Update on Real-World Evidence and DARWIN EU

CAT Industry Interested Parties Meeting
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Disclaimer

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Outline

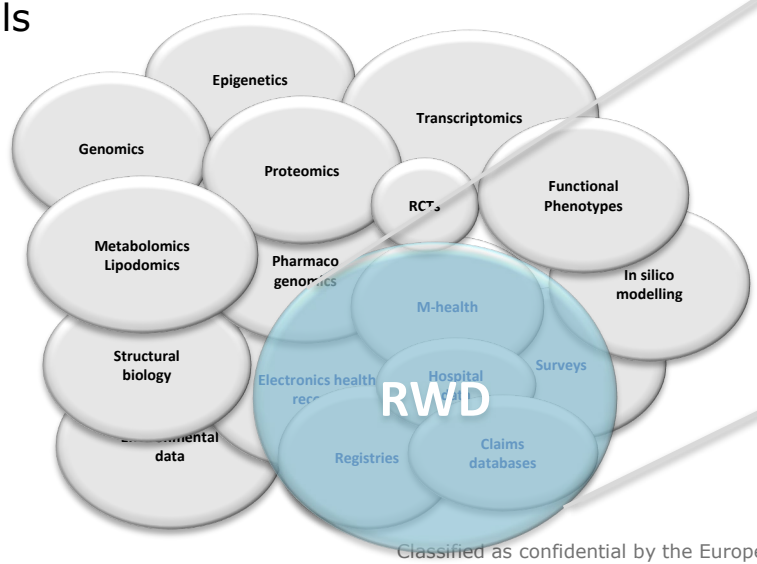
- Real-World Evidence (RWE) definition

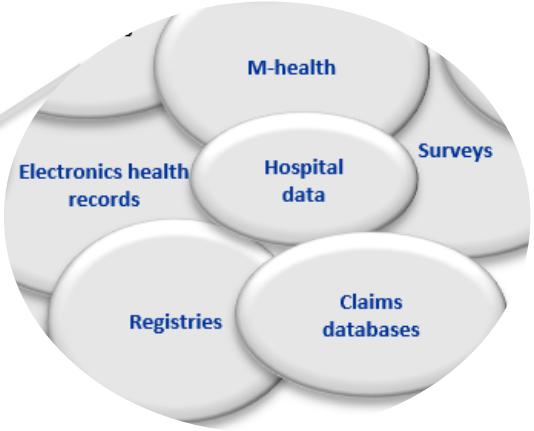
- European Medicine Regulatory Network approach to RWE
  - RWE in marketing authorisation applications
  - RWE provided by the network to support regulatory decision making

- How the vision will be delivered
  - DARWIN EU
  - Piloting with the committees

Real-World Data and Real-World Evidence

Real-World Data (RWD): routinely collected data relating to patient health status or the delivery of health care from a variety of sources other than traditional clinical trials



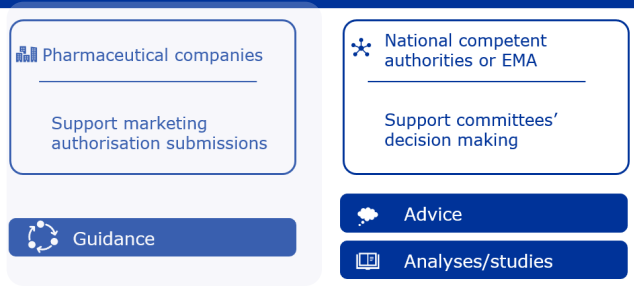


Real-World Evidence (RWE): information derived from analysis of real-world data

Use of RWD/RWE and the European Medicines Regulatory Network (EMRN) role

RWD/RWE provided by	Pharmaceutical companies	National competent authorities or EMA
RWD/RWE used to	Support marketing authorisation submissions	Support committees' decision making
EMRN role	Guidance	Advice Analyses/studies

RWD/RWE in marketing authorisation submissions



Aim

- To support submission of RWE of high validity and relevance and therefore optimal use of the RWE to support regulatory decision-making

How

- To support marketing authorisation applicants (MAAs) by providing guidance on the format and content of submission of RWE, e.g. *Guideline on registry-based studies (Oct 2021)*
- Templates and check-lists for feasibility analyses on appropriateness of RWE data sources (e.g. registries and electronic health care records)
- Standard definitions (internationally agreed), quality assessment criteria,…

On going initiative

- Study to characterise RWD/E included in applications and explore its contribution to decision making

