NOTES FROM A WORKSHOP ON THE IDENTIFICATION OF MEDICINAL PRODUCTS (IDMP)

11-12 September 2019

WHO, GENEVA

List of Participants

Brazil (ANVISA)

Monica da Luz Carvalho Soares

Canada (HEALTH CANADA)

Craig Anderson

EMA

Paolo Alcini

Francisco Peñaranda

IFPMA

Mümèn Gencoglu

Patrick Middag (Observer)

Vada Perkins (Observer)

Japan (PMDA)

Takashi Misu

Mariko Tsukuda

Morocco

Dilal Rarmili

Nigeria

Jennifer Ugochukwu Chukwumerije

Thailand

Chutamas Luangaroonchai

Kritsada Limpananont

UMC

Johanna Eriksson

Malin Fladvad

United States of America (FDA)

Mary Ann Slack

Ronald Fitzmartin

WHO

Raffaella Balocco

Emer Cooke

Antony Fake

Ayako Fukushima

Takahiro Goto

Noha Iessa

François X. Lery

Leticia Megias

Shanthi Pal

Michael Ward

Objectives and expected outcomes of the workshop

Emer Cooke, Head, Regulation of Medicines and other Health Technologies at WHO, opened the meeting and welcomed the participants. She introduced the meeting objectives which included a review of:

- the status of IDMP implementation and IDMP substance databases in selected regions/ countries, and
  differences and challenges in the IDMP implementation across various geographic regions and resource settings.

The expected outcome of the workshop:

- A clear articulation of the benefits and challenges of the global maintenance of PhPID
- Initial considerations for the necessary policy, processes, training and resources for scale-up in different geographic and resource settings
- Consensus to establish a working group and initiate the development of a plan for the global maintenance of PhPIDs
- Elements of a framework for further outreach and collaboration in the global implementation of the IDMP standards.

Ms Cooke noted that IDMP is meant to facilitate the global exchange of data for medicines and should be accessible for all countries.

Mary Ann Slack, Director, Office of Strategic Programs, CDER FDA, volunteered as chair for the meeting and Michael Ward, Coordinator Regulatory System Strengthening as co-chair. Malin Fladvad, WHODrug portfolio manager, was appointment rapporteur.

Introduction and recap of previous meeting

A short briefing of IDMP standard and usability was presented by the FDA, followed by a summary of the WHO proposal1, the context of global harmonisation, and the outcomes of the meeting in May 2018. The risk for disharmony in the implementation of IDMP at a global level was recognised, leading to possible local assignment for substance IDs, local controlled vocabularies and variations of PhPID algorithm. The benefits of adopting a proactive approach that would help address these

[1] The WHO proposal suggests that the Uppsala Monitoring Centre, UMC, will be responsible for the day-to-day operations of the global PhPIDs (validation/assignment and technical support) with the convening of an WHO appointed international working group of experts resembling the setup for the International Working Group on Drug Statistics Methodology (DSM). This DSM working group supports/oversees the work of the WHO Collaborating Centre in Oslo in assigning ATC (Anatomical Therapeutic Chemical) codes and Defined Daily Doses (DDD) to medicinal products. Pharmaceutical companies apply to the WHO CC in Oslo to have their products assigned an ATC and/or DDD. In analogy, UMC has already established processes for interactions with the Pharmaceutical Industry in the maintenance of WHODrug Global and has also over 40 years' experience in mapping of safety data from different regions and countries in the technical operations and maintenance of the WHO Global ICSR database, VigiBase.

challenges and achieve the goal of product and ingredient identification across regions were also acknowledged.

Status of IDMP implementation

Updates were provided by participants from US FDA, EMA/EU, Health Canada and PMDA on the status of implementation of IDMP and on the status of maintenance of the components of the IDMP.

The respective jurisdictions are at different stages and have different approaches in terms of regional implementation and it was evident that further work is required at a global level to ensure consistency in implementation of ISO standards forming the foundation for the PhPID. Especially, issues regarding pharmaceutical dose form standard, ISO 11239, need to be resolved. It was acknowledged that the success of global PhPID requires globally-recognised substance identifiers, ISO 11238. There is also concern on how to handle legacy data.

