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Data Analytics and Methods Task Force

EMA/HMA Big Data Stakeholder Forum 2022

Report of the EMA/HMA Big Data Stakeholder Forum - 1 December 2022

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Introduction

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

EMA, HMA and the EU regulatory network continue their journey towards the vision for data-driven medicines regulation through delivery of the European medicines agencies network strategy to 2025. Active dialogue with partners and stakeholders remains key to this work.

Informed by the feedbacks from experts and stakeholders, the second HMA-EMA Big Data Steering Group workplan 2021-2023 was published in August 2021.

In this context, the third annual Big Data multi-stakeholder forum took place on 1 December 2022 and aimed to:

- inform stakeholders on the delivery of data activities of the Network Strategy 2025,
- strengthen engagement and collaboration with stakeholders,
- look through a medicines regulatory lens to the European Health Data Space (EHDS).

The forum was opened and introduced by Emer Cooke (EMA Executive Director), Karl Broich (HMA Management Group Chairperson and President of BfArM), Olga Solomon (Head of Unit "Medicines: policy, authorisation and monitoring", European Commission) and Marco Greco (President of The European Patients' Forum).

Three hundred and seventy stakeholders participated in the Forum.

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

Session 1: Report on implementation of the HMA-EMA Big Data Task Force priority recommendations

The third BDSG workplan was published in September 2022 to continue to progress the activities launched in 2020 and to address new topics. An overview of 2022 deliverables and the new plan for 2022-2025 were presented. Significant progress continued in 2022 to enable the data transformation of the EU regulatory network and the delivery of these activities remains on track as per the Big Data Steering Group (BDSG) 2022 report (europa.eu).

'At the core of a successful MA dossier is excellent clinical evidence.' **Peter Arlett, EMA.**

Session 2: Big Data - DARWIN EU ® and data quality

This session provided feedback on DARWIN EU ® experiences after its first year, its use cases including Health Technology Assessment (HTA) bodies and Payer use cases, and the launch of the 1st EU data quality framework for medicines regulation.

Progress continued in 2022 for the establishment of DARWIN EU ® culminating with the launch of the first four studies (to support PRAC, COMP and CHMP) and the selection of the first 10 data partners that will provide access to ~26 million active patients to the EU regulatory network to generate RWE. After acceptance of the study protocol, fast delivery of study results is anticipated and many requests for future research questions have already been received by EMA. Finally, DARWIN EU ® is

participating to the EHDS2 pilot starting in 2023 with its EMA use case on natural history of coagulopathy (blood clotting) related events in COVID-19 patients and risk factors.

'European HTA collaboration on RWD is crucial to identify and access appropriate data source, promote good quality and avoid duplication of effort. Many uses cases for RWD exist.' **Niklas Hedberg, TLV [Health Technology Assessment bodies].**

'Payers' use cases for DARWIN EU ® are mostly in orphan drugs, advanced therapy medicinal products and oncology... also of interest for HTA and Regulators.' **Wim Goettsch, Zorginstituut Nederland [Payers].**

Built in collaboration with TEHDAS and stakeholders, the first draft EU Data Quality Framework for medicine regulation was launched for public consultation in 2022 and provides general definitions and considerations, applicable to a wide range of data sources for the purpose of characterising and assessing data quality for decision-making.

The main feedback from the public consultation related to the scope and applicability of the data quality framework, opportunities for international collaboration, harmonization on terminologies and better definition of maturity models. Next year, consideration on RWD quality will be explored.

'TEHDAS and EU medicines regulatory data quality frameworks are compatible... collaboration with EMA on the EHDS data quality and utility label should be next.' **Enrique Bernal Delgado [TEHDAS].**

'Industry welcomes the first EU data quality framework… more steps to maximise its utility and applicability are needed.' **Lisa Hampson, EFPIA [Pharmaceutical industry].**

'The EU data quality framework can help increase data quality in disease registries... It can already be used when developing electronic health record databases.' **Aldo Pietro Maggioni, ANMCO [Healthcare professionals].**

'Data quality is very important for rare disease and this framework is a big opportunity for this area…specific data quality recommendations for rare disease should be established.' **George Paliouras, Duchenne Data Foundation [Patients].**

Session 3: Big Data - data discoverability, skills, processes and capability

This session presented the progress on the EU Real World metadata list, the good practice guide and the catalogues of data sources and studies, on the work on Artificial Intelligence in medicines regulation and on the Clinical Trial Raw Data analysis pilot.

To prepare stakeholders in anticipation of the go-live of the real world data and observational study catalogues in 2023, EMA published the metadata list for real-world data sources and studies and released for public consultation the Good Practice Guide for the use of real-world metadata. Comments received focussed on the catalogue maintenance and content validation, interoperability with other catalogues (e.g., DARWIN EU ®, EDHEN), interlink with the data quality framework, scope of the data source catalogue, the importance of data source accessibility, the need for clarifications and definitions and proposals for additional data fields for specific metadata.

