EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

RWE and the Changing EU Landscape: EMA perspective

GETREAL INSTITUTE
PUTTING REAL WORLD EVIDENCE INTO PRACTICE

1st GetReal Institute Annual Conference
16 March 2023 | Utrecht, The Netherlands

Catherine Cohet
RWE Workstream, Data Analytics & Methods Task Force, EMA

Disclaimer

I have no conflict of interests

The views expressed in this presentation are mine and should not be understood or quoted as being made on behalf of or reflecting the position of the EMA or one of its committees or working parties

Outline

01 Evolving landscape of EU RWE guidance

02 Updates: RWE-related activities at EMA, DARWIN EU®, EHDS

03 Key messages

Current landscape of EU RWE guidance

Methodology Working Party (MWP)

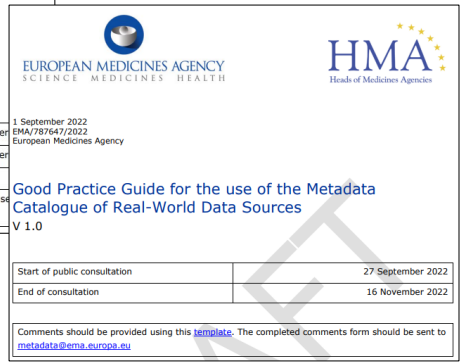
International collaborations (ICMRA, ICH)

Oct. 2021

Dec. 2021

May 2022

June 2022
Revision 11: July 2023



Consultations in 2022

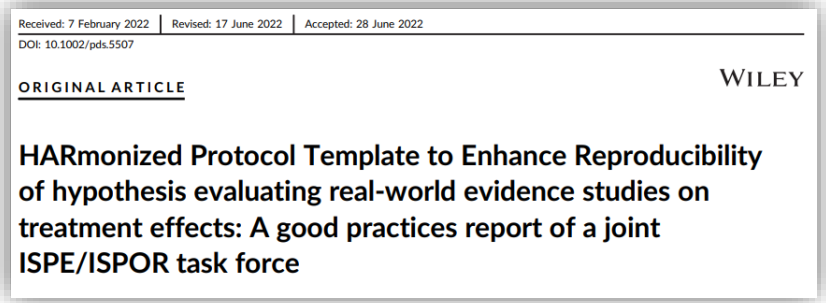
Revision ongoing

GVP Module VIII revision

- Triggered by entry into force in Jan 2022 of the **new EC Clinical Trial Regulation**
- Ongoing work
  - adapt **definitions**
  - **align** with new/updated **guidelines** (e.g., registry-based studies) and international standards (e.g., HARPER)
  - integrate appendix I and addendum
  - integrate **experience** of PASS assessors
  - amend **templates** for format and content of PASS protocol and report
- **Public consultation** end 2023 or early 2024

HARPER in the EU regulatory context

- Tool to promote transparency, reproducibility and harmonisation of NIS protocols by academics, companies and regulators
- Facilitates design of high-quality protocols and assessment by companies and regulators
- Compatible with legal format and content of GVP VIII, can be applied to PASS protocols
- Provides structure for evaluation of suitability of RWD sources for a given research question based on the forthcoming EMA metadata catalogue for data sources
- Used a template for generic protocols for DARWIN EU® studies


Received: 7 February 2022 | Revised: 17 June 2022 | Accepted: 28 June 2022
DOI: 10.1002/pds.5507

ORIGINAL ARTICLE

WILEY

HARmonized Protocol Template to Enhance Reproducibility of hypothesis evaluating real-world evidence studies on treatment effects: A good practices report of a joint ISPE/ISPOR task force

Wang SV et al. Value Health. 2022;25(10):1663-1672

Methodology Working Party

- Established by **CHMP** to leverage expertise in key areas: **RWE**, biostats, modelling/simulation, PK, PGx
  - **Product-related** support to EMA Committees and SA Working Party
  - Engagement with **stakeholders** (regulators, trade associations, patient/HCP organisations)
  - Preparation, review, update of **guidelines**/concept papers, **training** and workshops for assessors
- **EU experts** nominated by CHMP, 3-year **work plan**
- Info on mandate and procedures to become soon available

