20 December 2023
EMA/919710/2022
Data Analytics and Methods Task Force

HMA/EMA Big Data Stakeholder Forum 2023

Report of the HMA/EMA Big Data Stakeholder Forum - 4 December 2023

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Introduction

Understanding when to have confidence in novel technologies and in the evidence generated from Big Data will benefit public health by supporting medicines development, improving treatment outcomes and facilitating earlier patient access to innovative treatments.

As the journey towards data-driven medicines regulation accelerates, the fourth annual Big Data multi-stakeholder forum took place on 4 December 2023 at the EMA building in Amsterdam, enriched with virtual participation. It aimed to inspire stakeholders with opportunities for the future, discuss data-enabled opportunities to improve medicines development and regulatory decision-making, and, inform and strengthen collaboration with stakeholders and partners on the delivery of the data activities included the Network Strategy to 2025 (fourth update of the HMA-EMA Big Data Steering Group workplan).

The forum was opened by Emer Cooke (EMA Executive Director), Lars Bo Nielsen (HMA Management Group member and Director General of DKMA), Olga Solomon (Head of Unit Medical Products and innovation, DG SANTE, European Commission) and Marco Greco (President of The European Patients' Forum).

One hundred and sixty-five stakeholders participated in the Forum and many hundreds followed the broadcast of the event online.

This report offers a high-level summary of the forum presentations as well as highlights from the comments and discussion with stakeholders.

Session 1: Implementation of the HMA/EMA Big Data Task Force priority recommendations

This year marked the fourth year on the journey to realise the HMA/EMA vision of a data-driven regulatory system. The fourth BDSG workplan was published in July 2023 to continue to progress the activities launched in 2020 and to address new topics. An overview of 2023 deliverables and the new plan for 2023-2025 were presented. Significant progress continued in 2023 to enable the data transformation of the EU regulatory network and deliver the data activities of the European medicines agencies network strategy to 2025.

Session 2: Enabling the use and establishing the value of Real-World Evidence

Steady progress continues to enable the generation of Real-World Evidence (RWE) and its integration into EU regulatory and downstream decision-making .

DARWIN EU® celebrated its first birthday in early 2023 and promises to be instrumental in enabling the use of RWE. It increased access for the EU network to real-world data (RWD) sources, with twenty data partners either active or being onboarded. DARWIN EU® established standard analytical pipelines and codes and conducted several studies to support EMA scientific committees as well as ECDC, HTA bodies and payers. Learnings, not only from DARWIN EU® studies but also from other RWE pilots were published in 2023 in the report on the experience gained with regulator-led studies with RWE from September 2021 to February 2023. Complementary to this, to ensure high quality decision making in this rapidly developing environment, the Methodology Working Party is drafting a reflection paper on the use of RWD to generate RWE in non-interventional studies and is establishing a roadmap for the development of RWE guidance. Involvement of the regulatory and HTA networks in multi-stakeholders' regulatory science projects such as those in the MetReal cluster, ERAMET and INVENTS, will accelerate

the development of methodology, standards, use cases and framework(s) to assess credibility of novel approaches.

The EMA-HMA Catalogues of real world-data sources and non-interventional studies will increase the discoverability of data sources in Europe when they are rolled out to the public in quarter 1 of 2024. They will describe the RWD sources and studies through a set of collected metadata to help pharmaceutical companies and researchers identify and use such data when investigating the use, safety and effectiveness of medicines. Key functionalities of the catalogues were presented to the event's participants. To improve data quality in EU, the data quality framework for EU medicines regulation has been developed jointly with the Methodology Working Party and in close collaboration with TEHDAS Joint Action. It describes concepts applicable to all data sources used in medicine regulation across EU regulatory network. It will be published to stakeholders by the end of 2023 and a RWD deep dive annex is currently being developed for 2024.

