11 December 2023
EMA/238242/2023
European Medicines Agency

# Minutes – ninth DARWIN EU® Advisory Board meeting

Wednesday 24 May 2023 14:30 – 16:30 CET, virtual meeting

Co-Chairs: Emer Cooke (EMA) and Karl Broich (HMA)

| Item | Preliminary draft agenda | Name | Action | Mins |
|---|---|---|---|---|
| 1. | Adoption of draft agenda and minutes from the last meeting (6 February 2023) | All | For adoption | 10’ |
| 2. | Adoption of revised mandate | All | For adoption | 5’ |
| 3. | Update on DARWIN EU®<br>• Including call for data partners Phase II<br>• Phase I studies | Andrej Segec (EMA), Juanjo Abellan (EMA) | For information | 20’ |
| 4. | Ongoing and shortlisted studies | Andrej Segec (EMA) | For information | 15’ |
| 5. | RWE experience report & roundtable on establishment of DARWIN EU® | Stefanie Prilla (EMA), Andrej Segec (EMA), All | For information/ consultation | 30’ |
| 6. | Consultation on catalogue of standard data analyses | Juanjo Abellan (EMA) | For consultation | 15’ |
| 7. | Tour de Table | All | | 5’ |
| 8. | AOB<br>• Information items<br>○ Multi-stakeholder RWE and DQ workshop on 26 – 27 June | All | | |

| Role | Name |
|---|---|
| Present | Emer Cooke (EMA), Aurora Di Filippo (AIFA, IT), Elizabeth Vroom (UPPMD), Jesper Kjaer (DKMA, DK), Katharina Schneider (BfArM, DE), Lucie Moreau (HDH, FR), Magali Boers (LHD, LU), Markus Kalliola (SITRA, FI), Niklas Hedberg (TLV, SE), sara Rafael Almeida (EC), Sari Palojoki (ECDC), Wim Goettsch (ZINL, NL), Aldo Maggioni (ESC), Almath Spooner (EFPIA, EuropaBio, EUCOPE), Brian Bradbury (Amgen), Peter Arlett (EMA), Patrice Verpillat (EMA), Stefanie Prilla (EMA), Andrej Segec (EMA), Juan Jose Abellan (EMA), Maria Clara Restrepo-Mendez (EMA). |
| Apologies | Karl Broich (HMA, BfArM, DE), Claudia Furtado (INFARMED, PT), Hugues Malonne (FAGG-AFMPS, BE), Mahmoud Zureik (ANSM, FR), Johanna Seppanen (THL, FI). |
| Minutes | Sophie Groeneveld (EMA). |

Emer Cooke (EMA) opened the meeting and welcomed members to the ninth DARWIN EU® Advisory Board meeting. Due to technical difficulties, Karl Broich (HMA) was unable to join the meeting.

## 1. Adoption of draft agenda and minutes from the last meeting (6 February 2023)

The draft agenda as adopted without amendments. The minutes from the last meeting on 6 February 2023 were adopted and will be published on the EMA DARWIN EU® webpage.

## 2. Adoption of revised mandate

The revised mandate was circulated after the meeting on 6 February for members' review and comments. No comments were received during the consultation.

A question was raised on the two-year term indicated in the mandate, and whether there is an official process in place to determine when a member has served two years, and whether/how this member is replaced. It was clarified that the two-year period is extendable and will be reflected in the revised mandate before publication. Members were advised to inform the secretariat in case of issues with their memberships or nominations.

Subject to comments that will be addressed offline on the replacement mechanisms and appointing authorities, the revised mandate was adopted. The EMA management board will be informed at the upcoming June meeting. The revised mandate will be published on EMA DARWIN EU® webpage.