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

15 December 2022
EMA/CHMP/58124/2023
Human Medicines Division

Consolidated 3-year work plan for the Methodology Working Party (MWP)

Chairperson: Kit Roes

Vice chair: Kristin Karlsson

Work plan period: May 2022 – December 2024 (with a first review point after one year)

https://www.ema.europa.eu/en/committees/working-parties-other-groups/chmp/methodology-working-party

International collaborations

- HMA/EMA Big Data initiative in EU, US RWE framework, Health Products and Food Branch Notice in Canada
- Challenges remain (e.g., RWD/RWE definitions, data governance…)
- Opportunities from COVID-19: new collaborations, effective sharing of data, knowledge and experience

→ Call from stakeholders for international **convergence** and where possible, harmonisation

→ Building on ICMRA COVID-19 collaborations for observational studies → workshop in June 2022 to **identify areas for international collaboration**

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Health Canada

FDA U.S. FOOD & DRUG ADMINISTRATION

- July 2022: ICMRA statement on international collaboration to enable RWE for regulatory decision-making
- 4 focus areas for regulatory cooperation:
  - **Terminology** harmonisation
  - Regulatory convergence on RWD and RWE **guidance** and best practice
  - Readiness to address **public health** challenges and emerging health threats
  - **Transparency**
- Concluded that to progress, existing fora should be leveraged, notably ICH

- **ICH Reflection Paper** to engage ICH on convergence of terminology and format of protocols/reports, and inform assessment of RWD/RWE for regulatory purposes
- Impact: higher quality RWE that can substantively contribute to body of evidence supporting benefit/risk decision-making

  (status: under consultation by ICH MC)
- Complementary to **ICH M14** "*General principles on planning and designing pharmacoepidemiological studies that utilize RWD for safety assessment of a medicine*" (target early 2025)