After a reminder on the proposals for a European Health Data Space (EHDS), the 2-year HealthData@EU pilot was presented together with its use cases. The pilot sets out to learn about current user journey to data access and analysis and to test the principles of the proposed EHDS legislation for secondary use of healthcare data. One of the DARWIN EU® ongoing studies, to identify the risks of coagulation disorders in patient with Covid-19, is a use case for medicines regulators. Learnings so far have included variability in requirements and timelines for access to data across nodes/countries, variety of clinical coding systems and interpretation (i.e. requiring more time for creating standardized phenotypes in native data), the benefit of using a common data model, and opportunities and challenges of testing while building the technical infrastructure at the same time. Ultimately the EHDS has the potential to strengthen and accelerate the use of RWD and establish transparent and trustful collaboration.

Global progress in convergence with international partners on RWD continued in 2023 and contributes to establish further the value of RWE and enabling its use. Numerous initiatives are underway with public consultation on an ICH RWE Reflection Paper having taken place from July-September 2023, the consultation on ICH M14 Guideline development for post-approval safety studies using RWD expected in the new year, and with the re-purposing of the existing ICMRA COVID-19 RWE Working Group to focus on RWE in public health emergencies.

Front row comments included the views from stakeholders' representatives for payers, pharmaceutical industry, patients and healthcare professionals. Across stakeholders, the progress since the start of the BDSG four year ago was acknowledged, establishing a solid foundation to enable the use of RWE, improve data quality, set methodological guidance, convergence with international partners and piloting EHDS. For payers, RWE is useful for a variety of use cases to complement randomised clinical trials and DARWIN EU ® may provide a structure to access relevant data on a European level and facilitate collaboration between countries. Industry called for more shared information on DARWIN EU® studies that are expected to increase in number significantly in 2024, in particular to allow industry to be prepared in case of consultation on complex studies and called for standards to be developed on data quality for RWD. For patients, clear communication to patient communities is essential and DARWIN EU ® use cases can be far reaching, e.g. to help optimise the use of drug already on the market. For healthcare professionals, it will be important to ensure access to tools and data across Europe to release the potential of RWE for all stakeholders.

Session 3: Patient Experience Data (PED): realising the potential of PED in EU medicines regulation.

Reinforcing patient relevance in evidence generation is a key priority in the EMA's Network Strategy and the realisation of a data-driven regulatory network. Despite much progress in the EU in recent years, more efforts are needed to systematically include Patient Experience Data (PED) in medicines development and regulation.

Several regulatory initiatives are currently ongoing within the EU network. Anchored in the EU Network Strategy's delivery plan and CHMP's workplan, the drafting of a reflection paper on the best EU approach to define, generate, collect and analyse PED, and the exploration on how to improve transparency in the Assessment Report will be progressed in 2024. Complementary to this, the EMA action plan on PED will aim at establishing an overall EU strategy and approach, improving EU regulatory guidance and convergence with international partners, improving data quality and methodologies, realising opportunities with RWE and digitalisation, and strengthening training and expertise.

For EU regulators, PED is an important piece of the spectrum of evidence supporting medicines' development and evaluation, and such data are complementary to other data and relevant at different stages of the EU regulatory decision-making process, from clinical trial design and benefit/risk evaluation to pharmacovigilance and risk minimisation. EU regulators need reliable and representative PED with high quality standards that meet regulatory decision-making requirements. To optimise the use of PED, more work is needed especially on definitions, data collection methods, data quality and completeness and methodologies applied to PED. Such opportunities were discussed during the event. EU regulators also encouraged companies to liaise early with regulators through Scientific Advice or Qualification, to discuss best way to generate and collect PED, and have a case-by-case discussion on their specific development plans. Collaboration with patients' organisations will be critical to advance this work as well as with downstream stakeholders (HTAs, payers, healthcare providers).

