Introduction of the DARWIN EU® Coordination Centre

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Executive Director

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Disclosure

This presentation represents the views of the DARWIN EU® Coordination Centre only and cannot be interpreted as reflecting those of the European Medicines Agency or the European Medicines Regulatory Network.
How to increase the generation and use of RWE?

Skills, Methods & Technology (incl. DARWIN EU®)

Data Discoverability and Characterisation

Data driven decision making

Organisation, Processes and Governance

Others: EC, HTA bodies and payers, EU health agencies

NCAs

EMA scientific committees and working parties
DARWIN EU® is a federated network of data, expertise and services that supports better decision-making throughout the product lifecycle by generating reliable evidence from real world healthcare data.

**FEDERATED NETWORK PRINCIPLES**
- Data stays local
- **Use of Common Data Model** (where applicable) to perform studies in a timely manner and increase consistency of results
What will DARWIN EU® do?

- Provide scientific expertise in formulating and executing studies and analyses
- Maintain a catalogue of known, relevant data holders, continually ensuring the discoverability & quality of data held by data holders
- Maintain & expand the federated network of data partners, assisting new data holders in conforming with required standards for usage in regulatory context
- Conduct scientific studies and analyses on behalf of the EMRN and EMA scientific committees
- Deliver training, governance, support of business services
- Enable the EMRN, EMA and the scientific committees to make use of the EHDS in the context of medicines regulation, acting as EHDS ‘pathfinder’
### What analyses and studies will DARWIN EU® deliver?

<table>
<thead>
<tr>
<th>Category of observational analyses and studies</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Routine repeated analyses</strong></td>
<td>Routine analyses based on a generic study protocol</td>
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<tr>
<td></td>
<td>• Periodical estimation of drug utilisation</td>
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<td></td>
<td>• Safety monitoring of a medicinal product</td>
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<td></td>
<td>• Estimation of the incidence of a series of adverse events</td>
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<td><strong>Off-the-shelf studies</strong></td>
<td>Studies for which a generic protocol is adapted to a research question</td>
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<td></td>
<td>• Estimate the prevalence, incidence or characteristics of exposures</td>
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<td></td>
<td>• Health outcomes</td>
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<td></td>
<td>• Describe population characteristics</td>
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<tr>
<td><strong>Complex Studies</strong></td>
<td>Studies requiring development or customisation of specific study designs, protocols and Statistical Analysis Plans (SAPs), with extensive collection or extraction of data</td>
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<td></td>
<td>• Etiological study measuring the strength and determinants of an association between an exposure and the occurrence of a health outcome considering sources of bias, potential confounding factors and effect modifiers</td>
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<tr>
<td><strong>Very Complex Studies</strong></td>
<td>Studies which cannot rely only on electronic health care databases, or which would require complex methodological work</td>
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<td>• Studies where it may be necessary to combine a diagnosis code with other data such as results of laboratory investigations, or studies requiring additional data collection</td>
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## Budget and expected number of studies

<table>
<thead>
<tr>
<th>Phases/Options</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
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</thead>
<tbody>
<tr>
<td>Phases/Options</td>
<td>Phase I</td>
<td>Phase II</td>
<td>Phase III</td>
<td>Option 1</td>
<td>Option 2</td>
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<tr>
<td>Estimated budget (in million EURO)</td>
<td>4M</td>
<td>8M</td>
<td>8M</td>
<td>16M</td>
<td>16M</td>
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<tr>
<td>Routine repeated Analysis</td>
<td>At least 1 study</td>
<td>At least 6 studies</td>
<td>At least 30 studies</td>
<td>At least 60 studies</td>
<td>At least 60 studies</td>
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<tr>
<td>Off-the-shelf Study</td>
<td>At least 2 studies</td>
<td>At least 6 studies</td>
<td>At least 30 studies</td>
<td>At least 60 studies</td>
<td>At least 60 studies</td>
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<tr>
<td>Complex Study</td>
<td>1</td>
<td>4</td>
<td>At least 12 studies</td>
<td>At least 24 studies</td>
<td>At least 24 studies</td>
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<tr>
<td>Very complex Study</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>At least 1 study</td>
<td>At least 1 study</td>
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</table>
## Establishment of Data Network

