Position Paper

Principles for the Implementation of ISO IDMP Standards for EudraVigilance and Development of a Road Map - Final, 6th Oct. 2014

Executive summary

The 2010 Pharmacovigilance legislation[i] and more particularly Article 57(2) of Regulation (EU) No 1235/2010, introduced new requirements for marketing authorisation holders (MAHs) to submit electronically to EMA information on all medicinal products for human use authorised in the European Union (EU). This was to be completed by 2nd July 2012, using xEVMPD, which was selected as an interim format pending approval of ISO IDMP standards. Compliance with the above proved to be a challenging, lengthy and costly exercise, and the original overall objective to improve pharmacovigilance reporting remains to be met.

As a next step, a significant update to comply with ISO IDMP standards is due to be completed by July 2016, as required by the Commission Implementing Regulation (EU) No 520/2012[ii]. Industry sees the implementation of ISO IDMP standards as an opportunity to apply consistency to the information that is shared across the network of EU competent authorities and facilitate industry electronic interactions with the agencies. Nevertheless, implementation of these standards continues to have a major impact on all stakeholders, requiring a significant investment in process revisions and technology enhancements (see Annex 1 for actual costs incurred and cost estimates ~ €70M total using a sample of 14 EFPIA companies). The financial and business impact of divergent standards and requirements should not be understated. At a time of budget reduction or constraint for many, stakeholders are experiencing significant financial risk and uncertainty with duplicative demands driving rework and inefficiency, which is causing escalating and uncontrolled expense). Therefore, it is critical for all stakeholders to collaboratively develop the Road Map for IDMP implementation, and more particularly agree on its scope and timing to ensure successful implementation by all parties.

The requirements to comply with ISO IDMP standards by July 1, 2016 should be part of a cohesive plan that is vital to managing the cost and avoiding rework of the data in the future. The IDMP implementation especially needs to meet the following objectives:

- Facilitate the pharmacovigilance activities of medicines regulatory agencies worldwide.
- Support operational efficiency at agencies and industry level.
- Support standardisation of data across agencies databases.
- Achieve stepwise implementation to provide realistic project milestones and manageable budgets.
- Prioritisation of implementation steps to meet EU legal requirements, while also considering continued alignment with global implementation.

To achieve the above, industry has conducted a systematic review of processes and systems that will potentially be impacted by the migration to ISO IDMP. These are presented in this document, which should serve as a framework for the development of the Implementation Road Map in the EU. Industry especially expects that the Road Map will be detailed in phases, steps, milestones and dates, covering at least the principles outlined in this document.

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I. Introduction

The adoption of the ISO IDMP standards in the EU will have a significant impact across many aspects of the regulatory environment, not just in the EU but in other regions as well. Thus, a well-founded coordinated program is required and industry is calling for collaboration to ensure a consistent and harmonised implementation of the Regulation in the EU and in alignment with the US.

More specifically, industry is seeking assurance that the implementation of ISO IDMP Standards will be developed in a way that fully supports the aims of the Pharmacovigilance legislation and avoids unnecessary duplication of data across regulatory systems used in the EU Network. Additionally, this should be achieved in partnership with non-EU Regulatory Agencies (in particular the FDA) for a widely harmonised approach to implementation.

Timely development of the Road Map and associated Implementation Guidelines across agencies are key elements to successful implementation of the standards, avoiding redundant work and costs, while meeting the objectives of the Pharmacovigilance legislation.

II. Expectations from ISO IDMP and legal basis

ISO IDMP was developed in response to a worldwide demand for internationally harmonised specifications for medicinal products, and is expected to achieve the following:

- Facilitate interoperability of systems used for the performance of pharmacovigilance activities.
- Avoid multiplication of data coding and entry.
- Facilitate the regulatory activities of agencies worldwide, including the life cycle management of medicinal products information.
- Ease the exchange of medicinal product information amongst regulatory authorities.

The legal basis for adopting ISO IDMP standards in the EU is provided for in the Commission Implementing Regulation 520/2012, where Articles 25 and 26 define the use of internationally agreed ‘terminology’, and ‘formats and standards’.