Patients want their data to be used to support the development and use of safe, effective and lifesaving medicines. The BDSG workplan already includes key opportunities to leverage the HMA/EMA tools to enhance the use of PED for regulatory decision-making. The HMA EMA catalogues of data sources & non-interventional studies will be launching early in 2024 and they present an opportunity to make PED more visible and findable. The EU data quality framework for medicines regulation will include a deep dive on RWD in 2024 and is an opportunity to apply it to PED and contributes to its drafting in the foreseen public consultation. A research programme on establishing the value of PED is currently under discussion and will be discussed in the future with stakeholders. Patients' organisations are encouraged to participate actively in shaping HMA-EMA actions.

Front row comments included the views from additional stakeholders' representatives for the pharmaceutical industry, patients, healthcare professionals and academia. Patients recognised the lack of harmonised standards to capture PED and the methodological shortcomings making it difficult to meet regulatory requirements. Cultural and training gaps in patient organizations also exists and more effort on awareness and training are needed. Collaborare, a EURORDIS project, aims to allow patients to collect and share Major Contribution to Patient Care (MCPC) elements for each rare disease. It will help to understand how innovative solutions could therefore support regulatory decision-making (its use is currently piloted with EMA scientific committee for orphans medicines). In the paediatric domain, PED reporting tools should be user friendly and compatible with the daily life of patients. Patients and parents should be involved in the conception and design of PED tools. Existing frameworks can help to design PED with the involvement of patients and caregivers (e.g. PFMD [1]PED). Healthcare professionals

[1] https://patientfocusedmedicine.org/patient-experience-data-project/

are strongly engaged in advancement of patient care with the help of digitalization. Protecting patient data is a key consideration and adequate training of healthcare professionals is crucial as part of their role to educate and train patients in collecting and sharing PED. Academia also supported progress on PED as mentioned in the context of oncologic research, highlighting the importance of Quality of Life (QoL) questionnaires developed with EORTC to collect data on Patient Reported Outcomes following initial treatment and long-term evaluation of survivorship. For Industry, PED is critical. To accelerate progresses, the role of Scientific Advice and more broadly a clear pathway for engagement are important, with a clear roadmap and timelines. Formal guidance, best practices and multistakeholder collaboration are needed.

Session 4: Novel technologies and methods driving changes in evidence generation in medicines regulation

This session explored some of the novel technologies and methods for evidence generation that could impact EU medicines regulation now and in the future. Front row comments after each presentation in this session included the views from additional stakeholders' representatives for patients, healthcare professionals and industry.

The AI Workplan to 2028 has been developed in collaboration with the network and stakeholders to manage the increasing complexity in the area of AI and the need to collaborate and coordinate activities across the EU network to maximise the value extracted from AI. It covers activities across four domains (guidance, policy and product support; tools and technology; collaboration and change management; experimentation) and notably the finalization of the first EU reflection paper on AI. The front row comments highlighted the need for patients to build trust in AI via a collaborative approach, the opportunity of AI for healthcare professionals to reduce inequalities and for industry to increase efficiencies and complement traditional data collection methods.

Quantum computing is at the brink of becoming a technology that could impact drug development in the future. Using the laws of quantum mechanics for information processing, quantum computing can solve certain problems faster than classical computing and brings significant potential benefits for drug discovery and modelling biological functions or biochemical systems. The front row comments highlighted the promises for healthcare professional and for industry to increase efficiency and identify the best treatments for patients. Industry also noted the security challenges inherent to these super computers. For patients, this new technology was not considered a reality in the near future, but they need to be brought along this journey and digital literacy and digital inclusion should be kept in mind.

As example of advances in digital technologies to enable collection of Patient Experience Data, the Collaborare initiative led by EURORDIS was presented in more detail. It will enhance collection of patient-reported outcomes (PROs), patient preferences (PPs), and patient engagement (PE) data through community collaboration with the aim to identify and share Major Contribution to Patient Care (MCPC) in rare diseases. An AI language model will facilitate the initial capture and analysis of patient experience data, particularly in the context of orphan medicines. The front row comments recognised the value of such initiative thanks to its simplicity and accessibility and called for regulators and developers to consider such tools in the future.