IDMP status update - FDA

The importance of IDMP for public health is driving the implementation at FDA, and key benefits are within safety surveillance and potentially to support mitigation of drug shortages. Unlike EU, IDMP is not a regulated standard and there is no set timetable. There is a roadmap of intention describing the plan forward. The current FDA approach is focused on marketed products only. There is a current challenge with implementation of the pharmaceutical dose form standard of IDMP and mapping assessment activities have been conducted. FDA-GSRS[2] is used to register unique substances and control substance data. There are approx. 180 000 substances records are available in the tool. In 2019 the EMA-FDA IDMP Collaboration Framework was launched, including collaboration on GSRS/EU-SRS

IDMP status update – EU/EMA

Implementation in EU is driven through the SPOR[3] initiative. The SPOR applies to both human and veterinary medicinal products. In EU IDMP is part of the regulation, and there is an agreed roadmap for implementation of the different domains which is revised on annual basis. Due to the relocation of the EMA agency, the progress is a little behind the scheduled time. Currently the member countries are focusing on validation of substance data. Mapping of existing data to a central repository represents a 'mini-WHO' exercise. Data quality is currently an issue, with differences seen between data sent to EMA and member states. There is a commitment to resolve this quality issue in future phases of IDMP implementation by integrating IDMP in the regulatory processes. EU has its own instance of the GSRS (EU-SRS).

[2] Open Source Global Substance Registration System (GSRS) has been developed and is available at https://tripod.nih.gov/ginas/#/

[3] SPOR is short for Substances Products Organisations and Referentials in the IDMP projects of the EMA. SPOR data services will act as the vehicle for implementation of ISO IDMP standards in the regulatory and the e-health world

IDMP status update – Health Canada

Health Canada does not have an overarching implementation plan for IDMP at this time. However, work is underway to develop a plan. In the meantime, work is also underway to ensure technical and policy structures are in place to support different aspects of IDMP. Particularly for patient safety and product labelling projects. For example, requiring IDMP compliant data with new structured product labelling and implementing aspects of IDMP together with E2B(R3)/ICSRs.

IDMP status update - PMDA

According to Takashi Misu, PMDA is currently considering how to comply with the ICH/E2B(R3). No plans for a regional substance ID.

Concluding remarks

Both Ron Fitzmartin, Sr Informatics Advisor, CBER FDA and EMA representatives emphasised that implementing a global set of standards such as the IDMP is a time-consuming process. They had a common view of 2022-23 when their respective organisation could be able to handle global PhPIDs assuming that the issues identified with, e.g., substance IDs and dosage forms are resolved. Francisco Penaranda, Head of Business Data & Analytics Department at EMA described the implementation of IDMP as "a marathon, not a sprint". The importance of working with industry was also noted.

IDMP in low and middle-income countries

The situations in Brazil, Morocco, Thailand and Nigeria were shared and it was evident that there are challenges in culture, awareness, buy-in from stakeholders and processes such as migration of legacy data and in transfer from document to data. Different use cases such as life cycle management, import, reimbursement, were mentioned. The representative from ANVISA, Brazil, Monica da Luz Carvalho Soares, Health Regulation Expert ANVISA stressed the attention and interest from PROADI (Program for the development of the Brazilian National Health System), a program of the Ministry of Health of Brazil, which drives the standardisation initiative in Brazil: moving from documents to data as part of international convergence and digital transformation of regulatory information. The FDA also underscored the value in a step-wise approach and the implementation of components of the IDMP.

The IDMP Frequently Asked Questions document developed by International Pharmaceutical Regulators Programme (IPRP) IDMP Working Group was discussed. Suggestions for additional details on implementation and practical examples were raised by the representatives from Brazil, Morocco, Nigeria and Thailand.

Plans for the IDMP substance database in respective countries

EMA and FDA are still cleaning the data in their substance registration systems (FDA-GSRS and EU-SRS) requiring a deep level of expertise to define, register and maintain substances in varying levels of specificity. The current list of known FDA registered substances is published and available for anyone's use on FDAs website.

GSRS system is an open source solution and hence available to all who wish to implement the system. Running a substance registration function would require deep substance knowledge as well as close coordination with other GSRS systems to avoid fragmentation of the system and fragmentation of the substance data. All that wish to implement the GSRS system should learn from what has been done already (e.g., FDA-GSRS, EU-SRS, WHO/UMC) and avoid a situation where every regulator would establish their own version.

A global substance ID is required to create Global PhPIDs. It might beneficial to have an independent entity to provide substance lookup and registration service (either directly or through pre-vetting and handing over to EU or FDA) to regulators who aren't ready to make such a big investment. Any organization maintaining a substance registration system should be part of the overarching IDMP governance to ensure we are all maintaining substances to the same level of granularity. There may be a need to look at dossier information to create global substance IDs and proprietary data needs to be protected. However, if accurate information is available in the supplementary protection certificate (SPC) after approval, there may not be a need to access trade secrets for approved products. The pre-market use cases may be more difficult to tackle on a global level due to trade secrets, commercial confidential information (CCI), and similar that may be different within different regions.