III. Considerations for overall ISO IDMP implementation

The EU Road Map for the development and implementation of ISO IDMP standards must address the following key principles:

- Gap analysis of xEVMPD vs ISO IDMP.
- Migration.
- Implementation plan.

In addition to the above, industry would like to make the following specific recommendations:

1. ***Common understanding of the overall vision and scope of IDMP implementation***: all stakeholders, i.e. EMA, NCAs and MAHs, must have a common understanding of the overall vision and scope. Consideration must be given to the impact of IDMP implementation on other initiatives and corresponding systems considering the EU Pharmacovigilance legislation requirements, Horizons 2020 and ISO DTS 19256 (Medicinal Product Dictionaries) as well as other projects such as:

a. ICSRs – the use/submission of IDMP data in the ICSR.
b. xEVMPD – the migration/submission of IDMP data and the adoption/implementation of controlled vocabularies.
c. Regulatory Submissions (eCTD/NeeS) – inclusion of IDMP components within Module 1.
d. EudraCT and Clinical Trial Portal and Database, as introduced by Articles 80 and 81 of Regulation (EU) No 536/2014[iii].
e. EudraGMDP.
f. Serialisation as introduced by Directive 2011/62/EU[iv] (Falsified Medicines Directive).

2. ***IDMP Implementation Group***: an IDMP Implementation Group should be established under the EU Telematics Governance structure, and be responsible for the development, maintenance and progress against the Road Map along with the communication of those decisions/changes. Building on existing collaboration (through the Article 57(2) Implementation Working Group), this new group should include the following members: EMA, NCAs, Industry and Software Vendors.

3. ***Scope of data to be included:*** Structured Substance Information (SSI) should remain out of scope, as it is not required to meet the objectives of the Pharmacovigilance legislation. This was included in the original agreement from March 2012 on the scope of data to be collected to support Article 57(2) - see extract from EMA/140899/2012 of 5th March 2012:

"… As a result of discussions, the Agency looked at how the mandatory scope could be reduced while ensuring that the public health goals of the legislation and patient safety were not compromised. This has resulted in a reduction in the number of data fields which are mandatory. The main differences between the requirements published in July 2011 and those published in March 2012 are the following:

- *the Agency will not require the following data sets to be submitted by July 2012:*
  - *structured substance information (SSI),*
  - *indication if the product is subject to additional monitoring,*
  - *location of the pharmacovigilance system master file,*
  - *description of packaging information;…"*

4. ***Adoption of a set of global controlled vocabularies***: this should incorporate:
   a. GINAS – Global Ingredient Archival System for the substances
   b. UCUM – Unified Code for Units of Measure for the units of measure
   c. EDQM Standard Terms - Route of Administration
   d. EDQM Standard Terms - Dosage Form
   e. MedDRA – For adverse events and indication

5. ***Development of an end-to-end process map and data flow***: an end-to-end process map and data flow across all of the systems should be developed to understand the various data inputs and data usage, and to assure the supplied data are consistent. This is critical for industry to understand as it has typically used independent systems (and processes) to deliver information to agencies for a specific need e.g. Pharmacovigilance Adverse Event Reporting, Regulatory Submissions, xEVMPD and others.

6. ***Clear definition of business value***: such definition should be based on the data currently exchanged between parties, and on the data quality and control methodology, with harmonised EMA/NCAs business practices.

7. ***IDMP information as component of the submission process***: the IDMP information should be a component of the submission process so that the information is submitted once and updated based on the approval process improving the data quality, currency and reducing the burden of additional parallel information exchange.

8. ***Staged implementation***: the implementation should be driven by success and experiences allowing for the processes and systems to mature and for the stakeholders to gain an understanding prior to any expanded rollout or requirements.

9. ***Clear documentation***: documentation with specific examples for implementers to capture/convert the data consistently should be developed. Systems and processes should be designed using extensive code lists and dictionaries to limit room for interpretation of data requirements.

10. ***Timelines***: reasonable timelines should be set for the adoption of the various components of the Road Map, knowing that software solutions and new business processes take time to go through the development/testing/implementation life cycles.