'Healthcare data is a complex ecosystem… This is a gold mine we are not taking advantage from yet… We need governance to coordinate efforts and mitigate inequalities

in collecting data and generating RWE.' **Rosa Giuliani, ESMO [Healthcare professionals].**

'ENCePP expertise can be leverage… collaboration with other metadata catalogues is key to build a sustainable catalogue.' **Rosa Gini, ARS Toscana [ENCePP].**

'This is important work for researchers in the EU... Collaboration with other EU initiatives such as EHDS and HealthyCloud, are critical for the future of the EMA catalogues… Incentives for data holders should be considered to encourage data collection.' **Irene Kesisoglou, Sciensano [Research organisation].**

'Testing with all stakeholders including patients and healthcare professionals will be very useful to ensure the catalogues are searchable, downloadable and the best sustainable processes to collect and maintain the catalogues are established...' **Gianmario Candore, EFPIA [Pharmaceutical industry].**

'Discoverability of data sources and studies is key to strengthen the medicines regulatory process, especially for value added medicines' **Kelly H. Zou, Medicines for Europe [Pharmaceutical industry].**

Following the Joint HMA/EMA Workshop on Artificial Intelligence in Medicines Regulation in 2021, the EU regulatory network has progressed several activities to develop a framework to assess and validate AI, to support the development of guidelines, as well as to build partnerships with academic, research centres and international partners.

The expertise of the EU network is being strengthen with the new Methodology Working Party and the European specialised expert community on methodology. The drafting of a reflection paper on AI in medicines regulation has been initiated and will cover regulatory aspects of AI/ML tools in anticipation of a possible future EMA guideline. Academic partners are welcome to approach the EU regulatory network for collaboration.

'Transparency in AI is very relevant, and we need to work together, including with international partners, for a good regulation on AI… AI using devices are emerging more and more.' **Andre Dekker, Maastricht University [Academia].**

'The scope of the EU network work on AI is important and should provide guiding principles for developing AI in medicines regulations while leveraging existing expertise'. **Thomas Brookland, EFPIA [Pharmaceutical industry].**

'AI needs data to produce models and we need to encourage the creation of open data sources…Training bias and protection against cyber-attack are also very relevant in the field of AI… Patients need training and patient organisations can play a role to support data collection and improve quality'. **Julian Isla, Dravet Syndrome European Federation [Patients].**

'Use of AI has been focusing up to now on diagnosis, but we need to progress its use for clinical validation, e.g. prevention of severe adverse events during clinical trial.' **Aldo Pietro Maggioni, ANMCO [Healthcare professionals].**

The CHMP raw data pilot was launched in 2022 to clarify the benefits and practicalities of accessing and analysing individual patient data in initial Marketing Authorisation Applications (iMAAs) and post-authorisation applications.

Different resourcing scenarios will be explored, and the Danish Medicines Agency (DKMA) has been selected as the EMA contractor to support the pilot's execution and conduct individual patient data analyses.

A data protection impact assessment has been conducted and it was clarified that Policy 0043 is applicable to the raw data pilot, but data will be redacted in consultation with the relevant MAHs. Stakeholder engagement remains important for this pilot with the establishment of the Network Advisory Group on Raw Data (AGRD) and Industry Focus Group on Raw Data (IFGRD), and the creation of various guidances to support participants. An interim pilot report is expected in Q3 2023.

'Involvement of patients and their feedback have been translated into the work of EMA... The use of raw data to assess drug is a huge step forward… Building capacity and knowledge sharing in civil society should not be overlooked.' **Angela Bradshaw, Alzheimer Europe [Patients].**

'It is the right time for the EU network to pilot analysis of raw data for decision-making… Industry is pleased with EMA collaboration on the pilot… Data privacy remains essential.' **Hans Ulrich Burger, Roche [Pharmaceutical industry].**

'EMA has chosen the right approach to engage with stakeholders… Harmonisation across international regulatory authorities is needed to establish the minimum requirements to submit raw data.' **Prafulla Girase, Alexion [SME].**

Session 4: Big Data - data governance, international and veterinary

This session heard from the key actors of the European Health Data Space (EHDS), including the European Commission, TEHDAS Joint Action and a Health Data Hub (HDH). EHDS will work to set out rules, common standards, infrastructures and a governance framework for the use of electronic health data for healthcare, research, innovation, policy making and regulatory activities.

