EUROPEAN MEDICINES AGENCY

DARWIN EU

Scaling-up Real-World Evidence Generation for Regulators in Europe: DARWIN EU

INFARMED conference 25 September 2023

Presented by Dr Daniel Morales
European Medicines Agency, Data Analytics and Methods Taskforce – Real World Evidence

Recent developments

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By 2025 the use of Real-World Evidence will have been enabled and the value will have been established across the spectrum of regulatory use cases

- European Medicines Regulatory Network (EMRN) strategy to 2025 -

Use or RWE in regulatory applications

	Flynn et al. (2021) What was the Contribution of Real-World Evidence in EU?	Purpura et al. (2021) The Role of Real-World Evidence in FDA
Number of products reviewed	158	136
Period	Jan 2018 – Dec 2019 (submitted marketing applications, including non-published information)	Jan 2019 – June 2021 (approved marketing applications, only published information)
Number of products with RWE included	**63 (39.9%)**	**116 (85.2%)**
Therapeutic area	Oncology and anti-infectives	Oncology and anti-infectives
Key messages	• Widespread use of RWE to support evaluation of marketing applications • RWE in pre-authorization (1/3) and post-authorization (2/3) • RWE included to support safety (87.3%) and efficacy (49.2%) • Most common data sources were registries (60.3%) followed by hospital data (31.7%)	Successful use of RWE in regulatory approvals required: • fit-for-purpose data • good study design, appropriate data collection, and thoughtful data analysis • proactive communication with FDA

Three main areas for which RWD analyses can support regulatory decision-making

1 Support the planning and validity of applicant studies

- Design and feasibility of planned studies
- Representativeness and validity of completed studies

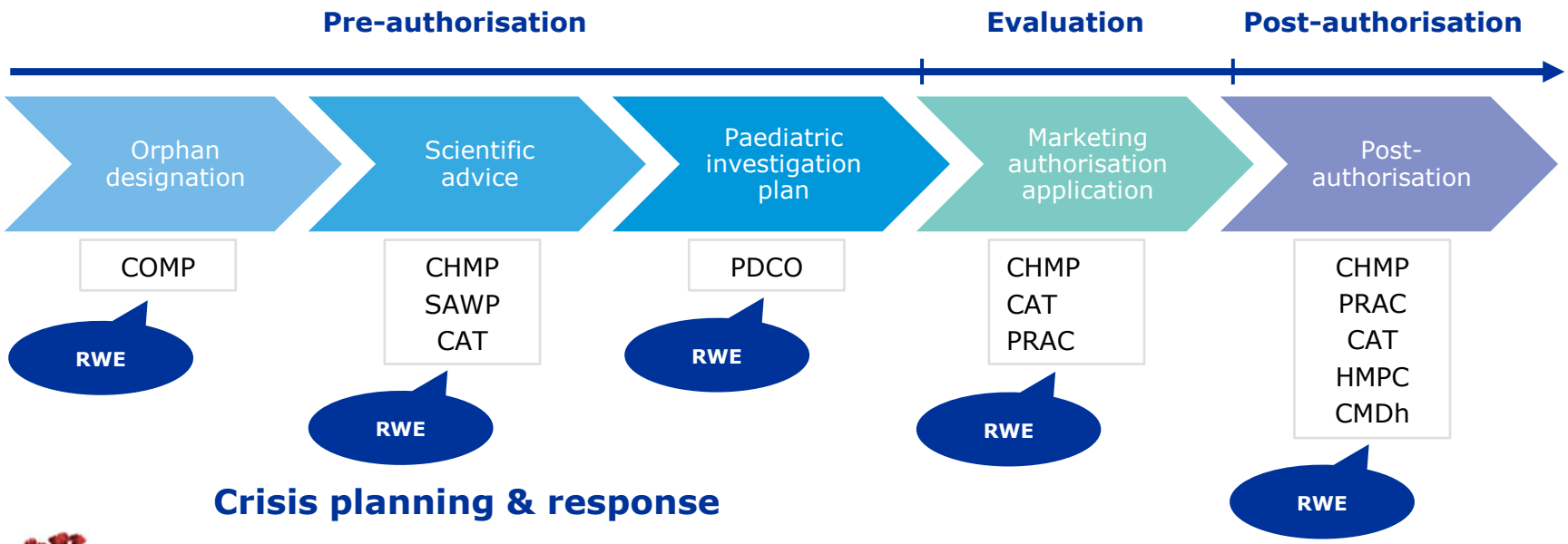
2 Understand the clinical context

- Disease epidemiology
- Clinical management
- Drug utilisation

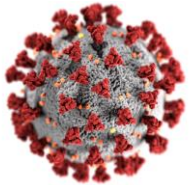
3 Investigate associations and impact

- Effectiveness and safety studies
- Impact of regulatory actions

Demand: RWE use across the medicinal product lifecycle



Crisis planning & response



- Monitoring the use of medicines to predict demand and shortages
- Understanding the disease natural history → development of vaccines and therapeutics
- Provide evidence for repurposing existing medicines
- Monitor the safety and effectiveness of vaccines and therapeutics post-authorisation

