6 February 2023
EMA/757688/2022
European Medicines Agency

Minutes – Seventh DARWIN EU® Advisory Board meeting

Thursday 8 September 2022 15:00 – 17:00 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 July 2022)	All	For adoption	10’
2.	Update on DARWIN EU®	Andrej Segec (EMA) and Sabine Brosch (EMA)	For information	10’
3.	Criteria for prioritisation of studies beyond Year 2	Juan Jose Abellan (EMA)	For consultation	20’
4.	Process for consulting/informing industry	Andrej Segec (EMA)	For consultation	20’
5.	EHDS2 pilot – link to DARWIN EU® • EMA use case	Malek Bentayeb (HDH), Mario Jendrossek (HDH), and Xavier Kurz (EMA)	For discussion	30’
6.	Tour de Table	All		
7.	AOB • Information items ○ Big Data Steering Group workplan 2022-25 and news announcement ○ 3rd Big Data Stakeholder Forum on 1 December 2022 ○ Multistakeholder workshop on Patient experience data in medicines development and regulatory decision-making – 21 September 2022	All		10’

Role	Name
Present	Katharina Schneider (BfArM, DE), Almath Spooner (EuropaBio, EFPIA, EUCOPE), Sari Palojoki (ECDC), Claudia Furtado (INFARMED, PT), Aurora Di Filippo (AIFA, IT), Niklas Hedberg (TLV, SE), Magali Boers (LHD, LX), Malek Bentayeb (HDH, FR), Markus Kalliola (SITRA, FI), Hugues Malonne (FAGG, BE), Wim Goettsch (ZINL, NL), Elizabeth Vroom (UPPMD), Brian Bradbury (AMGEN), Mario Jendrossek (HDH, FR), Xavier Kurz (EMA), Sabine Brosch (EMA), Andrej Segec (EMA), Maria Clara Restrepo-Mendez (EMA), Juan Jose Abellan (EMA)
Apologies	Jesper Kjaer (DKMA, DK), Sara Rafeal Almeida (EC), Mahmoud Zureik (ANSM, FR), Johanna Seppanen (THL, FI), Aldo Maggioni (ESC), Peter Arlett (EMA)
Minutes and admin support	Sophie Groeneveld (EMA)

Emer Cooke (EMA) and Karl Broich (Bfarm) welcomed the Advisory Board members and opened the meeting.

1. Adoption of draft agenda and minutes from the last meeting (6 July 2022)

The agenda was adopted with no changes. The minutes from the last meeting on 6 July 2022 were adopted and will be published on the DARWIN EU® webpage.

2. Update on DARWIN EU®

Andrej Segec (EMA) began the update on DARWIN EU® with the completion and acceptance of milestone 1 and milestone 2 deliverables, and the activation of Phase II of the DARWIN EU® contract. Notable deliverables include templates for study conduct (e.g. study outline, protocol and report; and code development), establishment of the scientific panel, template for data use agreement and the draft catalogue of standard data analyses.

Sabine Brosch (EMA), the data protection officer of EMA, presented the learnings following the finalisation of the Data Protection Impact Assessment (DPIA). The DPIA is an important step in the establishment of DARWIN EU® due to the nature of the research based on health data. The completion of DPIA minimises data protection risks during the collaboration between stakeholders with different interests, duties, rights, and roles. The use of data within DARWIN EU® extends its reach across and potentially beyond EEA, which is included among data protection considerations. Technology and organisational aspects of the DARWIN EU® Coordination Centre were also investigated. The DPIA, completed in August 2022, follows the preliminary DPIA performed during the tender in 2021, and addresses all processing activities known as part of the establishment. A review of the DPIA is planned for January 2023, as well as further updates of the DPIA as DARWIN EU® establishment progresses. The learnings from the DPIA include:

- Data protection by default and design should be a core element of any new project
- Rights to data protection and privacy are central to all processing activities
- Understand what type of personal data are processed at each step end-to-end
- Clearly define the actors involved and their roles and responsibilities

- Understand where your data goes – processor to sub-processor(s) - ensure compliance with transfer of personal data to third countries (international transfers)
- Systematically analyse, identify and minimise the data protection risks
- Be transparent towards data subjects – provide confidence that personal data are safe.

Andrej Segec continued with an update on the studies progress. Two off-the-shelf studies have been initiated so far. The first study is a disease epidemiology study, the second study is a drug utilisation study. The third study will be a drug utilisation study and will be initiated in the coming weeks. A fourth study is under discussion.

