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Summary report of the biannual Big Data Steering Group and industry stakeholders meeting

26 May 2023 – co-chaired by Jesper Kjaer (DKMA) and Peter Arlett (EMA), MS Teams

1. Welcome and opening remarks

The Co-chairs of Big Data Steering Group (BDSG) opened the meeting and welcomed participants representing the BDSG and pharmaceutical industry associations of ACRO, AESGP, AnimalhealthEurope, GIRP, EFPIA, EUCOPE, EuropaBio and Europharm SMC.

Objectives of this forum were to:

- Have open dialogue and hear industry's perspective on big data topics;
- Inform industry stakeholders on key progress concerning the BDSG workplan delivery.

As part of the opening remarks, Fia Westerholm (EMA) provided a short update on the ongoing review of the Network data governance. This activity involved a review of the BDSG and Network Data Board mandates which clarified the scope of these two groups, their stakeholder engagement model and composition. Pharmaceutical industry will be engaged in dedicated fora by both groups based on their workplans. The mandates have been approved by Heads of Medicines Agencies (HMA) and are pending the EMA Management Board approval in June. The revised mandates will be published on the EMA website in June/July 2023.

Jesper Kjaer (DKMA) briefed meeting participants on the annual update of the BDSG workplan to be completed and published by the end of the Summer. This update will contain new work items concerning stakeholder engagement and change management and a summary of such activities was presented to industry associations.

2. Big Data priority recommendations

2.1. DARWIN EU®

Andrej Segec (EMA) gave a short introductory summary on the DARWIN EU® network, including the onboarding of ten data partners and scientific studies conducted in 2022 as part of Phase I of the DARWIN EU® establishment. Further information is available on the DARWIN EU® website.

Participants were also reminded about the approach for consulting/informing industry on studies to be performed through DARWIN EU®:

- EMA will **consult** concerned MAHs for complex or very complex studies investigating the use, safety or effectiveness of one or several substances. Industry will be invited to provide comments on the study protocol (consolidated feedback across MAHs, if possible) and via the assessment report on the study results.
- For off-the-shelf (OTS) or routine repeated (RR) studies investigating the use, safety or effectiveness of one or several substances, EMA will **inform** industry using the existing processes such as the assessment report, committee agenda and minutes, and publication in the EU PAS Register. These studies use standardised analytics and have shorter timelines. In this context EMA initiated a consultation with industry stakeholders on the DARWIN EU® catalogue of standard data analyses. Study protocols (once accepted) and study reports (once completed and reviewed by EMA and relevant committees) are made available via EU PAS Register.

Consultation on the catalogue of standard data analyses for OTS/RR studies

Prof. Daniel Prieto-Alhambra (DARWIN EU® Coordination Centre) presented on the standardised analytics for RWE studies in DARWIN EU®, including the rationale and benefits of the chosen approach.

This catalogue is publicly available on the DARWIN EU® website and will be updated quarterly (e.g. following consultations or new use cases incorporation). Industry was invited to submit their comments on the catalogue of standard data analyses for the OTS/RR studies by email to andrej.segec@ema.europa.eu. The consultation is open until 30 June 2023.

EFPIA expressed their interest to participate in the consultation and provide consolidated comments by the given deadline.

Participants were informed that a workshop on RWE methodologies and heterogeneity of data results will take place in Q4 2023. This will provide a further opportunity to discuss standardised analytics for RWE generation.

Engagement with HTAs/Payers

Juan Jose Abellan (EMA) provided a short summary on the DARWIN EU® interaction with HTAs/Payers. A workshop was held in October 2022 to better understand how DARWIN EU® can support decision making for HTAs and Payers including identification of potential use cases. Two studies on the natural history of multiple myeloma and non-small lung cancer treated with immunotherapies were agreed to be piloted subject to the feasibility assessment. The interaction with HTAs/Payers is coordinated via their representatives at the DARWIN EU® Advisory Board.

Peter Arlett (EMA) complemented that although still on a learning journey, EMA and EU regulatory network saw value on leveraging DARWIN EU® and the RWE strategy for the benefit of decision making and bodies such as HTAs and Payers. The dialogue, in this respect, will continue and intensify over the coming months.

Industry associations asked for clarification on the measures taken to ensure adequate quality of RWD used in studies and Juan Jose Abellan (EMA) explained that DARWIN EU® uses a comprehensive qualitative assessment based on Khan's data quality framework (DQF). This will be complemented by

the first version of the EU Data Quality Framework (final version to be published in July), which encompasses principles from several data quality frameworks including Khan's DQF.

In relation to the data sources selection for individual studies, industry asked for greater visibility on how DARWIN EU® evaluates representativeness and reliability of selected data sources. This would help industry to understand how to interpret study results in the context of the limitations of the data source.

Real-world evidence studies coordinated by EMA to support regulatory decisions

Stefanie Prilla (EMA) introduced a report drafted by EMA to take stock of the experience gained to date in conducting RWD studies to support the EU regulatory decision-making. The report covers the period from September 2021 to February 2023 and considers three existing pathways available to EMA for RWE generation: studies conducted in-house, studies conducted via DARWIN EU® and studies commissioned via the Agency's research framework contracts.