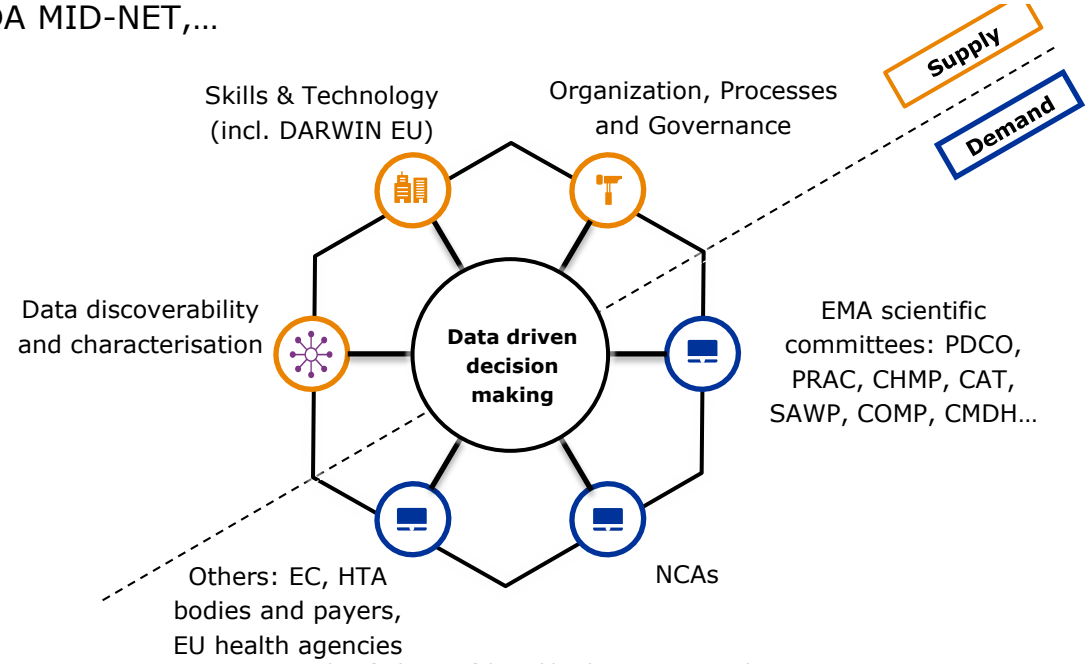
RWE by EMRN

- International regulators have been establishing systems for generating the evidence needed, e.g FDA Sentinel system, Health Canada CNODES, PMDA MID-NET,…

Pharmaceutical companies
Support marketing authorisation submissions

National competent authorities or EMA
Support committees' decision making

Guidance
Advice
Analyses/studies



Data (and studies) discoverability and characterisation

A catalogue of data sources (including registries) is being developed - Q4 2022 (TBC)

- The catalogue will be a newer and better version of the current ENCePP Resources Databases, focusing on data sources available in EU
- The catalogue will be searchable, and will include metadata describing the main characteristics of each data source
  - E.g. population size, demographics, type of care covered, diseases of interest covered,…
- In the future, information on quality of the data source might also be included

A catalogue for studies based on EU PAS Register will also be delivered - Q4 2022 (TBC)

- Useful to identify what studies have been done on a disease/product and which data sources have been used

Sources of evidence for regulatory committees

Requests or obligations to pharmaceutical companies

Analysis of public information including public scientific literature

1 **Studies** on the electronic health databases accessible in-house

2 **Studies procured** through the EMA framework contracts

3 **DARWIN EU** (starting from 2022)

3 Coming in 2022: Data Analysis and Real-World Interrogation Network - DARWIN EU®

DARWIN EU is a federated network of data, expertise and services

EU Medicines Regulatory Network

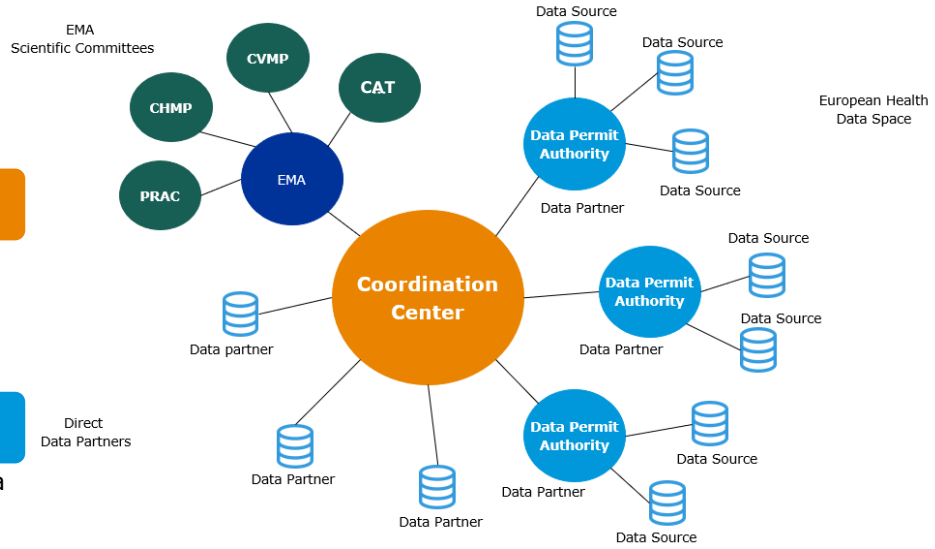
- **EMA** - provides leadership, setting standards, contracting studies, **overseeing**
- **EMRN -** including EMA scientific committees and working parties, national competent authorities (NCAs) and the European Commission: **request studies** via EMA

