and linkage to this data through use of 2D barcodes on packaging
	
	o Support translations of this information into other languages
	
	o Link the information to the IDMP product data to be stored in the PMS and SMS
	
	In order to achieve the requirements above further iterations of the ePI standard will be required to transform free text sections in structured data.

Data Standardisation Strategy | Product Information

ISO IDMP

Theme	Use cases

Product Information	• The ISO IDMP project helps to implement the EU SRS and SPOR SMS systems, improving the identification of active ingredients of medicinal products.
	
	• We received use cases to further expand the scope of the ISO IDMP project to include
	   o Structured information on the manufacturing site information of the active substances to support GXP processes and inspections
	
	   o Structured information to enable comparisons of manufacturer data held by (other) international authorities
	
	   o Captured veterinary specific requirements related to target species and antimicrobials data to align with veterinary union product database (UPD)
	
	To achieve this, adapting the current SPOR SMS & PMS systems to support the ISO IDMP specified substance group level 2 & 4 would be required. In addition, this would require that the associated FHIR message exchange format would need to be adapted to support the specified substance level 2 & 4.

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Data Standards Strategy | Product Information

GXP (Good practice quality guidelines and regulations)

Theme	Use cases
Product Information	o Development of standardized template for all inspections data (GXP, GCP, PMF) and others o Enable risk-based tracking for interactions between product quality and inspections of the manufacturing sites. In order to do this the quality information currently provided in PDF format within an eCTD submission needs to be structured using the specified substance level 2 part of the ISO IDMP standard o Use of specified substance level 4 of the ISO IDMP standard which captures the manufacturing sites and quality information. With these enhancement the full linkage of manufacturing sites of the active pharmaceutical ingredient (API) to the finished medicinal product manufacturing site would be made much easier In order to achieve this, a new project would need to be established in order to analyse the information and IT systems affected to determine the best approach for a data standard. Also, adapting the current SPOR SMS & PMS systems to support the ISO IDMP specified substance group level 2 & 4 would be required. The associated FHIR message exchange format would need to be adapted to support the specified substance level 2 & 4.

Data Standardisation Strategy | Product Information

Product Quality

Theme	Use cases
Product Information	o Usage of an international standard for the quality raw data to handle product quality assessments, as currently this data is collected in PDF format The adapting of the current SPOR SMS & PMS systems to support the ISO IDMP specified substance group 4 would support this requirement. Also, a project to identify and categorise the quality raw data needs would need to be established so that an appropriate data standard can be identified or developed

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Data Standardisation Strategy | Clinical Trials

Theme	Use cases
Clinical Trials	o Structured format of the clinical trial protocol design to enable comparative analysis of data across different trials o Development and incorporation of the clinical study design into the clinical trial protocol currently under development in ICH M11. The future ICH M11 standard should then be adopted used for capturing the protocol data o Enabling harmonised approach for data exchange between registries and the linking and comparing of different trials to each other. The adoption of CDISC (AdAM) standard for the collection of summary clinical trial patient data reports could help achieve this o The work to create a standard for clinical trial protocols and study design should be reviewed to see if it could be extended to include observation studies. This would then avoid the need to support two separate standards for capturing study design and study registration information. Experts from the network would need to be identified in order to define detailed requirements and provide input into the creation of such a data standard.

Data Standardisation Strategy | Data Quality

Theme	Use cases
Data Quality	o Data quality needs to be further developed in order to align datasets and find patterns that lead to improved treatments for patients. Hence data quality should be achieved by having standardisation in place. Aligned data enables high quality on data storage, access, extraction and analysis. The starting point will be to explore the specific requirements alongside reviewing relevant parts of the ISO 8000 set of standards.

Data Standardisation Strategy | Observational Studies / RWE

Theme	Use cases
Observational Studies / RWE	o Develop an internationally agreed common data model as currently each country and healthcare system have a unique approach to how the data is generated and fed into the pertinent database for research and analysis
	o Adopting RWE for registry studies, structuring of electronic health records facilitating re-use and sharing of data across countries instead of dealing with different formats/ different ways of recording data.
	o Have medical terminology in place that is translated into all EU languages (e.g. MedDRA). This would help the researchers and the public health domain as well as the development of IT tooling
	o A veterinary specific RWE data standard is needed in order to collect data on farm animals from farms and other sources.
	o Further structuring the ENCepp database and having links to associated risk management plans or risk minimisation data. Also implementing a studies registry would be useful

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Data Standards Strategy | Artificial Intelligence