Countdown to 2025

Enabling use

Towards delivering the 2025 RWE vision

EMA studies using in-house databases

- **Primary care** health records from the **France**, **Germany, UK, Italy, Spain** and **Romania.** Some data sources include data on specialist.

Studies procured through EMA FWCs

- New framework contract (FWC) since September 2021: services of **8 research organisations** and academic institutes
- Access to **wide network of data sources**: 59 data sources from 21 EU countries
- Ability to leverage external **scientific expertise**

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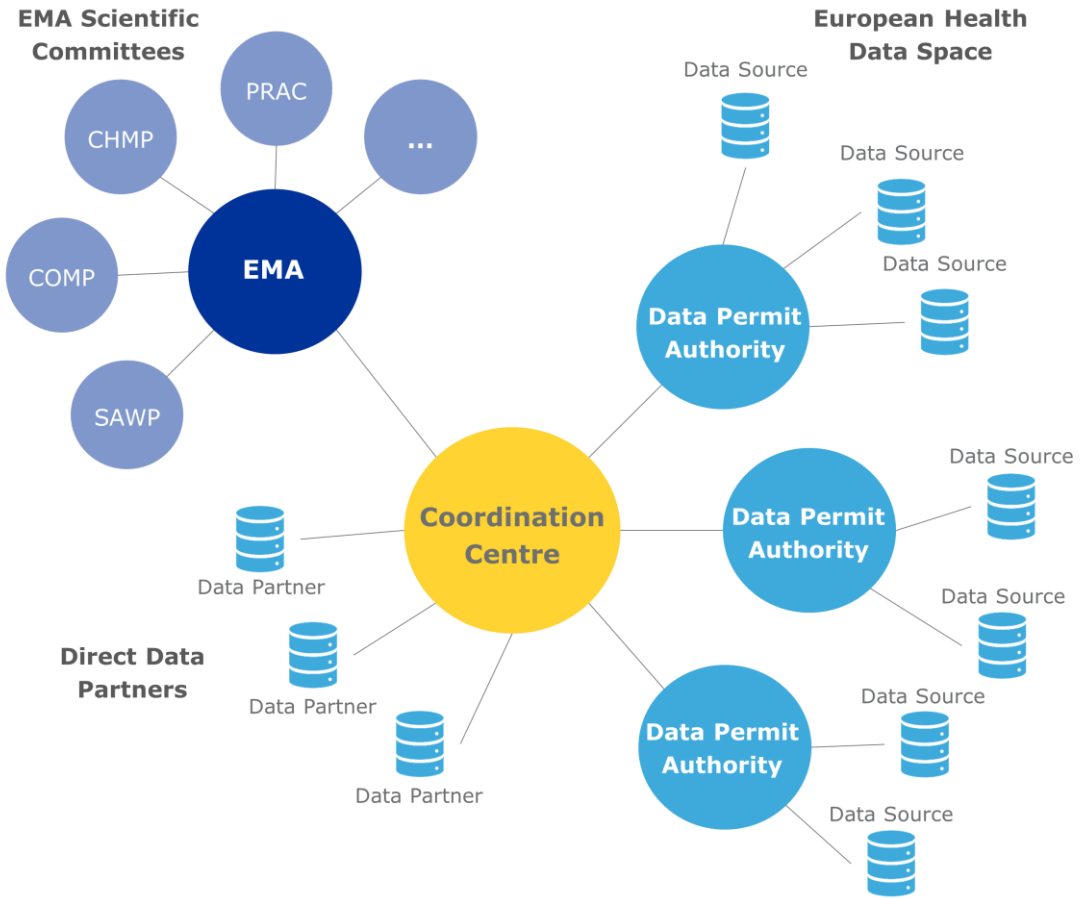
DARWIN EU®

- Coordination Centre launched February 2022
- Onboarded first **10 data partners**
- **First studies** finalised
- Additional 10 data partners are foreseen to **be added each year** for 2023-2025