The Coordination Centre

- **Establishes** and **maintains the network** (including onboard/maintain data sources), manage the **execution of scientific studies**

Data Partners, incl. Data Permit Authorities

- **Partners** who have access to data, or who may request analyses in a data source and provide results to the Coordination Centre
- This includes **Data Permit Authorities** (DPAs), already existing or to be created as part for the European Health Data Space (EHDS)



3 DARWIN EU® - High level timelines

2021

- Selection of the Coordination Centre provider

Phase I and II - 2022/2023

- Establish connectivity with EHDS and existing Data Permit Authorities
- Start recruiting and onboarding the data partners
- First catalogue of standard data analyses available
- Start running pilot studies to support EMA committees - first benefits delivered

Phase III - 2024

- DARWIN EU® to be fully operational and routinely supporting the scientific evaluation work of EMA and NCAs' scientific committees

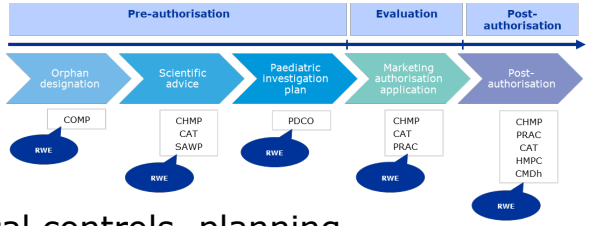
Operation - 2025/2026

- DARWIN EU® to continue to evolve
- Full integration with the EHDS

3 DARWIN EU® Advisory Board

- Mandate
  - Provide strategic advice and recommendations to the project team on the establishment of the DARWIN EU capability and its use of the European Health Data Space
  - Ensure continued coordination and alignment with relevant European initiatives and policy
  - Support two-way communication with the stakeholders
- Stakeholders
  - European Commission, National Competent Authorities (NCA), HTA, Payers association, Data Permit Authorities, Joint Action TEHDAS, EU patient associations, EU healthcare professional associations, European Centre for Disease Prevention and Control agency (ECDC), and European pharmaceutical industry (as observer)
  - Through collaboration, we will deliver more for public health

DARWIN EU® - Benefits



- National and EU **regulation of medicines**
  - **Drug development** – disease epidemiology, unmet need, historical controls, planning
  - **Authorisation** – contribution to BR, controls, extrapolation to general and/or special populations
  - **Post-authorisation** – benefit-risk monitoring, extension of indication, risk minimisation measures

DARWIN EU will significantly **increase the capacity** of the Network to undertake high-quality observational studies based on real-world data

- **Additional benefits** as EU partners participate and access the platform:
  - **European Commission** – key use case for the European Health Data Space
  - **National governments** to support health policy and delivery of healthcare systems
  - **HTA bodies and payers** to support better quality decisions on cost-effectiveness
  - **EU health agencies** - use cases specific for EFSA, ECDC, ECHA, JRC
  - **EU patients** - faster access to innovative medicines and safe and effective use

RWE generated through regulators – Use cases

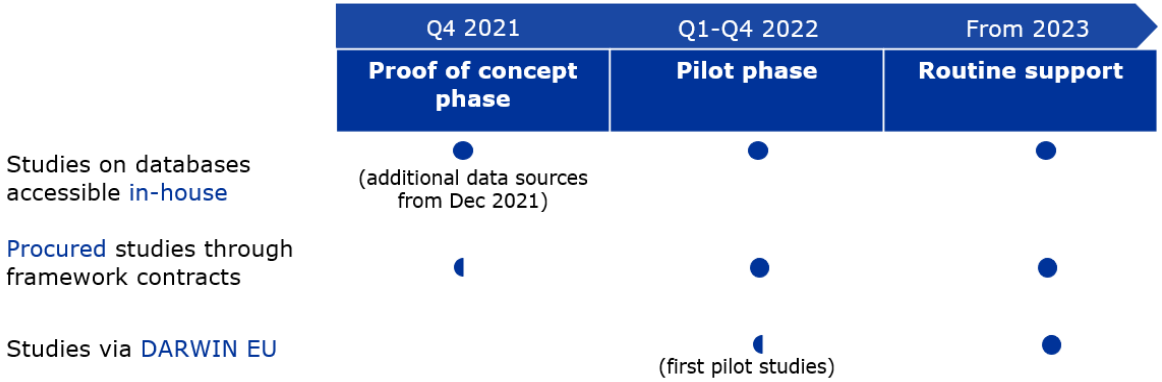
From a regulatory perspective, RWE aims to support committees' decision-making in three main areas