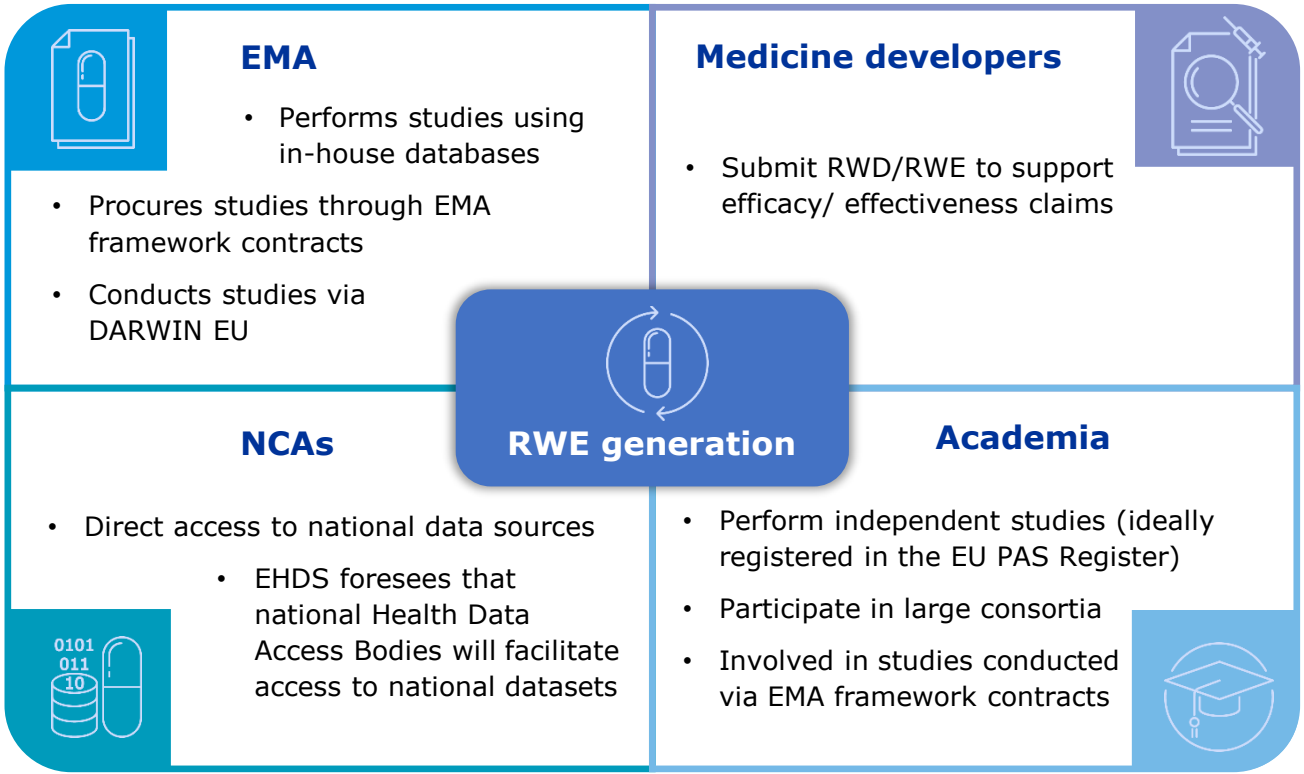
Outline

01 Evolving landscape of EU RWE guidance

02 Updates: RWE-related activities at EMA, DARWIN EU®, EHDS

03 Key messages

Who delivers RWE in the EU?



Three main areas where RWD analyses support decision-making

1 Support the planning and validity

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

2 Understand the clinical context

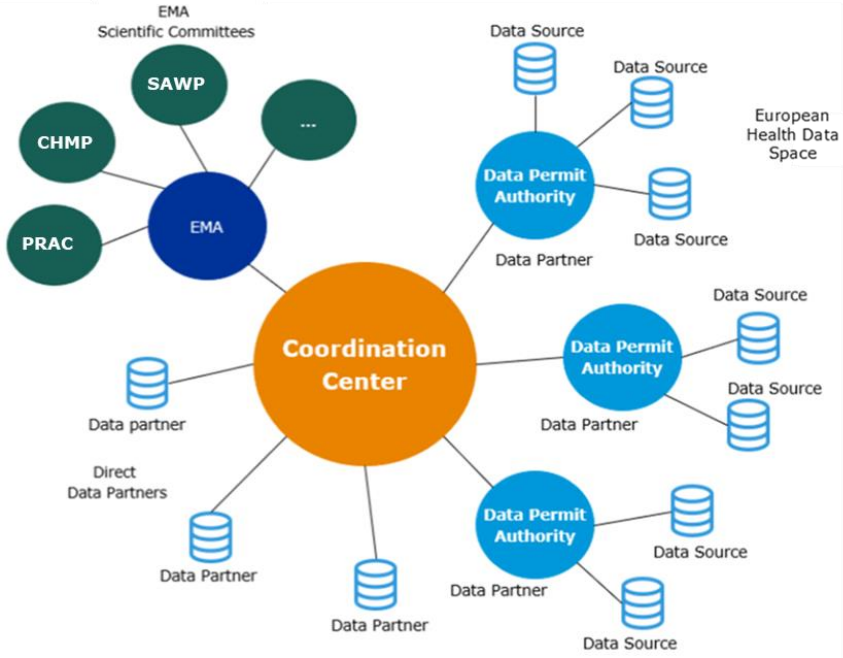
- Disease epidemiology
- Clinical management
- Drug utilisation

3 Investigate associations and impact

- Effectiveness and safety studies
- Impact of regulatory actions

DARWIN EU®: key tool for EU regulators

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**



High level timelines

2021

- Selection of the Coordination Centre provider

2022/2023

- Coordination centre set-up, incl. operational processes and governance
- Establish connectivity with EHDS and existing Data Permit Authorities
- First catalogue of standard data analyses available
- Start recruiting and onboarding data partners
- Start running pilot studies to support EMA committees