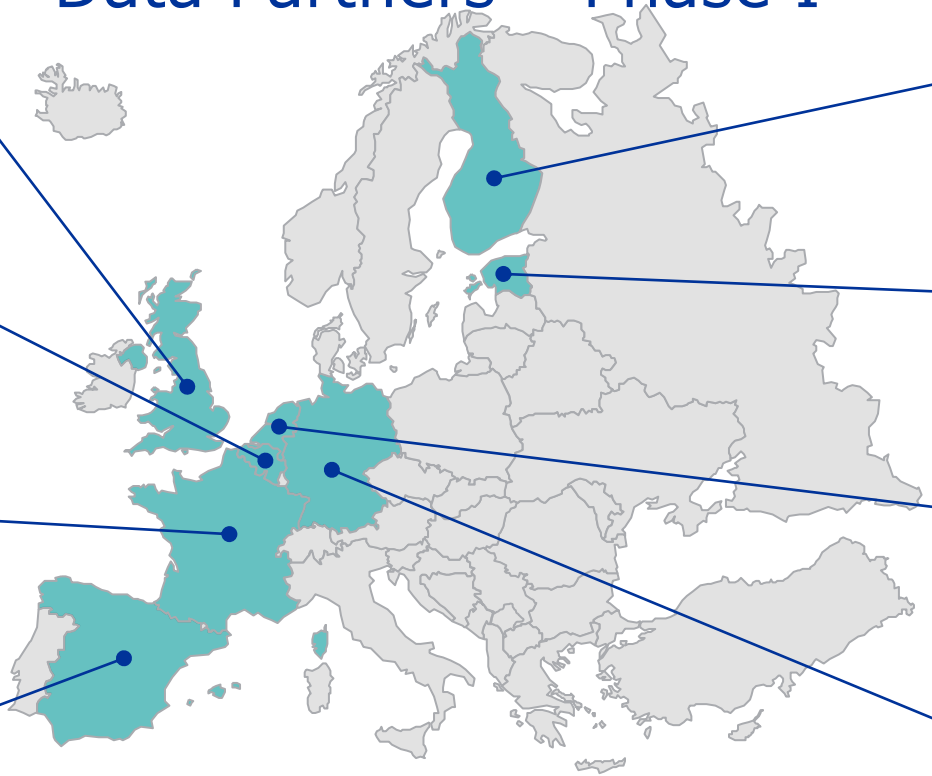
DARWIN EU® is a federated **network** of **data**, **expertise** and **services** that supports better decision-making throughout the product lifecycle by generating reliable **evidence from real world healthcare data**



FEDERATED NETWORK PRINCIPLES

- Data stays **local**
- **Use of OMOP Common Data Model** (where applicable) to perform studies in a timely manner and increase consistency of results

Data Partners – Phase I



UK

1. Clinical Practice Research Datalink (CPRD GOLD)

Belgium

2. IQVIA Belgium Longitudinal Patient Data

France

3. Bordeaux University Hospital

Spain

4. IDIAPJGol
5. Parc Salut Mar Barcelona, Hospital del Mar (IMIM)

Finland

6. Auria Clinical Informatics at Hospital District of Southwest Finland (HDSF)

Estonia

7. University of Tartu (Biobank)

Netherlands

8. Integrated Primary Care Information
9. Netherlands Comprehensive Cancer Organisation

Germany

10. IQVIA Germany Disease Analyser

~26 million active patients

Currently **selecting Phase II DPs** via **open call for expression of interest**, then Phase III to follow

Ongoing studies

Background all-cause **mortality rates in patients with severe asthma aged ≥12 years** old [EUPAS103936]

CHMP
Complex

EHDS coagulopathy of COVID-19

EC/EHDS
Complex

Effectiveness of **COVID-19** vaccines against severe COVID-19 and post-acute outcomes of SARS-CoV-2 infection.

ECDC/VMP
Complex

Drug utilisation study on co-prescribing of **endothelin receptor antagonists** (ERAs) and **phosphodiesterate-5 inhibitors** (PDE-5is) in pulmonary arterial hypertension. [EUPAS106052]

CHMP
OTS

Multiple myeloma: patient characterisation, treatments and survival in the period 2012-2022 [EUPAS105033]

HTA/Payers
OTS

Drug utilisation study of **medicines with prokinetic properties** in children and adults diagnosed with gastroparesis

NCA
OTS

Naloxone use in treatment of opioid overdose. [EUPAS105644]

CHMP
OTS

Drug utilisation study of prescription **opioids**. [EUPAS105641]