Theme	Use cases
Artificial Intelligence	o Requirement scoping in terms of specific business use cases needs to be further followed up on and quantified. Moreover, expert involvement is required to investigate usage of AI in pharmaceuticals. o In addition, in the context of AI, standardisation is required not only for data but also for the procedural and ethical aspects. The specific set of standards to explore is the ISO/IEC JTC 1/SC 42. The development of these requirements should be further defined in the context of ongoing projects within the EMRN and can feed into future updates of the strategy document

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Data Standardisation Strategy | Scientific Memory

Theme	Use cases
Scientific Memory	o Recording of Actions, discussions and decisions in harmonised and systematic way across the full lifecycle of medicinal products is needed. This scientific memory would facilitate the recording and retrieving past decisions such as details on the degree of efficacy, acceptance of a single arm study, requests for a comparative trial, product name based search, active substance based search, indication of consultation by external experts nominated by the committee, indication of withdrawn products and many more This requirement should lead to a set of best practices for recording and structuring this type of data. Although the data to captured is specific to regulated medicinal products domain this type of activity can be facilitated by adapting parts of ISO 9001 Evidence based decision making to the process of recording this data.

Data Standardisation Strategy | mHealth (Mobile Health)

Theme	Use cases
MHealth	o Utilising data from personal health tracking devices during clinical trials, real world evidence and observational studies would substantially enhance the amount of data which could lead to better and more informed decisions. Hence, it would be worthwhile to implement a data standard that would enable the collection and use of data coming from mobile health (mHealth) devices for clinical trials and research For this topic an expert group should be formed in order to elaborate the requirements and subsequently lead to a project to bring this initiative further. The set of standards to be explored is the ISO TC215 (guidance on usage of devices in clinical trials for product authorisation).

Data Standardisation Strategy | Omics

Theme	Use cases
Omics	o Develop a standardized way of presenting product information (e.g. clinical particulars, contra-indications) in the area of Omics o Standardize the technical part (lab assessment communication) of the clinical trial protocol related to omics in order to capture information regarding sequence annotations, quantitative data or read alignment. For this purpose, a new set of omics standards needs to be developed and further scoping of requirements and standardisation of the common data format and associated terminologies is required

Data Standardisation Strategy | Environmental Risk Assessment

Theme	Use case
Environmental Risk Assessment	o Currently environmental risk assessments are received as unstructured PDF files which limits the use and reuse of the data contained in these document. In order to improve the usage of this data an expert group should be established in order to review the CDISC SDTM standard for data collection of risk assessment data.

Data Standardisation Strategy | Electronic Submissions

Theme	Use cases
Electronic Submissions	o eAF is intended to become a HL7 FHIR based standard for MAA and variations to existing authorisation. This scope should be reviewed to see if it would also meet the needs pre-application phase activities such as scientific advice and orphan medicine status. eAF could then be used to cover the whole lifecycle of medicines and act as a means for populating IRIS (including human and veterinary data) with all the metadata required to run regulatory processes supported in IRIS. o Compared to eCTD v3, eCTD v4 supports submission and reuse of PDF documents made in previous submissions. Nevertheless, the EMRN is in the process of transitioning towards the use of structured data which means that PDF files will become less common in the process of exchanging data. Therefore, other methods for data exchange such a FHIR messaging which would allow a more agile way of working should be considered. This would apply to both, the human and veterinary submissions.

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Thank you!

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Data Standards Strategy | Objectives per goal

Goals

- # 1 - Availability and accessibility of (human and veterinary medicines)

Objectives

1. Collaborate with stakeholders and SDOs to adapt or develop a new standard to deliver **improved human and veterinary product information** in **electronic format** (**ePI**).

2. Improve submission requirements to ensure that essential manufacturing information is accurate and submitted in a **format that is conducive to electronic receipt, storage and usage**.

3. Support **international harmonisation of data elements and terminology** to help enhance and facilitate **analysis of human and veterinary drug utilisation datasets**.

4. Support the **data collection and submission of product information once and used by many systems** within EMRN and internationally to facilitate data sharing and decision making.

5. Engage with HL7 SDO to organise and participate in FHIR Connectathons to **increase the maturity level of FHIR resources used by ISO IDMP implementation** and other regulatory use cases.

6. Collaborate with stakeholders and SDOs to extend **ISO IDMP** and the underlying FHIR messaging for **supporting Vet use cases** and Union Product Dictionary terminologies.

