ICMRA Summit 2022

Dublin, Ireland, Tuesday 8th of November 2022

Opening Remarks
Participants were welcomed to Dublin and thanked for attending the first in-person ICMRA Summit since Rome 2019 due to the COVID-19 pandemic. Now that the COVID-19 pandemic has entered a new phase, participants were challenged to reflect on lessons learned to identify how best to prepare for future emergencies as a global network of medicines regulatory organisations.

Session 1 Challenging Our thinking on Pharmacovigilance
Chair: Australia (TGA)
Panel: South Africa (SAHPRA), Sweden (MPA), South Korea (MFDS), Saudi Arabia (SFDA) and UK (MHRA)

The Chair opened the session by highlighting the many ways in which COVID-19 changed global approaches to pharmacovigilance (PV) and how ICMRA became an important platform for sharing information concerning emerging safety signals in "real-time". Timely sharing of information helped to identify, confirm, and ensure an appropriate response to validated safety signals leading to greater confidence in regulatory decisions.

Opening Panel Presentations
SAHPRA shared their pre-COVID-19 PV experience in LMICs, noting a heavy reliance on paper-based reporting tools, low awareness of training in PV among key stakeholders, and limited collaboration on PV within national health systems and at regional level. Implementation of the AU 3S (Smart, Safety, Surveillance) Project aimed to address these issues with a view to improving collaboration, implementing digital health tools, and strengthening safety expertise and decision-making leading to improved safety across the lifecycle of priority products.

MPA highlighted spontaneous reports from consumers were approximately four times higher than healthcare professionals (HCPs). However, a greater proportion of reports from HCPs were linked to serious ADRs compared to reports from consumers. Spontaneous reporting, combined with the use of national health registries to evaluation potential safety signals, were important sources of information to inform public health and regulatory decision-making.

In response to COVID-19, MFDS extended their adverse event reporting systems to include emergency use COVID-19 products and enhanced post-evaluation safety monitoring using real world data. This enabled the provision of important safety information to clinicians in real time to inform prescribing and dispensing recommendations. Further information was provided on the medical record observation & assessment for drug safety common data model (MOA-CDM) used in Korea to facilitate active surveillance.

SFDA highlighted the importance of clear safety communication to proactively address mis- and disinformation. In addition to the development of a dedicated website continuously providing up-to-date communications, SFDA developed plain language videos communicating important safety information concerning the use of medicines specifically targeting groups with limited access to HCPs.

Challenges associated with monitoring safety information in particular populations were highlighted by MHRA, including the limited pre- and post-approval safety information to support regulatory

decision-making. The combination of spontaneous reporting systems capable of dealing with high volumes, combined with rapid evaluation of potential safety signals, formal epidemiological studies and global collaboration facilitated a global approach to PV during the pandemic. The need to extend ICMRA's vaccine PV model to include other public health issues was highlighted.

Main Panel Discussion Themes
Regular, timely and transparent communication was highlighted as critical to ensuring continued public trust and confidence in vaccine safety. When communicating on complicated issues, regulators should openly acknowledge limitations in our understanding, while at the same time emphasise the dynamics nature of evidence generation leading to public health recommendations.

Greater engagement across the entire healthcare system is critical, including HCP and National Immunization Technical Advisory Groups (NITAGs). This is especially important when there are perceived differences in advice concerning benefit-risk profiles.

Finally, early planning for organised data collection to support regulatory decision-making is critical, particularly for specific populations, in addition to rapid evidence generation and evaluation. There is a need to provide recommendations on based on evidence.

Key Consideration for ICMRA and PV Working Group:
- Critically review responses undertaken to date and identify actions to support future approaches to PV and information sharing.
- Ensure regulators take a people-focused approach and actively engage in open dialogue.
- Consider the value-add for new tools supporting communication (e.g., social media, videos etc.,), in addition to technologies such as AI to support rapid evaluation of safety signals.
- Develop and improve methodologies for ways of working together that support information exchange.
- Strengthen and enhance collaborations with stakeholders across the health system.
- Preparedness to combat hesitancy

Session 2 – Innovation and the Future Opportunities - Regulators working together
Co-Chair: Ireland (HPRA) and US (FDA)
Panel: Canada (HC), Brazil (ANVISA), EMA, US (FDA), Japan (PMDA) and Switzerland (Swissmedic)

The Co-Chairs highlighted the rapid pace of science-based technological and medicinal product innovation, and the importance for regulatory agencies to capitalise on potential opportunities to protect public health through effective regulation. Another important issue that requires consideration is the availability of appropriate development pathways to support the availability and access to innovative products.