PRAC
OTS

OTS = off-the-shelf study

Challenges of federated networks

Challenges of federated networks

Related to the databases content

- Differences in the underlying health care systems;
- Different mechanisms of data generation and coding schemes;
- Differences in data quality

Related to the organisation of a network

- Different ethical and governance requirements
- Implementing quality controls procedures
- Speed

Future perspectives

DARWIN EU® establishment in 2022 and 2023

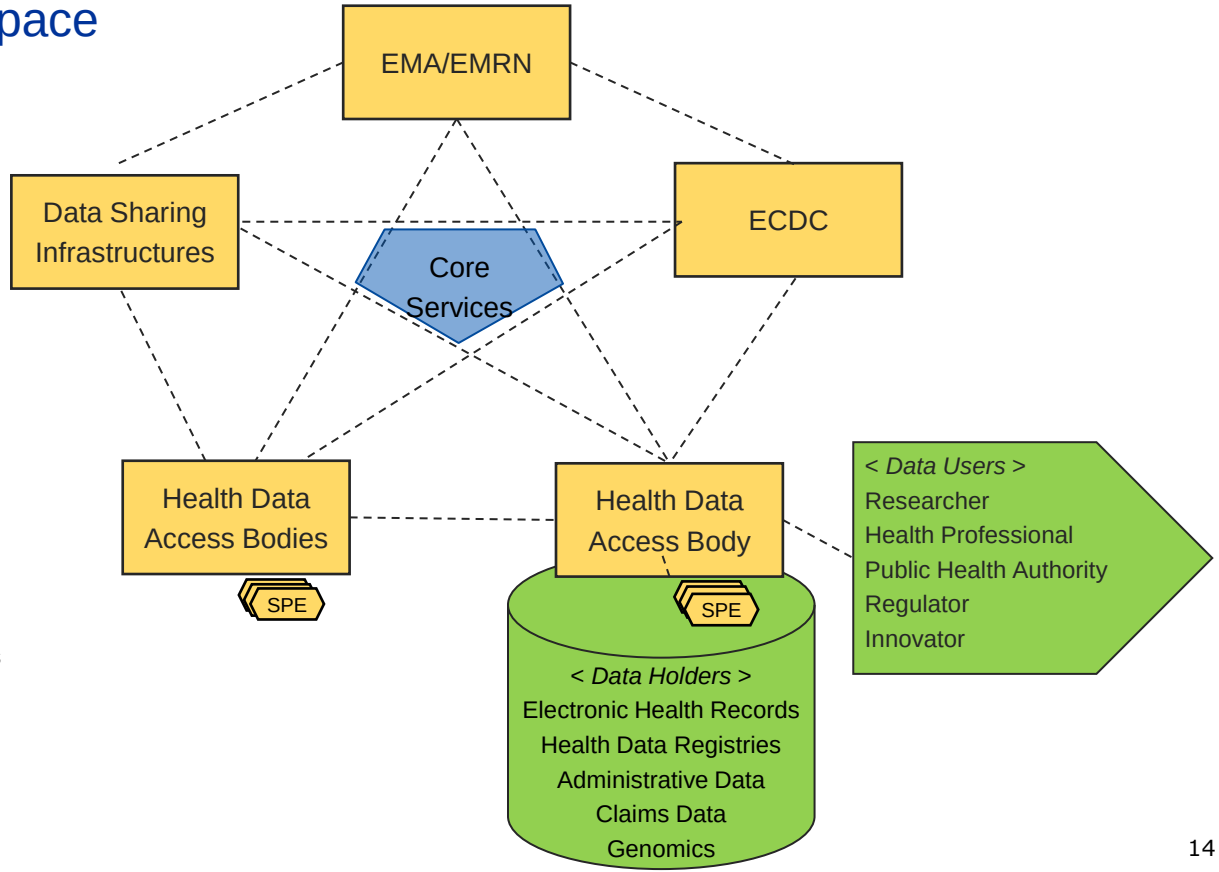
- ✓ 2nd year of establishment in progress, delivery on target and according to plan
- ✓ Focus on selection of further Data Partners and study conduct (various use cases)
- ✓ Establishment of standard analytical pipelines and codes

		Phase I	Phase II	Phase III	Option I	Option II
Studies	Off the shelf	2	6	30	60	60
	Routine repeated	1	6	30	60	60
	Complex study	1	4	12	24	24
	Very complex	0	0	0	1	1
Data Partners (total)		10	20	30	40	40

Database expression of interest

European Health Data Space

- **New infrastructure for secondary uses of health data**
- Connecting health data access bodies and data sharing infrastructures
- Several health data access bodies are established, or in the process, across Member States



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