The onboarding of data partners is progressing well, with finalisation of onboarding to be expected by end of September/October. Following the completion of onboarding an EMA news announcement will follow. Following the completion of first RWE studies provided by DARWIN EU®, another news announcement is expected which will share the results of the studies and their impact on decision making as well as their benefits and accessibility in the EU PAS register.

In discussion, it was clarified that during the creation of the templates for the study protocol and study report, the output of the initiative HARmonized Protocol Template to Enhance Reproducibility (HARPER) has been considered. It was also clarified that the Data Use Agreement (DUA) has a number of clauses for the use of data, confidentiality, data sharing, obligations of the roles etc. The document is anticipated to be made public at a later stage in the establishment. Several Advisory Board members expressed interest in obtaining more information on the DPIA (e.g. data flows, legal background etc.), most of which will be shared at the dedicated webinar. Further clarifications on the DPIA were made regarding the use of fully anonymised data: it is the intention to receive anonymised and aggregated results from data partners. In the operational phase, the CC may also consider using pseudonymised data which will be assessed via a revised DPIA.

3. Criteria for prioritisation of studies beyond year 2

Juan Jose Abellan (EMA) presented the criteria for prioritisation of studies beyond year 2, starting with a summary of the three different pathways EMA has at its disposal to obtain RWE (EMA analysis using in-house accessible healthcare databases, funded studies via the framework contracts, and DARWIN EU®). Focusing on DARWIN EU® studies only, the capacity is expected to increase over time reaching nearly 150 studies annually. The proposed criteria for prioritisation will be applied in situations where the demand exceeds the capacity of DARWIN EU®.

<u>The primary criteria for selection of studies are:</u>

- Feasibility and timelines for obtaining results (e.g. need for secondary care data)
- Public health impact
    - Unmet medical need
    - Size of exposure
- Chronological order

<u>Secondary criterion for selection is:</u>

- Methodological advances

Emer Cooke (EMA) opened the discussion with the advisory board. Members commented that from a reimbursement perspective, a criterion was proposed when the product is (to be) conditionally approved by EMA, to support the generation of complementary evidence. Another criterion proposed was the need

for joint effort across borders – multi-national/EU-wide context. In the context of rare diseases, from a payers' perspective, a similar criterion was proposed as the need for multi-national network to perform a study which could not be completed nationally. Under methodological advances, looking into Patient Reported Outcomes and Quality of Life data to support payers' decision making was also proposed and endorsed by the patient representative. From a NCA perspective, under public health impact, it was proposed to prioritise studies with direct impact on risks for populations, for example evaluating serious adverse drug reactions, serious diseases with high mortality or hospitalisation rates.

In discussion, it was also clarified that multi-national studies are at the core of DARWIN EU® - and has proved especially important for decision making in the context of rare diseases. EMA will update the list of criteria and present the final list to the Advisory Board at a future meeting **(action EMA).** Emer Cooke thanked the members for their contributions.

4. Process for consulting/informing industry

Andrej Segec (EMA) presented the approach for consulting/informing industry on studies performed via DARWIN EU®. The objectives of the consultation were to identify in which scenarios industry should be informed or consulted and at which time point(s) during the study conduct. The approach is driven by transparency and should make use of the already established processes, such as the publication of committee minutes and agendas, EPARs, and the study protocols and reports in the EU PAS Register.

The proposal is to consult concerned Marketing Authorisation Holders (MAHs), when conducting complex or very complex studies on the use, safety or effectiveness of one or several substances. Industry will be invited to provide comments on the study protocol and, later, via the Assessment Report on the assessment of the results. The utility of received comments in a consolidated way across MAHs where possible was noted. When conducting Off the Shelf (OTS) and Routine Repeated (RR) studies investigating the use, safety or effectiveness of one or several substances, EMA will inform industry. In this scenario, industry is to be informed using existing processes outlined in the previous paragraph (EU PAS Register).

EMA will consult at various timepoints during the study conduct. The proposal is for EMA to inform industry of (very) complex studies' initiation to inform industry to expect consultation in the following stages of the study conduct. EMA proposed to inform industry of the protocols of OTS and RR studies via their publication in the EU PAS register and only consult industry on the protocols of (very) complex studies. EMA will subsequently consult industry on the study report of (very) complex studies for which industry will provide comments via the Assessment Report. Finally, industry will be informed of the final report of all studies via publication in the EU PAS Register.