2024

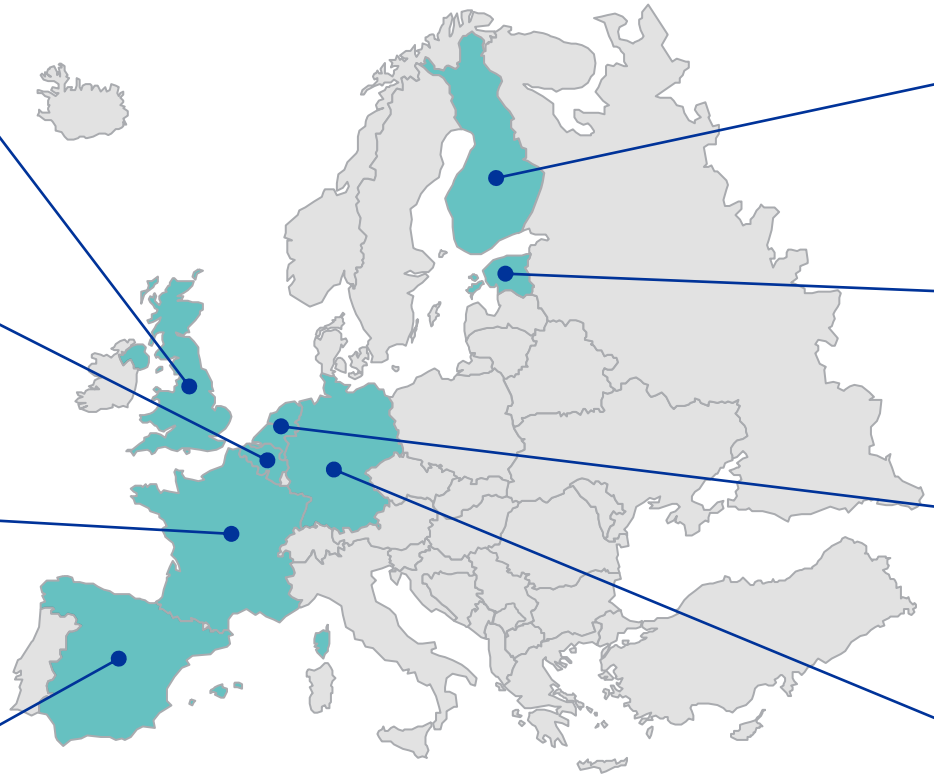
- DARWIN EU® to be operational and routinely supporting the scientific evaluation work of EMA's committees and NCAs by delivering studies and maintaining data sources

2025/2026

- DARWIN EU® to be fully operational and yearly evolves to meet the needs from the EU regulatory network
- Full integration with the European Health Data space (EHDS)

Onboarding of data sources: 10 each year from 2022 to 2025 (total of **40+**)

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

Types of analyses/studies delivered

Category of observational analyses and studies	Description
Routine repeated analyses	**Routine analyses based on a generic study protocol** • Periodical estimation of drug utilisation • Safety monitoring of a medicinal product • Estimation of the incidence of a series of adverse events
Off-the-shelf studies	**Studies for which a generic protocol is adapted to a research question** • Estimate the prevalence, incidence or characteristics of exposures • Health outcomes • Describe population characteristics
Complex Studies	**Studies requiring development or customisation of specific study designs, protocols and Statistical Analysis Plans (SAPs), with extensive collection or extraction of data** • 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
Very Complex Studies	**Studies which cannot rely only on electronic health care databases, or which would require complex methodological work** • 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

Studies/use cases - Phase I

Type	Studies	Data Partners	EMA committee	EU PAS Register #
Off the Shelf	**Population level epidemiology** study on prevalence of **rare blood cancers** from 2010.	NL, ES, UK, BE, DE	e.g., COMP	EUPAS50800
Off the Shelf	Patient level **drug utilization** study of **valproate-containing medicinal products** in women of childbearing potential from 2010	NL, ES, UK, BE, DE, FI	PRAC	EUPAS50789
Off the Shelf	Patient level **drug utilisation** study of **antibiotics** on the Watch list of the WHO AWaRe classification, 2010-2021	NL, FR, ES, DE, UK	PRAC – CHMP AMR strategy CMDh EMA V-Div (→ECDC)	EUPAS103381
Complex	Background all-cause **mortality rates in patients with severe asthma ≥12 years** old	NL, ES x2, UK, EE	CHMP PRAC	

What next?