<table>
<thead>
<tr>
<th></th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
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<tbody>
<tr>
<td>Data Partners On-</td>
<td>up to 10 additional</td>
<td>up to 10 additional</td>
<td>up to 10 additional</td>
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<td>Boarded</td>
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<tr>
<td>Data Partners Connect</td>
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<td></td>
<td>Up to 20 following the ones already on-</td>
<td>Up to 40 following the ones already on-</td>
<td>40 following the ones already on-boarded in</td>
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<tr>
<td>ed &amp; to be Maintained</td>
<td></td>
<td></td>
<td>boarded in Years 1 and 2</td>
<td>boarded in Years 1, 2 and 3 (i.e 30), plus 40 following the ones already on-boarded in Years 1, 2, 3 and 4.</td>
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</table>
What is the DARWIN EU® process for conducting studies?

NCA/EMA Committee
- Identify question that may impact committee decision
- Integrate within EU regulatory decision-making process

NCA/EMA Committee
- Define the research questions
- Evaluate feasibility

Coordinating Centre (NCA/EMA may be consulted)
- Create protocol & code
- Contact Data partners
- Manage study governance
- Receive, check, analyse aggregated data
- Compile results in study report

Data Partners (may include NCA/EMA)
- Receive and run the code on their own databases
- Send aggregated data to the Coordination Centre

Share aggregate data & reports with requester (support integration/assessment)
Which data sources will DARWIN EU® use?

Data sources will be onboarded over time taking into account the following criteria:

- Data sources collecting health data routinely and representative of the different types of real-world data in terms of data elements, setting (primary & secondary care), population, origin (e.g. electronic health care records, claims)

- Data sources which collectively provide a broad geographical cover

- Data sources containing patient-level data with a unique patient identifier linking all records relating to a given patient

- Medicines prescribed or dispensed identifiable with quantities (e.g. doses, package size) and dates allowing to calculate cumulative doses and duration of use and linked to individual but unidentifiable patients

- Clinical events formally coded, with accurate dates and linked to individual but unidentifiable patients

- Data already converted or planned to be converted into a common data model

Selection criteria are currently under discussion
Setting up the DARWIN EU® Coordination Centre
Call for tenders: a two stage process from June 2021 – Feb 2022
DARWIN EU® Coordination Centre

Executive Director
Prof. Peter Rijnbeek
Head of the Department of Medical Informatics
Erasmus MC

Deputy Director
Prof. Daniel Prieto Alhambra
Erasmus MC, Oxford University

Deputy Director
Associate Prof. Katia Verhamme
Erasmus MC

Contractor

Sub-contractors

Erasmus MC
University of Oxford
SYNAPSE
IQVIA
The Hyve
ODYSSEUS DATA SERVICES INC
DARWIN EU® Implementing a paradigm shift

• A highly needed paradigm shift for the **fast** delivery of **reliable** evidence for regulatory decision-making on the utilisation, safety and effectiveness of medicinal products throughout their lifecycle

• A long-term investment needed to significantly scale up the number of studies on more databases and improve public health.

Not possible by simply scaling up the traditional approaches.
What is needed to facilitate observational studies at scale?

- Data interoperability
- Standardised analytics
- Technical Infrastructure
- Data network
Improving interoperability of data

• Increasing productivity to an industrial level requires the automation of the analytical processes, which in turn cannot be done without a rigorous standard representation of the data.

• Full interoperability of the data is needed with respect to structure (syntactic interoperability) and coding systems (semantic interoperability) by using a Common Data Model (CDM)
Generating Reliable Evidence using a Common Data Model

We need to make studies repeatable, reproducible, replicable, generalisable, and robust.

A Common Data Model will enable standardised analytics to generate reliable evidence.
The OMOP Common Data Model

• It is maintained by the Observational Health Data Sciences and Informatics (OHDSI) initiative with an active European Chapter (www.ohdsi-europe.org).

• Many tools are available for data standardisation, data quality, and data analysis.

• It is designed for federated querying and analytics, whereby applications are run locally by the data partners and only aggregated results are shared. This privacy-by-design approach is compliant with data protection requirements.

• It has been used in many observational studies including studies that informed regulatory decision-making.