Helping Members States and the Commission in developing and promoting concepts for sharing of data in secondary use for purposes in the context of the EHDS, TEHDAS has surveyed various countries across EU to analyse their national data governance models and presented in the forum some of their findings. Generally, there are positive views on the impact and added value of the EHDS for secondary use of health data, and political will to join. However, countries note that there is work needed to clarify the governance aspects of EHDS and consider diversity in current national governance structures. Communication with all stakeholders, including citizens, will be critical to ensure equal benefit for all countries and stakeholders, transparency and build trust.

Also informing the development of the EHDS, the HDH is leading the European consortium to build a first version of the EHDS2 and test concrete cross-border use cases with 17 partners across 9 countries. This EHDS2 pilot will cover important pieces of the overall EHDS user journey. It will build the IT infrastructure connecting the data platforms and EU central services in a network allowing information exchange, develop a standardised descriptive metadata catalogue and provide guidelines for data standards (for semantic interoperability, data quality and data transfer security).

'EHDS development is positive but digital identification of healthcare professionals and sharing of medical dossiers should also be considered… Burden on healthcare professionals should be avoided.' **Ilaria Passarani, PGEU [Healthcare professionals].**

'The EHDS has been awaited and will create new roles for patients and patients' organisations… Pitfalls from the GDPR regulation should be avoided and anonymised

data should be shared without consent.' **Julian Isla, Dravet Syndrome European Federation [Patients].**

'EHDS will help unleash the potential of big data... A greater role for data curators should be considered, as they can also enhance quality of data.' **Michael Bierl, EUCOPE [SME].**

The session then provided a status on implementation of the Data Standardisation Strategy for medicinal products data, healthcare and study data, safety and risk management data and submissions data.

Participants to the forum were next offered a view on an international collaboration initiative in the area of Pharmaceutical Quality Knowledge Management System (PQ KMS). It aims to reduce regulatory complexity, standardize and harmonize structured electronic data for regulatory submission and standards in regulatory review, assessment and inspection. Moving from unstructured data in PDFs to structured machine readable manufacturing/CMC data submitted using cloud-based systems promises to provide opportunities for advanced analytics and machine learning approaches, which to date have been underutilised in manufacturing and CMC, and it will significantly increase the efficiency of the regulatory decision-making.

Another international collaboration initiative was presented during the forum. Building on the collaborations on observational studies initiated during the COVID-19 pandemic, regulators identified during ICMRA workshop on RWE in 2022, four areas for future regulatory RWD and RWE international collaboration: harmonisation of terminologies for RWD and RWE, regulatory convergence on RWD and RWE guidance and best practice, readiness to address public health challenges and emerging health threats, and transparency.

Finally, this session concluded with presentation of feedback of the second Veterinary Big Data Stakeholder Forum that aimed to identify and prioritize a list of initiatives to feed into the Veterinary Big Data work plan for the coming years. Since the last forum, awareness on Big Data in the veterinary domain has increased and a coalition of willing has been established. Cooperation with stakeholders should continue to establish data-driven and evidence-based decision-making practices underpinning innovation in the Veterinary Medicines Regulation domain for animal and public health.

Session 5: View to the future

This session provided an overview of EU research and innovation activities on Big Data & RWE and upcoming funding opportunities. This covered the areas of personalised medicines, rare diseases, infectious diseases preparedness, Covid-19 response, and European infrastructures. The European Commission has put a lot of efforts from the last 12 years to support research in the EU via FP7, Horizon 2020, Horizon Europe and Innovative Medicines Initiative Europe's partnership for health.

The last initiative HORIZON-HLTH-2022-TOOL-11-02 (New methods for the effective use of real-world data and/or synthetic data in regulatory decision-making and/or in health technology assessment) is of particular relevance for the current activities of the European Health Data Space, BDSG and DARWIN EU ®.

To continue to prepare for the future, this session concluded with a horizon scanning for big data topics, presenting the early signs of important developments for medicines and public health. Ultimately this will help to initiate the adaptation of the EU regulatory system, foster high-quality development, and ensure innovations reach patients.

'As patients need to remain involved, building knowledge and skills is important to get their engagement…patients organisation are a multiplier of knowledge and capacity.' **Kaisa Immonen, EPF [Patients].**

'Different stakeholders do horizon scanning from their own perspectives…. Considering various levels such as processes, methods, tools… Next needs will be for Alzheimer disease…We need also to prepare data for historical, background, epidemiological datasets where therapies will soon come.' **Niklas Hedberg, TLV [HTA].**

'Harmonisation of legislations should not be overlooked...Horizon scanning needs to consider the growing importance and impact of digital devices, also in creating the needed infrastructures for the EHDS, while acknowledging the differences between the pharmaceutical industry and the variety of the medical device industry'. **Giedre Kvedaraviciene, COCIR [Tech-Medical Devices industry].**