IV. Scope of transition from xEVMPD to IDMP

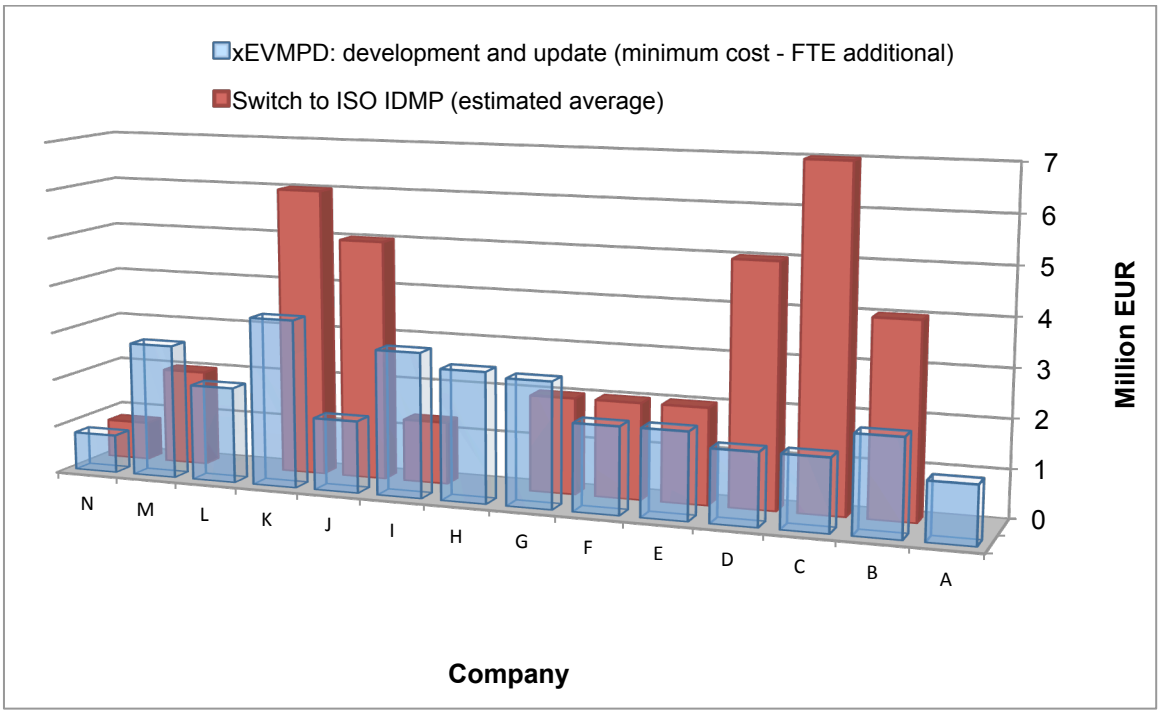
1. Migration of the existing xEVMPD data to IDMP format should occur with the same data scope as the existing content.
2. Implementation of the Controlled Vocabularies must occur consistently across the EU network, with clear ownership and maintenance processes.
3. The business value of the existing dataset must be demonstrated and it should be verified that the original overall objective to improve pharmacovigilance reporting has been met.

V. Conclusion and next steps

Industry looks forward to on-going dialogue with EMA as plans for development and implementation of the ISO IDMP standard unfold, and is available to respond to any questions in relation to this systematic analysis.

Annex 1: cost in Millions euros of the xEVMPD development and update, and estimate of the switch to ISO IDMP – Data provided by 14 EFPIA member companies

This chart illustrates the combined *actual* cost of XEVMPD across 14 companies **exceeded €28M**; cost of the ISO IDMP switch is conservatively forecasted to exceed **€38M** across these same companies. Therefore, a sampling of 14 EFPIA member companies indicates a combined expenditure of at least **~ €70M.**



[i] Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products (*Official Journal L 348, 31.12.2010, p. 1–16*)

[ii] Commission Implementing Regulation (EU) No 520/2012 on the performance of pharmacovigilance activities provided for in Regulation (EC) 726/2004 and Directive 2001/83/EC of the European Parliament and the Council (*Official Journal L 159, 20.06.2012, p. 5–25*)

[iii] Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (*Official Journal L 158, 27.05.2014, p. 1-76*)

[iv] Directive 2011/62/EU of the European Parliament and the Council of 8th June 2011 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products (*Official Journal L 174, 01.07.2011, p. 74-87*)