• The European Health Data and Evidence Network (EHDEN) project is investing €17M private/public funding in standardising health data to the OMOP-CDM through the Innovative Medicines Initiative (www.ehden.eu).
From Source Data to the OMOP CDM: Extraction Transform Load (ETL)

- Fully documented process
- Process is supported by tools and procedures
- Applied to a large number of database
- Quality control mechanism in place -> DQD, Inspection Report
Standardising the analytics

• A catalogue of open source standardised analytics is needed to support “all” regulatory decision-making on the utilisation, safety and effectiveness of medicinal products.

Will require alignment on the priority and choice of the analytical methods, and the standardised output!
Standardising the analytics

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  Will require alignment on the priority and choice of the analytical methods, and the standardised output!

- Development will be driven by initial studies taking different complexity levels into account.

- The standardised analytics will be based on available tools and methods developed in the OHDSI community.
Creating a strong technical infrastructure

Required components:

• Collaboration Space for CC and Study Teams
• Analytics Platform
• Study Execution Platform
• Training Platform
• Service Desk
• Source Control Repository
• DARWIN EU Website

Will build on prior work

Will be developed using short sprints during the establishment phase
Operating a high-quality Data Network

• Selection of data partners
  1) Prioritisation of already converted data sources
  2) Potentially mapping highly valued data sources

• All data sources will go through a quality control process approved by EMA
Establishment and Evolution of the Coordination Centre

Executive Board

Director

Advisory Boards
- Scientific (SAB)
- Ethical (EAB)
- Data Source Prioritisation Committee (DSPC)
- General Assembly (GA)

Development
- QA/QC Procedures
- Vocabulary Extension
- CDM Development
- Methods Research
- Analytical Tools
- Dashboarding
- Training Material
- Protocol Templates

Operations
- Study execution
- Network management

Technology
- Infrastructure
- Security
- Collaboration Environment
- Analytics Platform
- Source Control Repository
- Website
- Service Desk
- Training Platform

Management
- Secretarial
- Legal / Contracting
- Finance
- COI management
- Risk management
- Reporting
- Recruitment
- Outreach
Operations

Study teams should leverage:

1) Common Analytics
2) Phenotype Library
Network teams should leverage:
1) Common ETL Tools
2) Established QC mechanisms
Implementation roadmap

**Phase I - 2022**
- Start running pilot studies to support EMA committees – **first benefits delivered**
  - Coordination Centre set-up
  - Data Protection Impact Assessment
  - Start recruiting and onboarding data partners
  - Pilot with the EHDS model and existing Data Permit Authorities
- Consultation of stakeholders

**Phase II - 2023**
- Support the majority of Committees in their decision-making with reliable RWE by 2023

**Phase III - 2024**
- Up scale delivery and capacity to routinely support the scientific evaluation work of EMA’s scientific committees and NCAs by delivering studies and maintaining data sources.

**Operation - 2025/2026**
- DARWIN EU® to be fully operational and yearly evolves to meet the needs from the EU Regulatory Network
- **Integration with the EHDS**
DARWIN EU® - Coordination Centre immediate next steps

- **Formation** of the coordination centre: governance team, technology operations team, governance & boards

- **Project management** (e.g. project plan, risks management, reporting)

- **Strengthening** of the coordination centre:
  - Requirements & solution design
  - Conflict of Interest management process
  - Mandate and composition of the Scientific Panel
  - Change management plan

- **Strategic oversight** of the coordination centre:
  - Management plan and Business plan

- **On-Boarding of data sources templates**:
  - On-boarding specifications, data use agreement

- **Execution of studies templates**:
  - Feasibility assessment form, study outline/protocol/report, Agreement for Study Participation
More Information

Data Analysis and Real World Interrogation Network (DARWIN EU) | European Medicines Agency (europa.eu)

Coordination Centre website – coming soon in 2022!

• For questions to the Coordination Centre, please contact: enquiries@darwin-eu.org

For regular updates on DARWIN EU® Subscribe to the Big Data Highlights newsletter by sending an email to: bigdata@ema.europa.eu
EUROPEAN OHDSI SYMPOSIUM

Symposium: June 24th
Workshops: 25-26th

“We’ll meet again for one journey ahead

Call for participation
Deadline May 6th

Organised by:
Erasmus MC
Health Data Science