This review was conducted to:

- Understand the needs for RWE by EU decision makers, the ability and capacity of the current EMA-RWE framework to respond to these needs and the usefulness of the RWE provided.
- Understand the suitability of available RWD sources and pathways, and the methodological challenges of data collection, study design and reporting.
- Review the process for receiving study requests, proactively offering and conducting RWE studies and identify opportunities for improvements.

Overall, the review showed that the current RWE generation framework with its three evidence generation pathways is able to address a broad range of research questions and help support decision-making in a variety of regulatory contexts and procedures. Still, a number of studies were not feasible especially when the conditions were not identified and/or medicines of interest were not used in the primary care setting, or in case of rare diseases and short procedural timelines. This is expected to change in the future with the capacity and agility of DARWIN EU® expanding over the coming years.

This report also presents learnings and recommendations to further enable the use of RWE and support EU network decision-making. These recommendations will be considered by the Big Data Steering Group and the DARWIN EU® Advisory Board.

The draft report is currently under consultation within the EU network and should be finalised by the end of June 2023 when the main findings will be published. Furthermore, a multi-stakeholder workshop on RWD quality and experience in use of RWE for regulatory decision making will take place on 26-27 June 2023 and offer an additional opportunity to discuss this report in more detail.

2.2. Data quality & representativeness

Ana Cochino (EMA) updated the meeting participants on the progress with the Data Quality Framework including the real-world data use case following its public consultation in Q4 last year:

- The framework has been updated to incorporate feedback received during the public consultation and is undergoing internal review before the consultation/communication with the Network. The final document is expected to be published in July 2023.

- As part of the multi-stakeholder workshop on RWD quality and experience in use of RWE for regulatory decision, a half day on 26 June will be dedicated to address the data quality topic through the sessions listed below:
  - Development of the Data Quality Framework – status update and next steps;
  - Use cases: approach for assessing and improving data quality;
  - Systems and processes underpinning real-world data;
  - Data quality metrics for real-world data;
  - Data quality in the context of a regulatory/research question.
- The discussions and output of the workshop will contribute to the development of the RWD chapter of the Data Quality Framework. The draft RWD chapter will be released for public consultation in Q3 2023.

EFPIA enquired about opportunities for industry's active participation in the workshop to possibly demonstrate a use case on how industry tried to implement the initial Data Quality Framework including sharing its challenges and solutions to overcome those challenges. EMA welcomed this suggestion and will liaise with EFPIA to incorporate this request in the workshop agenda.

2.3. International initiatives

Kelly Plueschke (EMA) gave an update on the ICH Reflection Paper – "*International harmonisation of real-world evidence terminology, and convergence of general principles regarding planning and reporting of studies using real-world data, with a focus on effectiveness of medicines*" - that EMA has developed in collaboration with Health Canada and FDA following the July 2022 ICMRA statement on international collaboration to enable RWE for regulatory decision-making. The ICH reflection paper underwent review by the ICH Management Committee, which agreed on the proposal to develop two guidelines on:

- RWD/RWE terminology, metadata and assessment principles; and
- RWD/RWE protocol & report format and study transparency.

The Reflection Paper includes an Annex that lists the large number of already existing regulatory guidance that will require synergy seeking when developing the proposed new ICH guidelines.

In June 2023, the paper will be presented to the ICH Assembly to seek support for public consultation. If agreed, this consultation will comprise various engagement activities involving multiple stakeholders.

Catherine Cohet (EMA) presented on the ICH M14 guideline - "*General principles on planning and designing pharmacoepidemiological studies that utilize RWD for safety assessment of a medicine*" highlighting that:

- The main scope is on safety studies, focusing on protocol development;
- The work is well under way, with the guideline establishment targeted in January 2025;
- Very shortly the draft guideline will be circulated for the internal ICH party consultation including industry members, and public consultation is planned to start in Q3 2023.

New RWE guidance development work (regulatory and non-regulatory) progresses at a fast speed and high volume, therefore there is a need to leverage the momentum and explore synergies and collaboration opportunities from a European but also a global perspective.

In response to a question as to how this international work feeds into the BDSG activities, it was explained that the BDSG workplan has a dedicated workstream on international initiatives aiming to ensure that European developments harmonise with global initiatives on big data use in regulatory decision making.

3. Wrap up and conclusions

The BDSG co-chairs thanked the meeting attendees for their participation and contribution to this meeting. The various multi-stakeholder workshops planned for this year will allow plenty of opportunity to progress the discussions held during today's meeting.

EFPIA expressed their appreciation to the BDSG for their collaborative approach on big data activities and willingness to consider industry's input on the DARWIN EU® standardised analytics for OTS/RR studies, request for more visibility on assessment of selected data sources for studies via DARWIN EU® and active collaboration in the RWD quality and experience in use of RWE for regulatory decision-making workshop in June 2023.