Use case objective	**Support the planning & validity of applicant studies**	**Understand clinical context**	**Investigate associations and impact**
Use case category	Design and feasibility of planned studies	Disease epidemiology	Effectiveness and safety studies
	Representativeness and validity of completed studies	Clinical management & drug utilisation	Impact of regulatory actions

Pilot-based approach to iteratively refine and implement RWE processes and use cases

Interacting with scientific committees to agree PoC and pilots

- PRAC: implementing the lessons learnt from 2019-21 pilot
- SAWP: pilot starting in 2021
- CAT, COMP, PDCO: PoC in 2021, pilot starting in 2022
- CHMP: Pilot starting in 2022



Aim to support the majority of Committees in their decision-making with valid and reliable evidence at EU level by 2023

Conclusions

Aim

Pharmaceutical companies	National competent authorities or EMA
Support marketing authorisation submissions	Support scientific committees' decision-making with valid and reliable evidence at EU level

On-going work

Further analysis ongoing to evaluate the impact and usefulness of RWE in MA
On-going initiatives to increase both the generation and the use of RWE
Pilot-based approach to iteratively refine and implement RWE processes and use cases

Vision 2025

Role of RWE established across spectrum of regulatory use cases
Regulation more data-driven: includes analysis of CTs and RWD
Better evidence supports better decisions on medicines for patients

Any questions?

Further information

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What should be the criteria for acceptability of RWE?

WHAT

Data source

Adequate: amount of information needed for regulatory decision-making, e.g. sufficient sample size and sufficient information on patient characteristics, treatments (doses, duration of prescription, formulation), morbidities and risk factors

High quality: derived from real-data sources of demonstrated quality and accuracy (validation)

Methods

Internal validity: accurate representation of what it intended to measure (i.e. no bias)

Consistency

Across countries/data sources, or differences can be explained

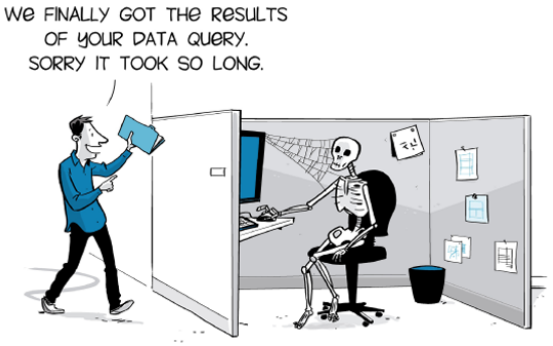
HOW

Transparency

Replicability

A priori specification

Timeliness



Studies on databases accessible in-house and procured

1 Studies on electronic health databases accessible in-house (EMA)

- Currently three primary care databases (UK, FR, DE)
- 99 EMA in-house analyses or studies performed from 2013
  - The studies supported evidence needs of EMA Committees, mainly Pharmacovigilance (PRAC)
- PRAC pilot: November 2019 - January 2021
- On-going procurement to increase geographical representation and access to hospital prescribing

2 Studies procured through the EMA framework contracts

- Allows access to different data sources and scientific expertise
- 30 studies funded from 2010, e.g.
  - vAACine covid-19 monitoring readinESS (ACCESS): background rates for adverse events of special interest
  - Ranitidine - potential risk of cancer associated with N-nitrosodimethylamine (NDMA)
- A new framework contract, with a broader set of organisations and data sources from October

3 DARWIN EU® - Process for conducting analyses and studies

NCA/EMA Committee	NCA/EMA	Coordinating centre in consultation with EMA	Data Partners (may include NCA/EMA)
Question that impacts committee opinion	Evaluates relevance and feasibility of RWD Define the research questions	Create protocol and programming code Contact relevant Data partners Manage specific study governance (ethics,…)	Receive and run the code on their own DBs
			Aggregate data and results sent to the coordinating centre
Integrate data and reports in the assessment report	Share aggregate data and reports with committees (and support integration/assessment)	Receive, check, analyse aggregate data Compile the results in a study report	

Key principles

- Data stays local
- A common data model will help performing studies timely and increasing consistency of results