## 3. Update on DARWIN EU®

Andrej Segec (EMA) presented the update. A number of milestones have been achieved since February 2023. Phase II of the DARWIN EU® contract is in progress, with timely completion of deliverables and milestones. EMA is progressing and focusing on the study conduct and onboarding of new data partners in Phase II, with an anticipated total of 16 studies, and 10 additional data partners. The Data Protection Impact Assessment (DPIA) update is in progress and expected to be delivered in Q3 2023. The board was informed of the news announcements and the LinkedIn Interview on Real World Evidence in Medicine Regulation on 20 April 2023. Further updates include the launch of the DARWIN EU® Coordination Centre website in March 2023 with details on the network, studies and analytics, as well as the open call for expression of interest in becoming a DARWIN EU® data partner.

A summary of the results from the open call was presented by Juan Jose Abellan (EMA). As of 1 May 2023, 66 expressions of interests were received from a mix of EU and non-EU data sources and containing data from a variety of healthcare settings. It was clarified that the criteria for prioritisation of data partners includes (in the second order) the frequency of requested study topics e.g. research questions on oncology, which can inform the selection of data partners. The open call for data partners is open-ended, meaning that data holders can apply at any point. However, the list of interested data partners will be reviewed at least twice a year by the CC and EMA (e.g. 30 April and 31 October 2023). Periodically, EMA may re-advertise the open call for expression of interest for the next phase of onboarding.

A summary of the results of the first three completed studies was presented, as well as their assessment and impact on regulatory decision-making. The first three study reports are published in the EU PAS Register (EUPAS50800, EUPAS50789 and EUPAS103381). In terms of next steps, EMA will be selecting Phase II data partners and continue progressing on the conduct of Phase II studies. EMA will publish a report on the experience with Real World Evidence (RWE) studies (see agenda topic 5). A consultation on the catalogue of standard data analyses is ongoing with the Methodologies Working Party (MWP) and Industry (see agenda topic 6 for more information). A multi-stakeholder workshop on Real World Evidence and data quality is planned for 26 and 27 June 2023.

A further discussion took place on the selection of data partners for individual studies, and their fitness-for-purpose assessment. It was clarified that the selection is based on feasibility assessment and the availability of data to answer all the research objectives, with 5-6 data sources selected per study. The fitness-for-purpose assessment, to support the interpretation of the results, is anticipated to be included in each study at the study-protocol stage. Finally, the drug utilisation study on antibiotics is expected to be repeated in the future in additional data partners and/or adding a number of new antibiotics.

# 4. Ongoing and shortlisted studies

A number of RWE studies initiated in phase II of the DARWIN EU® contract were presented to the board in confidence for information. These studies range from complex to Off-the-Shelf studies, for a number of stakeholders including EMA scientific committees as well as ECDC, HTA/Payers and EHDS. A further shortlist of studies, planned for the remainder of Phase II, was also presented, noting that these may or may not be initiated pending their feasibility and overall priority. It was clarified that as soon as the study protocol (for any study) is accepted, it will be published in the EU PAS register.

Brian Bradbury representing the industry commented on a study focusing on treatment patterns, asking whether adjustments for confounding and bias are incorporated in these analyses. It was clarified that Off-the-Shelf studies are typically descriptive studies and will not contain adjustments, although they may contain sensitivity analyses. Finally, it was clarified that it is the intention to make the analytical codes used in the studies available to the public, via GitHub.

# 5. RWE experience report & roundtable on establishment of DARWIN EU®

Stefanie Prilla (EMA) presented an overview of the results from the report on the experience gained by EMA with regulator-led studies from September 2021 to February 2023. An overview of the ongoing RWE pilots was presented with various committees and SAWP, as well as pilot studies planned for HTA/Payers and ECDC. At EMA, RWE studies can be conducted using three main pathways: 1. Using the healthcare data sources available to EMA in house, 2. Via DARWIN EU®, and 3. by research organisations included in the Agency's framework contracts. Overall, 61 research topics were considered during the reporting period, resulting in 30 studies that were initiated, of which 27 studies were completed. For these,

feedback was received in 18 cases on the usefulness of the studies and 12 responders indicated that the results were considered supportive for the assessment.