- Prioritisation, selection, **onboarding** of next 10 DAPs, open call for of interest
- Prioritisation and initiation of **studies** in Phase II
- Data Protection Impact Assessment update

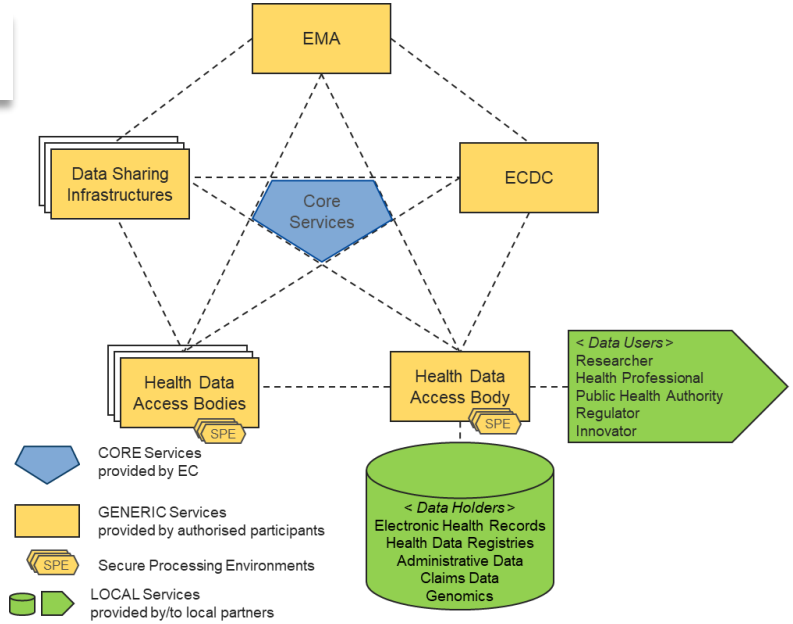
By 2025, ~150 studies/year

- How to capture and generate analyses of **Patient Experience Data** (PED) - e.g., PROs may be held and analysed in DARWIN EU®
- Patient representatives involved in BDSG/ DARWIN discussions
- Work on Big Data and PED closely coordinated at EMA

- Publication of **RWE experience report** to evaluate opportunities & challenges of all RWE (from DARWIN, in-house data sources, and framework contracts) provided by EMA to support committees Sept. 2021-Feb. 2023 (report mid 2023)

European Health Data Space

- EC proposed legislation to enable **effective use of health data** in the EU
- Primary use of health data for care (MyHealth@EU) and re-use (**HealthData@EU**: new **infrastructure** connecting data access bodies and data sharing infrastructures)
- Several health data access bodies established, or in the process, across MS
- Pilot phase: 5 **use cases** to inform HealthData@EU (legal, governance, infrastructure, data quality, capacity, digitalization) → reports in Q3 2024
- Integration of DARWIN EU® will be tested **DARWIN as pathfinder/node**



Natural history of coagulopathy (blood clotting) related events in COVID-19 patients and risk factors

Led by EUROPEAN MEDICINES AGENCY

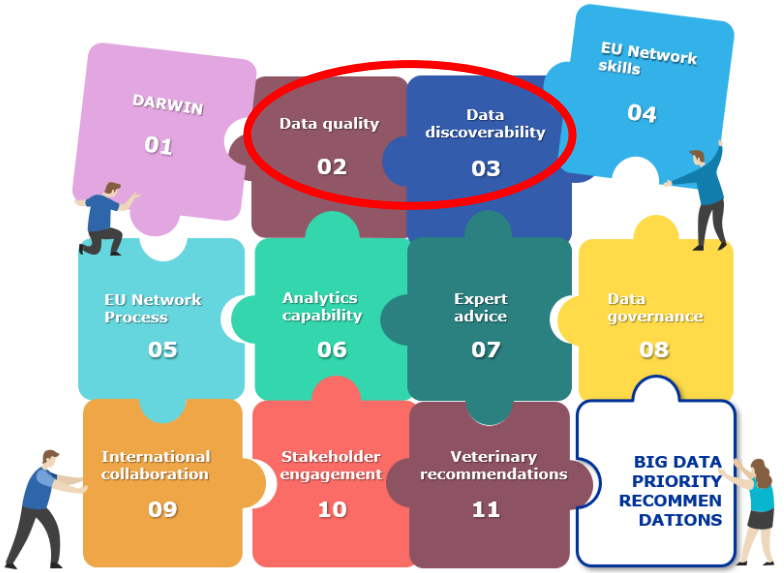
EMA use case: Research teams and data nodes from Finland, France, Denmark and Croatia