The use of external data, such as digital twins and external controls, can accelerate further evidence generation. AI will enable the generation of digital twins with synthetic data. The use of such methods will facilitate the sharing of sensitive data across organisations and EU regulators, allow to generate synthetic control arms from available cohort studies and/or RWD, simulate studies, and interpolate/extrapolate. The front row comments highlighted across stakeholders the potential to complement traditional methods, to reduce bias and the lack of diversity in clinical trials, to address

ethical challenges and benefit rare diseases. It is the time to start talking about this in multistakeholder collaboration forum to advance this field, to start developing regulatory guidance and establish validity, credibility and value for regulators to support their decision-making.

Session 5: Keynotes from featured speakers

Today's world is moving rapidly, and new technologies are emerging. Information manipulation is becoming a risk, and reliable sources of information are critical for an informed and engaged society and a trusted regulatory system. This session looked further ahead and discussed how data analysis can supercharge evidence-based decision making and how data can be used for a better-informed society.

Science and technology are converging. Scientific breakthroughs in medicine extended our lives, and HealthTech innovations changed the way we deliver health and care, but we need to go one step further as 80% of our health are driven by the conditions in which we are born, grow up and aged. Current health systems are reactive care systems, waiting for people to get sick. They need to transform into proactive, predictive, ultimately preventive health systems that keep people healthy. The AI4HealthyCities launched by the Novartis Foundation intends to use the power of data, AI and public private partnerships to decipher underlying drivers for cardiovascular health and health inequities and drive actions and policies to improve the heart health of population-level. EU contains 11 of the 25 globally most innovative countries. We need to seize the opportunity of living in a data- and tech-driven era to transform health systems, generalize data-driven decision making for planning and policy making in health and use the power of data, technology and AI to strengthen drivers of population health and narrow health inequities. The front row comments with the event chairs and participants also saw in this initiative links to the future European Health Data Space (EHDS) that holds promise to unleash the potential of data regarding access and research for better health, policies and innovation.

Misinformation, particularly when it is presented as being scientific has been proved to increase vaccine hesitancy. Since 2010 the vaccine confidence project has been monitoring public confidence in immunisation programmes by building an information surveillance system for early detection of public concerns around vaccines. By collecting and analysis structured and unstructured data around vaccines from various sources (surveys, social listening, media monitoring and crowdsourcing), it allows early response and engagement with the public to ensure sustained confidence in vaccines and other health interventions. The IRIS academic research group has also been created to develop the practical tools/methodologies that could be used by governments or NGOs to tackle misinformation. To prepare to tackle misinformation, building a Social Listening System is essential: Prepare, Listen, Understand and Engage. Crowdsourcing for understanding misinformation online appears to be a useful mechanism, to mitigate the challenges of traditional surveys or social listening methods and see how misinformation spreads on private social networks. By detecting early a new, emerging narrative in private spaces, a more efficient social listening in public spaces can then be implemented. AI will democratise disinformation and allow the average person to create and spread the messages as they wish. AI is also a threat to traditional search engines (and social media) and could replace search engine's place as a go-to source for information, disrupting the existing information landscape and creating a completely new information environment. Generative AI models will soon become a new target for those who seek to shape the information debate on a topic e.g. vaccine confidence or climate change. Access to key social platforms' data also causes erosion of trust in government, science and big tech companies. AI is here to stay, so we need to be faster with data collection and analysis (e.g social listening/crowdsourcing) and be prepared (e.g. build social listening systems before a crisis). The front row comments with the event chairs and participants also discussed the recommendation of

debunking misinformation, the need to create trust and help the 'hesitant' users with providing them reliable of information.

Closing remarks

The event was closed by the event co-chairs, Jesper Kjaer (DKMA, BDSG co-chair) and Peter Arlett (EMA, BDSG co-chair) and participants were informed about the future engagement opportunities in 2024.