Data Standards Strategy | Objectives per goal

Goals

- # 1 - Availability and accessibility of (human and veterinary medicines)

- # 2 - Data analytics, digital tools, and digital transformation

Objectives

1. **Refine Electronic Health Records (HER), therapeutic area and terminology standards** to help generate high quality RWD/RWE datasets for analysis.

2. **Develop and promote use of international AI standards**, focusing on regulatory use cases that help augment or improve clinical research, regulatory review and pharmacovigilance practices.

3. **Establish an EU framework for data quality/representativeness across the range of regulatory decisions**. Collaborate with European and International stakeholders to define /adopt standard quality principles and metrics in prioritised key areas/data fields to foster trustworthiness and regulatory acceptability, as well as facilitate the creation of data quality frameworks within EMRN.

4. Develop/adapt standards or/and technical specifications to directly **access externally maintained veterinary data, metadata and evidences** and transform them in reliable, traceable, auditable, legal and ethical information to enhance decision making.

5. Develop/adapt **m-health related standards** for improving field trials, e.g. regulatory compliant 'virtual trials'.

6. Collaborate with SDOs, researchers and providers for **efficient high-quality RWE data collection on the farm level and on the individual 'animal patient' level for analysis**.

Data Standards Strategy | Objectives per goal

Goals

- # 1 - Availability and accessibility of (human and veterinary medicines)

- # 2 - Data analytics, digital tools, and digital transformation

- # 3 - Regulatory science and innovation

Objectives

1. Evaluate and **support efforts to implement new standards for the submission of regulatory data** (e.g., model-informed drug development, omics, and clinical outcomes assessment).

2. **Foster and promote use of standards** to help support clinical trial semantic interoperability and data exchange across the EMRN and its stakeholders.

3. **Develop, adopt or adapt existing standards to better align and structure regulatory submissions** to support review and analysis of rapidly evolving domains of research and innovation such as drug–device combinations, predictive toxicology and artificial intelligence.

4. Leverage efforts to **establish human and veterinary novel science and innovation platforms** between the EMA, the EMRN and academic research centres to inform data standards activities.

5. Engage with HL7 SDO and EMRN stakeholders to **adapt FHIR resources for use in the regulatory environment** for data exchange.

6. Engage with SDOs to develop/adapt standards to **address legislative compliance and adherence to international formats** as introduced by the VICH guidelines.

Data Standards Strategy | Objectives per goal

Goals

- # 1 - Availability and accessibility of (human and veterinary medicines)

- # 2 - Data analytics, digital tools, and digital transformation

- # 3 - Regulatory science and innovation

- # 4 - Antimicrobial resistance and other emerging health threats

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Data Standards Strategy | Objectives per goal

Goals

- # 1 - Availability and accessibility of (human and veterinary medicines)

- # 2 - Data analytics, digital tools, and digital transformation

- # 3 - Regulatory science and innovation

- # 4 - Antimicrobial resistance and other emerging health threats

- # 5 - Supply chain challenges

Objectives

1. Promote and support the creation of key ISO IDMP medicinal product and substance identifiers to **help identify and validate products** approved in the EMRNU and other regions.

2. Identify and align key medicinal product data elements and other information used **for cross-border information exchange** use cases such as prescription, and dispensation, international patient summaries.

3. **Leverage structured Chemistry, Manufacturing and Control (CMC) information** (e.g., facility location, production information, up-to-date view of the CMC processes) to help improve inspection and compliance efficiency.

4. Collaborate with international stakeholders to support **an electronic, interoperable system to better identify and mitigate drug shortages and risks associated** with pandemic or bioterrorism threats that impact public access and distribution.

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Data Standards Strategy | Objectives per goal

Goals

- # 1 - Availability and accessibility of (human and veterinary medicines)

- # 2 - Data analytics, digital tools, and digital transformation

- # 3 - Regulatory science and innovation

- # 4 - Antimicrobial resistance and other emerging health threats

- # 5 - Supply chain challenges

- # 6 - Sustainability of the EU network and operational excellence

Objectives

1. **Develop, implement, and maintain standards, global identifiers and terminologies** used for electronic human and veterinary regulatory submissions.

2. **Promote innovation and digitalisation** in pre-clinical and clinical trials by strengthening the EMRN adoption and use of standards.

3. Ensure **program activities and objectives are aligned and integrated into** the overall planning and execution of related **IT and other regulatory science initiatives**.

4. **Contribute to the Common European health data space** as set by the European Commission's strategy for data.

5. Collaborate within EMRN and other European/international stakeholders to initiate pilots to **provide feedback/demonstrate that existing or under development standards on particular areas of interest** are capable to support regulatory use cases within Europe and different jurisdictions.