Some other updates…

Expected in **Q1 2023**:

- Publication of the final **Data Quality Framework** (following public consultation)
- Publication of the final **Good Practice Guide** on use of real-world metadata (following public consultation)

→ supports go-live by early 2024 of **catalogues** of EU **RWD sources** and **observational studies**



By **Q4 2023**:

- Migration from **ENCePP** Resources database and EU PAS Register and data enrichment; new and improved ENCePP website
- Launch/publication and maintenance of new EU real-world **metadata catalogue**

Registries and **HTA** workshop end 2023

Key messages

By 2025, **transformation to data-driven regulation**

→ **Use of RWE** will have been enabled and its value will have been established across the spectrum of regulatory use cases

→ **DARWIN EU®** network as part of **EHDS** will support better decision-making

→ Through public searchable **catalogues**, **data** will be **discoverable** and of known **quality** and **representativeness** allowing choice of optimal data sources, enabling regulators to guide development and expertly assess study results

→ Suite of EU and international **guidelines** and **standards** available to help industry and regulators develop and supervise medicines

→ Guided by **patients** and working with **stakeholders** to deliver data transformation to support the development and use of better medicines for patients

Better evidence supports innovative medicines for patients and safer and more effective use

Further information

DARWIN EU

Big Data

Big Data Highlights

Subscribe for updates:
bigdata@ema.europa.eu

EMA data quality framework for medicines regulation

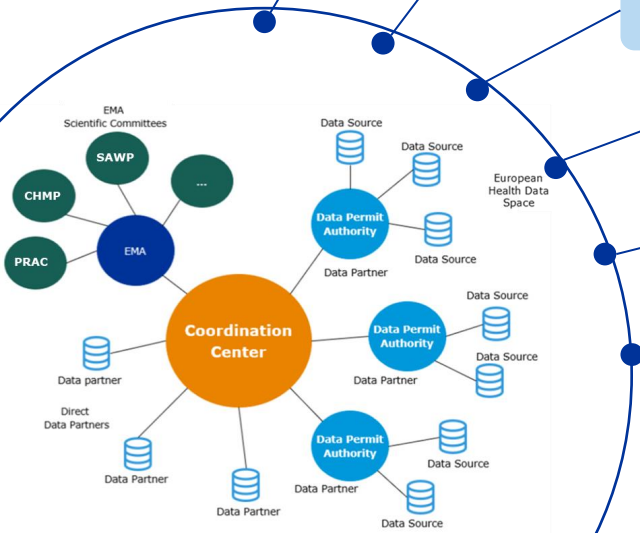
EMA events

catherine.cohet@ema.europa.eu

Official address Domenico Scarlattilaan 6 • 1083 HS Amsterdam • The Netherlands
Telephone +31 (0)88 781 6000
Send us a question Go to www.ema.europa.eu/contact

Follow us on **@EMA_News**

DARWIN EU®: key tool for EU regulators



Provide **scientific expertise** in formulating and executing studies and analyses

Maintain a **catalogue** of known, relevant data holders, continually ensuring **discoverability & quality** of data held by data holders