Opening Panel Presentations
HC provided an overview of model-informed drug development (MIDD) to optimise clinical trial designs, population selection for clinical trials, and dosing recommendations particularly in hard-to-reach populations for practical or ethical reasons. Prior knowledge based on pre-clinical and clinical information, for example, contribute to the development of different types of models to inform drug development.

ANVISA discussed the use of paediatric extrapolation and guidelines to accelerate clinical drug development by waiving the need to conduct specific studies in children referring to ICH E11A.

Despite not having a specific guideline in place and limited technical capacities in ANVISA, a number of market authorisation applications (MAH) submitted to ANVISA incorporated paediatric extrapolation. The importance of upskilling reviewers to evaluate pharmacokinetic models and simulations to support MAHs was identified as critical.

EMA described their clinical evidence; vision 2030, highlighting that the research question should drive the selection of specific methodologies and types of supporting data collected, including real-world data (RWD) and other novel forms of evidence, to support decision making. The EMA also discussed DARWIN EU, increasing use of real-world evidence (RWE) studies to support regulatory decision-making, and how ICMRA provides an important platform to support collaboration, convergence, and development of best practices concerning the use of RWE.

To ensure the continued availability of quality medicines, FDA presented on their initiatives to support the development and adoption of advanced manufacturing technologies including the activities in ICH Q13. In addition to providing research funding, there are centre-specific initiatives aimed at developing regulatory frameworks and guidance documents, engagement with key stakeholders, and provision of opportunities for developers to access early regulatory advice programmes.

PMDA presented on the effectiveness of authorisation pathways to facilitate accelerated patient access to medicines. Breakthrough, PRIME and SAKIGAKE are all examples of expedited regulatory pathways supporting the accelerated evaluation of MAAs across different regions. To facilitate future preparedness, regulators should consider innovative technologies and methods for more expedited pathways, in addition to greater utilisation of collaborative procedures. Importantly, regulators must ensure compliance with approval conditions and initiate enhanced post-marketing safety surveillance following authorisation.

Swissmedic outlined their Swissmedic 4.0 initiative, which aims to collect practical experience and identify opportunities and risks of digital transformation. When evaluating potential digital transformations, Swissmedic 4.0 considers human, organisation/process and technological outcomes in parallel. Additional details of the application of AI to support PV activities was described, including the use of LiSA and TRICIA to automate literature reviews and aspects of adverse event reporting, respectively.

Main Panel Discussion Themes
The future application of IT-based tools, such as machine learning and AI, were highlighted as important areas for consideration, especially in the context of rare diseases where evidence is limited due to small populations and numbers of patients. Data analytics, patient-focused digital end points and modelling can help provide additional evidence to complement available pre-clinical and clinical data for rare diseases.

Another important consideration raised during discussions was the importance of data quality, standards, and interoperability. Poor quality data limits the translation of RWD into RWE, which are both complementary to traditional forms of evidence derived from appropriately designed

Finally, engagement with key external stakeholders, including the (bio)pharmaceutical industry and academia is critical. Ultimately, these are the main sites for innovation and regulators should engage at appropriate timepoints along the health product lifecycle to facilitate development and authorisation.

Key Consideration for ICMRA:

- Further investigation of the value-add and application of IT-based tools to support regulatory decision making with a particular focus on rare diseases
- How to best support and develop ICMRA as an important platform to facilitate information-sharing
- To identify key areas of innovation to allow ICMRA focus and share best practice. A number of participants highlighted the potential for collaboration in relation to AI and also expressed an interest in a cross-cutting approach related to rare diseases. A focus on orphan-designated neurology conditions ("neuro-orphans") was suggested to expedite clinical development with a modelling approach in close collaboration with interested agencies to further explore regulatory decision-making based on patient-generated data (RWD)
- Importance of human and cultural openness to change to realise the benefits of science-based innovation