WHO proposed to form a working group to define best practices, on how to identify/validate new substances and the level of details needed for global substance registration. A separate group should define the objectives of and the expertise needed to form this working group.

Overarching objective for access to high quality WHO-UMC maintained PhPIDs (Global PhPIDs)

The objectives for a WHO-UMC maintained PhPIDs service were discussed. A proposal for a first phase of the service was drafted, including business case and operating requirements:

- Compelling use cases exist for WHO-UMC maintained PhPIDs
- WHO-UMC maintained PhPIDs will only be generated for authorized products
- WHO-UMC maintained PhPIDs use global substance IDs, dose forms, strength and reference strength
- All users (regulators and industry) are able to use and request substance IDs
- Users understand the different components of IDMP and their practical value
- Users need to be able to understand what product elements a PhPID describes (for example, #123456 = paracetamol 200mg, tablet)
- All users are able to use or map PhPIDs to global dose forms, strength and reference strength
- Users are able to identify WHO-UMC maintained PhPIDs

Additional critical requirements for governance of PhPID services

- The data needs to be of high quality
- Technical solutions are automated as far as possible to avoid requirements of staffing (at regulators)

The question of an appropriate governance framework should be re-evaluated closer to the timeframe when stakeholders are likely to be able to generate global PhPIDs.

PhPID for veterinary products

A question was raised regarding whether the PhPID generation and maintenance undertaking also include veterinary products. EMA is implementing IDMP for both the human and veterinary domain and would prefer an integrated system for generation of PhPID for both product types. The ISO standard for PhPID does not currently specify information about the type of product (i.e. Human or Veterinary) it applies to.

Use cases that drive global PhPIDs

UMC made a brief introduction on the need for harmonized drug information for Pharmacovigilance. Several use cases for PhPID were identified, whereupon the group decided to elaborate on benefits and hypothetical examples for a selected number:

- Pharmacovigilance including Signal detection, Medication Errors & Pharmacoepidemiological studies (benefit/risk assessments)
- Reimbursement and purchasing
    - Comparing for example price differences between countries
- Stock outs and shortages
    - Be able to identify comparable products to be used
- Cross border prescriptions
- Supporting information sharing in-between authorities (evaluation, approval etc)
    - Efficiently identify products with the same ingredients in drug submissions

In addition, the following use cases were identified:

- Identifying different medicinal product safety issues
    - Antibiotic resistance
    - Similar product names (but with different active substances)
- Environmental impact
    - To set limits for import based on how much of a particular chemical is used
- Health expenditure
    - To complement ATC/DDD
- Industries need to keep track of portfolio of products, what and where a product is approved/manufactured
- Inspections
- Market access
- Drug needs in neglected clinical areas
- Special access to nonmarketed drugs for practitioners treating patients with serious or life-threatening conditions when conventional therapies have failed, are unsuitable, or unavailable.
- Product Withdrawal

Training, promoting and awareness of IDMP to WHO Programme for International Drug Monitoring

Participants discussed how to engage more broadly with different stakeholders to find out what is needed with regard to training and promoting awareness. For example, is it possible to provide information of what investment is needed for each regulatory authority to start using IDMP, that is, 'to get in the game' and utilize IDMP? The following ideas were suggested on building awareness and promotion:

- Briefing at the Annual Meetings of the WHO Programme for International Drug Monitoring.
- Circulate information about webinars, e.g. FDA and EMA are broadcasting regularly
- Create a training video
- Add IDMP information in UMC training efforts
- Survey countries on additional questions/needs.

IPRP was suggested to be a good forum for promotion of IDMP, to raise awareness and make information accessible for both industry and regulatory agencies. Preferably, more countries should be represented in IPRP.

Actions arising and recommendations

- The group to have frequent meetings to update on progress and discuss implementation approaches. Next meeting should be within 6 months.
- Nature and participation of the group to be further refined, as discussions and progress towards IDMP implementation mature.
- The group to agree on next steps for PhPID, including possible pilot and business case for WHO-UMC maintained PhPID, to give the background and value of the initiative.
- Development of the PhPID service should follow the pace of the development and implementation of IDMP in a stepwise and pragmatic approach.
- Group to elaborate on the use cases for PhPID
- Investigate the need and feasibility of incorporating veterinary medicines into WHO-UMC maintained PhPID
- No efforts should be duplicated; interact with other groups working with IDMP (ISO, IPRP)
- A separate group should define the objective, expertise and membership needed to form a working group for creation and maintenance of global substance IDs
- Present update at IPRP meeting in October and discuss possible collaboration with ISO/WHO.
- Developed communication material including minutes to be published on IPRP homepage.