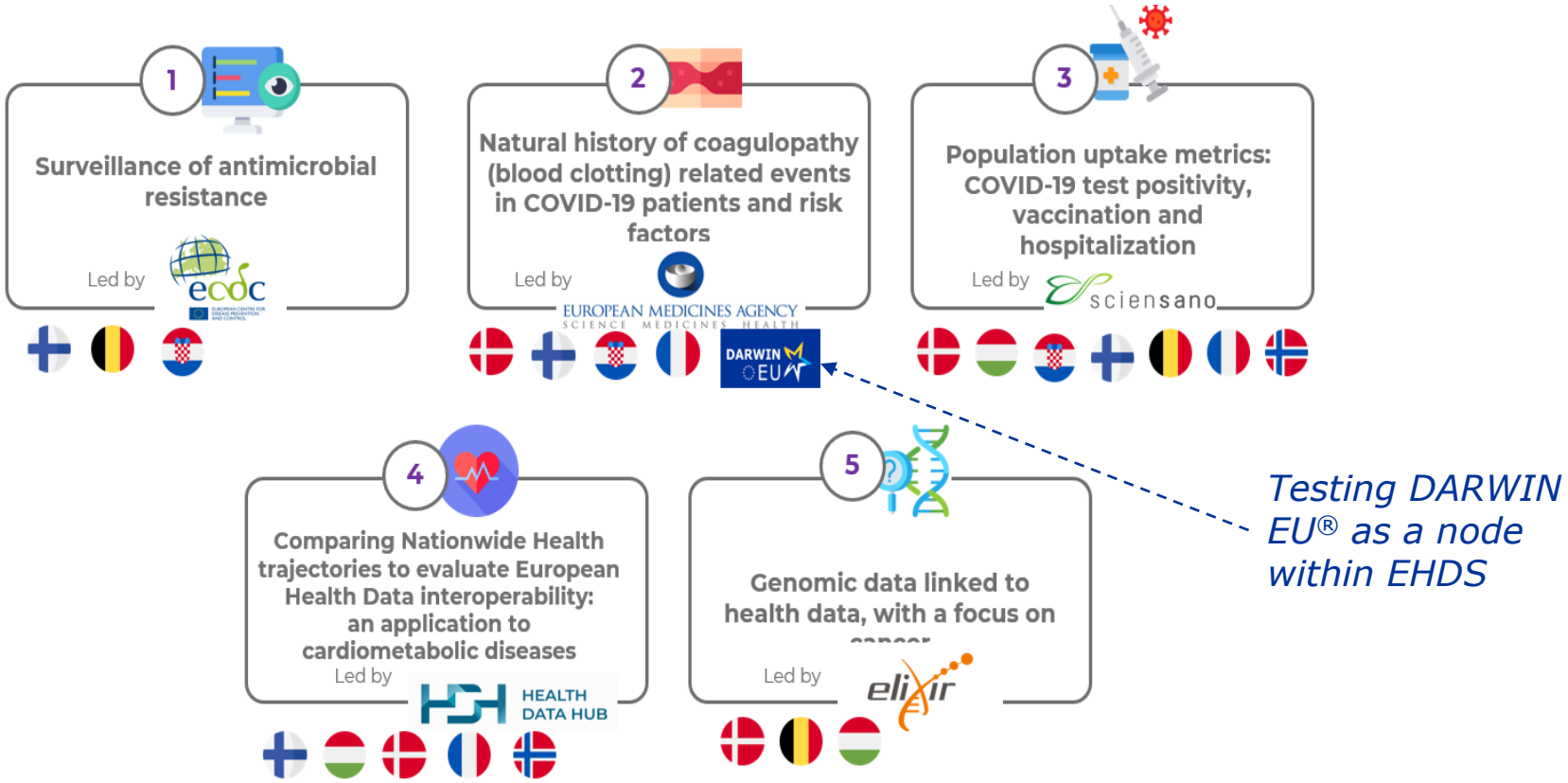
Maintain & expand the **federated network** of data partners, assisting new data holders in conforming with required standards for usage in regulatory context

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'

EHDS pilot


1
Surveillance of antimicrobial resistance
Led by
ecdc
2
Natural history of coagulopathy (blood clotting) related events in COVID-19 patients and risk factors
Led by
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH
DARWIN EU
3
Population uptake metrics: COVID-19 test positivity, vaccination and hospitalization
Led by
sciensano
4
Comparing Nationwide Health trajectories to evaluate European Health Data interoperability: an application to cardiometabolic diseases
Led by
HEALTH DATA HUB
5
Genomic data linked to health data, with a focus on
Led by
elixir
Testing DARWIN EU® as a node within EHDS