Session 3 – Public Health Emergencies and Living with COVID-19
Chair: Canada (HC)
Panel: Denmark (DKMA), Colombia (INVIMA), Nigeria (NAFDAC), EMA, WHO

Keynote Address
Dr. Mike Ryan (WHO) expressed his sincere thanks for global regulatory efforts to ensure COVID-19 medicines and vaccines remain safe, effective and of sufficient quality, and for operating in such a rapid and transparent manner. Using a science-based approach to decision-making to maintain trust among key stakeholders was highlighted as critical, especially when faced with external political pressures. Ensuring safe, scalable, and equitable quality care is key to prepare for future global public health emergencies.

In addition to the need for developing better metrics to assess preparedness and systems, open, regular, and transparent communication was highlighted as a fundamental aspect for development. It was recommended that regulators develop more public-facing platforms to better communicate in plain language important health-related information to mitigate the effects of mis- and disinformation.

Opening Panel Presentations
DKMA discussed key successes Denmark and the European region experienced during the pandemic. Maintaining public trust through a strong commitment to transparent communication and collaboration with health system partners were highlighted as key successes. In the context of the Danish response, the application of IT systems to help mitigate shortages of medicines and medical devices was also important.

INVIMA described regulatory developments taking place during the pandemic for the Colombian agency. This included, among other things, reliance on Good Manufacturing Practices (GMP) certificates issued by PIC-S agencies. While there was reliance on the assessments of other agencies within the South American region, not all organisations' regulatory systems are equally able to support this.

NAFDAC highlighted challenges faced by African countries during the pandemic, including a lack of information and receipt of vaccines in a timely fashion, in addition to limited capabilities to perform adequate safety monitoring and testing. Limited digital connectivity was another issue impacting

transparency and regulatory activities. There was, however, strong reliance in the region and support from international partners concerning information sharing, supply chain monitoring and some PV activities.

EMA outlined regulatory flexibilities introduced to ensure continued supplies of safe and effective medicinal products in Europe, and efforts taken to provide regular trustworthy communications so that important safety information reaches the public. It was highlighted that perfect preparation does not exist, and there is a need to implement processes and procedures in an adaptable manner. Finally, when data is limited, the importance of information sharing and leveraging collective regulatory knowledge is vital to support decision-making.

WHO stressed that structural issues remain within the global regulatory network. Specifically, approximately 70% of the world's regulatory agencies do not have sufficient capabilities or the appropriate technical expertise to ensure quality regulatory processes. Access to quality medicines and health products requires an integrated approach with all stakeholders. The need to strengthen local regulatory authorities, while at the same time increasing reliance, is a priority for WHO.

Main Panel Discussion Themes
The importance of clear, transparent, and authentic communication was again highlighted as critical to the COVID-19 pandemic and important for future public health emergencies. The avoidance of overly technical language, acknowledgement of existing gaps in our knowledge and how those gaps will be filled, are central to effective communication to build trust.

Ensuring the health and wellbeing of staff and avoidance of burnout was another matter highlighted. Having adequate access to support systems is important, in addition to further investment to increase resources. The exceptional level of dedication and commitment to ensure the availability of safe and effective medicines demonstrated by agency staff is not sustainable.

Inequitable distribution of vaccines and other health products, in addition to inequalities in regulatory agencies were identified as areas requiring attention. Greater harmonisation, leading to increased levels of reliance and collaboration between global regulatory agencies, combined with capacity building are central in preparing for future health emergencies based on understanding their scientific foundation. ICMRA was highlighted as an important platform to support international harmonisation and information-sharing scientifically and to achieve consensus for mutual evaluation amongst regulatory agencies, especially for vaccines, medicines, and diagnostics.

Key Considerations for ICMRA
- How to enhance communications and engagement with stakeholders.
- How to address equitable access to needed preventative measures and treatments
- ICMRA is an important platform to leverage common learnings, but also address what will come next (layered emergencies).

Closing Remarks
Participants were thanked for their valuable contributions, and identification of ICMRA as an important platform to support continued dialogue, information-sharing and reliance between global regulatory agencies. The Chair thanked the HPRA for their excellent job in hosting and informed participants that ICMRA would reflect on how to develop and action key consideration identified during each session and closed the meeting.