The majority of the research topics emerged in the context of scientific assessments by PRAC and PDCO, followed by COMP and SAWP. An overview of the studies conducted via DARWIN EU® was presented. From study protocol until final report, the process for conducting the study took a median of 131 days. Data sources from 8 different European countries were used in year 1 studies, with at least 5 data sources per study. A number of recommendations derived from this review were presented:

- Need for wider access to additional, more diverse and complementary data sources, including additional European countries.
- Explore the possibility for early identification of RWE study needs and to accelerate RWE generation.
- Interaction with RWE sponsors (especially via the RWE liaison groups and EMA product team/RWE community) is essential and should be continued and intensified.
- Education and knowledge tools are needed, linking to the Big Data Steering Group's pharmacoepidemiology curriculum.
- Make available information on data provenance, quality and completeness (fit-for-purpose databases) to help interpretation of study findings.
- Promote the availability of RWE framework and related processes.
- Trigger systematic reflections of RWE needs and further streamline processes.

**Post meeting note**: the full report is now available on the EMA website: real-world-evidence-framework-support-eu-regulatory-decision-making-report-experience-gained_.pdf (europa.eu)

Emer Cooke (EMA) opened the floor for reflections from the board on the first year of establishment. Reflections from the Advisory Board members included endorsement from industry perspective, on the importance of clarity for selection of data sources in the context of their limitations and fitness for purpose in particular protocols and studies to help interpret the study findings.

It was clarified that the speed at which a study in DARWIN EU® is conducted is dependent on the type of use case and the urgency (e.g. safety issue). In 2022, data partners were only onboarded towards the end of the year and first analytical pipelines were being developed, which had an impact on the duration of the studies. Over time, with new data sources onboarded and standardised analytics, the ambition is to conduct studies in a matter of weeks or few months.

The board noted that methods and means for communication of results to various stakeholders will be important (e.g. communicating the results of the pilot study for HTA/Payers). Peter Arlett (EMA), on behalf of EMA, expressed commitment to intensifying the dialogue between HTA and Payers' associations. Further discussions will be held on how to optimise the communication links and payers'/HTA use cases with the increase in capacity of DARWIN EU® studies in the coming years.

# 6. Consultation on catalogue of standard data analyses

The catalogue of standard analyses consultation was introduced by Juan Jose Abellan (EMA). This catalogue consists of analytical pipelines developed/under development to address common research questions using Real World Data (RWD). The goal is to be able to use these standard (pre-defined) packages to run RWD studies in a matter of weeks, subject to institutional approvals. A first version of the catalogue is available on the DARWIN EU® Coordination Centre website: Standardised Analytics (darwin-eu.org). Quarterly updates of the catalogue are foreseen. The catalogue is currently under consultation with the MWP and will start industry consultation on 26 May 2023.

Members of the Advisory Board were also invited to comment. Comments can be provided in writing, via email, until end of June 2023, to the EMA secretariat. The board welcomed the opportunity for consultation.

## 7. Tour de table

None.

## 8. AOB

Building on the experience of the use of Real World Evidence for regulatory purpose and the conclusions of the previous activities around data standardisation, metadata, data quality and DARWIN EU®, EMA is organising a multi-stakeholder workshop on 26-27 June 2023: Multi-stakeholder workshop on Real World Data (RWD) quality and experience in use of Real World Evidence (RWE) for regulatory decision-making | European Medicines Agency (europa.eu). Advisory Board members were invited to participate face-to-face or virtually.

Emer Cooke (EMA) welcomed the progress on DARWIN EU®, thanked the Advisory Board members for their participation, and closed the meeting.

**Topics for future meetings:** Benefits analysis, repurposing, role of DARWIN EU® in the international RWE landscape

**Next meeting:** September 2023 TBA