Álmath Spooner, the industry representative in the DARWIN EU® Advisory Board, welcomed the principle of complexity as a driver for consultation and that industry will be consulted for complex studies. It is also proposed to consult on non-complex studies where these types of studies may also have an impact on decision making. Industry representatives will now disseminate the proposal with trade associations and provide feedback in a months' time.

From a national agency perspective, Niklas Hedberg (TLV) supported the proposal but also stated that the view on this might differ between HTA agencies in Europe. It was also clarified that data from industry will not be included in DARWIN EU® studies, as it is important to differentiate evidence generated from industry vs DARWIN EU®. The DARWIN EU® Advisory Board will discuss the updated proposal at the next meeting.

5. EHDS pilot – link to DARWIN EU®

Mario Jendrossek (HDH) presented on the EHDS2 pilot project. The Health Data Hub (HDH) is a French organisation that aims to ensure easy, unified, transparent and secure access to health data to improve quality of care and support for patients. The EHDS proposal aims to overcome several obstacles for a well-functioning data economy and health data sharing. The HDH is involved in two main prefigurative instruments led by the European Commission: TEHDAS joint action and the EHDS2 pilot.

The HDH have been selected to lead this project by the European Commission in July 2022. They will start the project on 1 October 2022 and run it until end of September 2024. Multiple consortiums are involved in the EHDS pilot, from EU agencies (EMA included), national platforms and international research infrastructures. The consortium will aim to answer the European Commission's call for project to concretely test the EHDS in practice by creating a network of data platforms at European level, by conducting cross-border research use cases, and provide recommendation for the future EHDS.

The pilot project will create the first European network for secondary use of data projects, containing a metadata search portal, data access request portal and other central services. Within the network, project leaders will be able to query metadata catalogues of all nodes and ask for data access in several nodes with a single data application form.

In the coming days, HDH will receive the final list of 3 to 5 use cases selected by the European Commission to run during the pilot. EMA will be an authorised participant and consortium partner within the EHDS2 pilot project. EMA's use case on thrombosis (see below) will aim to leverage DARWIN EU®, among other platforms. DARWIN EU® and the EHDS2 pilot are two complementary and synergetic projects for the secondary use of health data.

5.1. EMA use case

Following the introduction of the EHDS pilot, Xavier Kurz (EMA) presented further details on the proposed EMA use case. EMA's use case will aim to investigate the *natural history of coagulopathy and use of antithrombotic agents in COVID-19 patients and persons vaccinated against SARS-CoV-2.* The study has previously been conducted via the EMA Framework Contract and the results of this study may be used for benchmarking (EUPAS40414). This is an important use case that will test the way DARWIN EU® will be integrated in EHDS in the future. Six specific objectives of the study were presented, increasing in level of complexity, which will be chosen by data partners while considering their capability and the data they hold.

It will be important to evaluate how the data from the different nodes will be combined, considering data available in the Common Data Model (CDM) via DARWIN EU® and data available in other nodes in native format. It was also clarified that the CDM is not a pre-requisite for becoming a node in the EHDS pilot. In the future, some data sources, such as some registries for example will not be converted into a CDM. The objective will be to see how the different data sources can be combined in a single study in a meaningful way.

6. Tour de Table

Niklas Hedberg (TLV) raised a point about the Horizon Europe projects that have been announced in August, asking for a brief overview from the European Commission members of these new projects in relation to RWE.

7. AOB

A number of information items were shared with the Advisory Board members:

- Recently published Big Data Steering Group workplan 2022-25 and its news announcement
- Announcement of the date for the 3rd Big Data Stakeholder Forum on 1 December 2022
- Multistakeholder workshop on Patient experience data in medicines development and regulatory decision-making – 21 September 2022

Markus Kalliola (SITRA) also raised the workshop bringing together TEHDAS, EHDS2 pilot, 1Million Genomes project to be held on 26 September 2022, for which EMA/DARWIN EU® has also been invited, to identify synergies and common ground.

Karl Broich (BfArM) thanked all the members of the Advisory Board for their feedback and continued collaboration, and welcomed the progress and updates on the establishment of DARWIN EU® which is on track to deliver benefits, and closed the meeting.

Next meeting: December 2022, postponed to February 2023