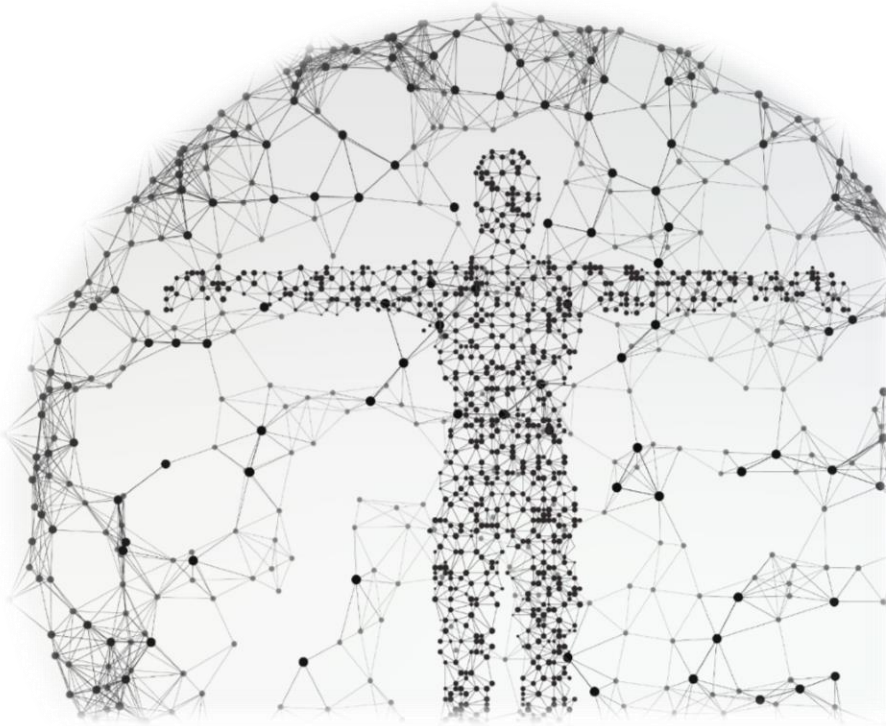
Coordination Centre

DARWIN EU®

Prof. Dani Prieto-Alhambra
University of Oxford, Erasmus MC
Deputy Director, DARWIN EU® Coordination Centre

ENCePP plenary, 30 November 2022



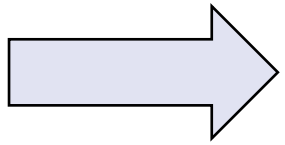
Disclosure

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.

RWE generation for regulatory purposes: Challenges and solutions

Generating Real-World Evidence (RWE) from Real-World Data (RWD)

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

RWE for regulatory purposes needs to be:

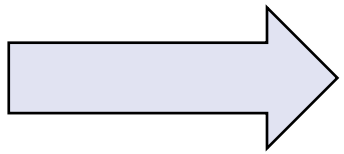
- **Fast, transparent, scalable and reproducible**
- Representative (of EU regions)

The challenge

The European Union (EU) has a rich and diverse healthcare data landscape.

However, this diversity brings challenges in terms of a common data structure, terminology, and governance.

There is limited access to data, and the processes for accessing and analysing data for regulatory purposes are slow and complex.

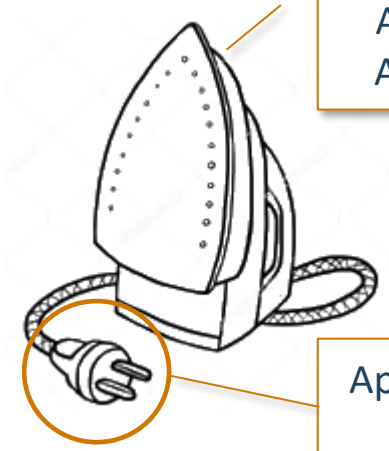


Data Analysis and Real World Interrogation Network (DARWIN EU®)

The challenge: bespoke analytics for heterogeneous data

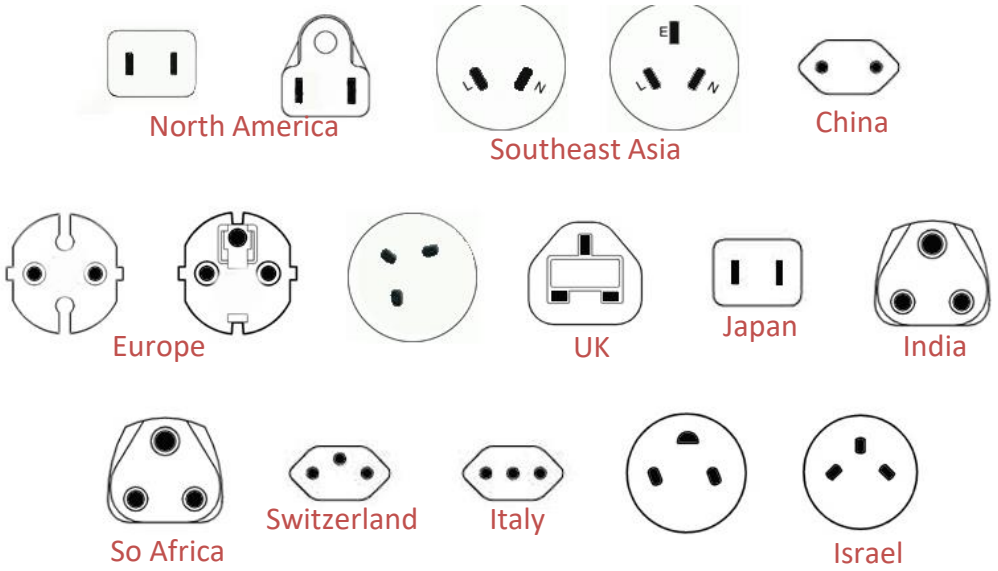
- Increasing productivity to an industrial level requires the automation of the analytical processes, which in turn cannot be done without a rigorous standard representation of the data.
- Full interoperability of the data is needed with respect to structure (syntactic interoperability) and coding systems (semantic interoperability) by using a Common Data Model (CDM)

Current Approach: “One Study – One Script“

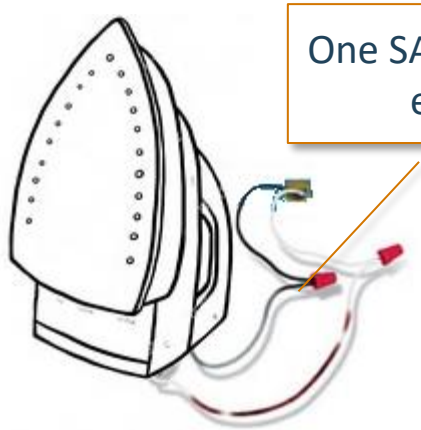


Analytical method: Adherence to Drug

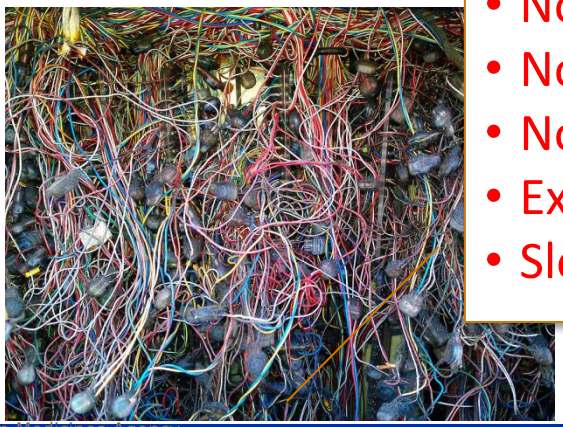
Application to data



Current solution:

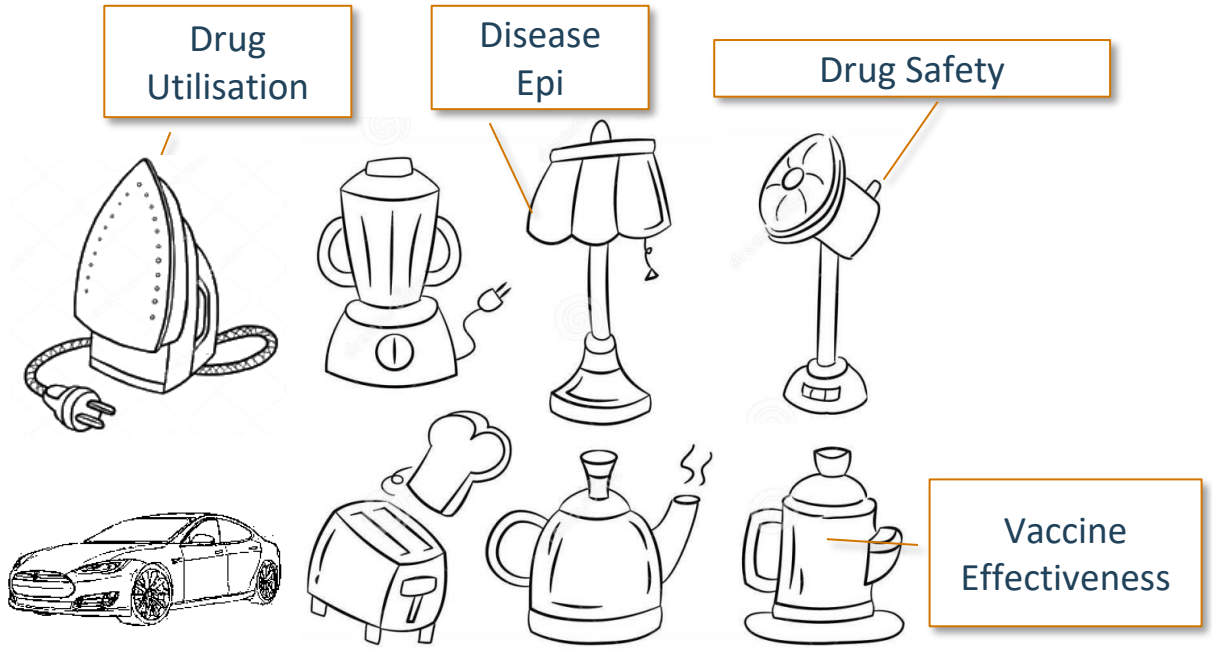


One SAS or R script for each study



- Not scalable
- Not transparent
- Not reproducible
- Expensive
- Slow

Solution: Data Standardization and Standardised Analytics



Standardized analytics → Standardized data

8

Setting up the DARWIN EU® Coordination Centre

DARWIN EU® Vision

To establish and maintain a framework supporting better decisionmaking throughout the lifecycle of medicinal products with timely, valid and reliable evidence from real world healthcare.

Objectives:

1) To establish and maintain a continually enlarging network of accessible observational data sources
2) To execute all steps of high quality non-interventional studies with the network
3) To make the study results available to the EU Regulatory network to support decision-making

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

Erasmus MC
Universitair Medisch Centrum Rotterdam

Sub-contractors

UNIVERSITY OF OXFORD

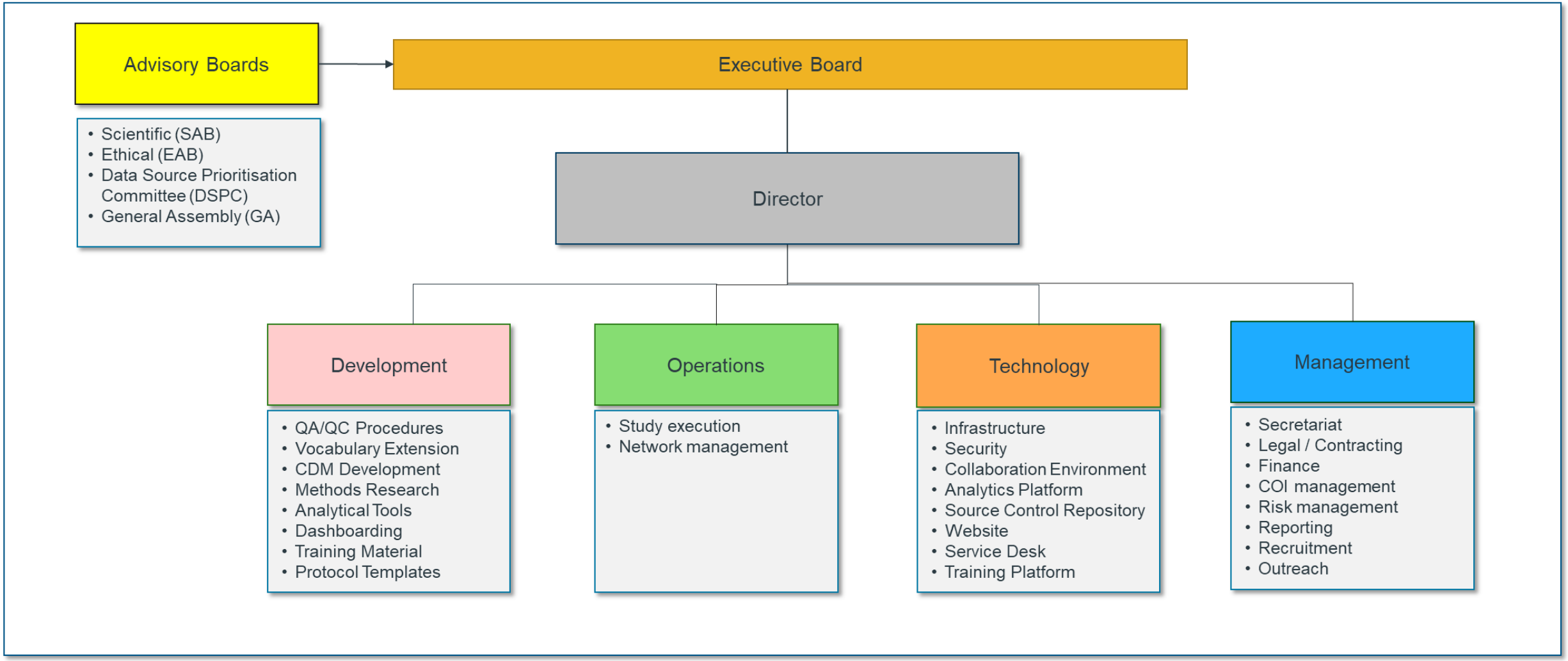
SYNAPSE
RESEARCH MANAGEMENT PARTNERS

IQVIA

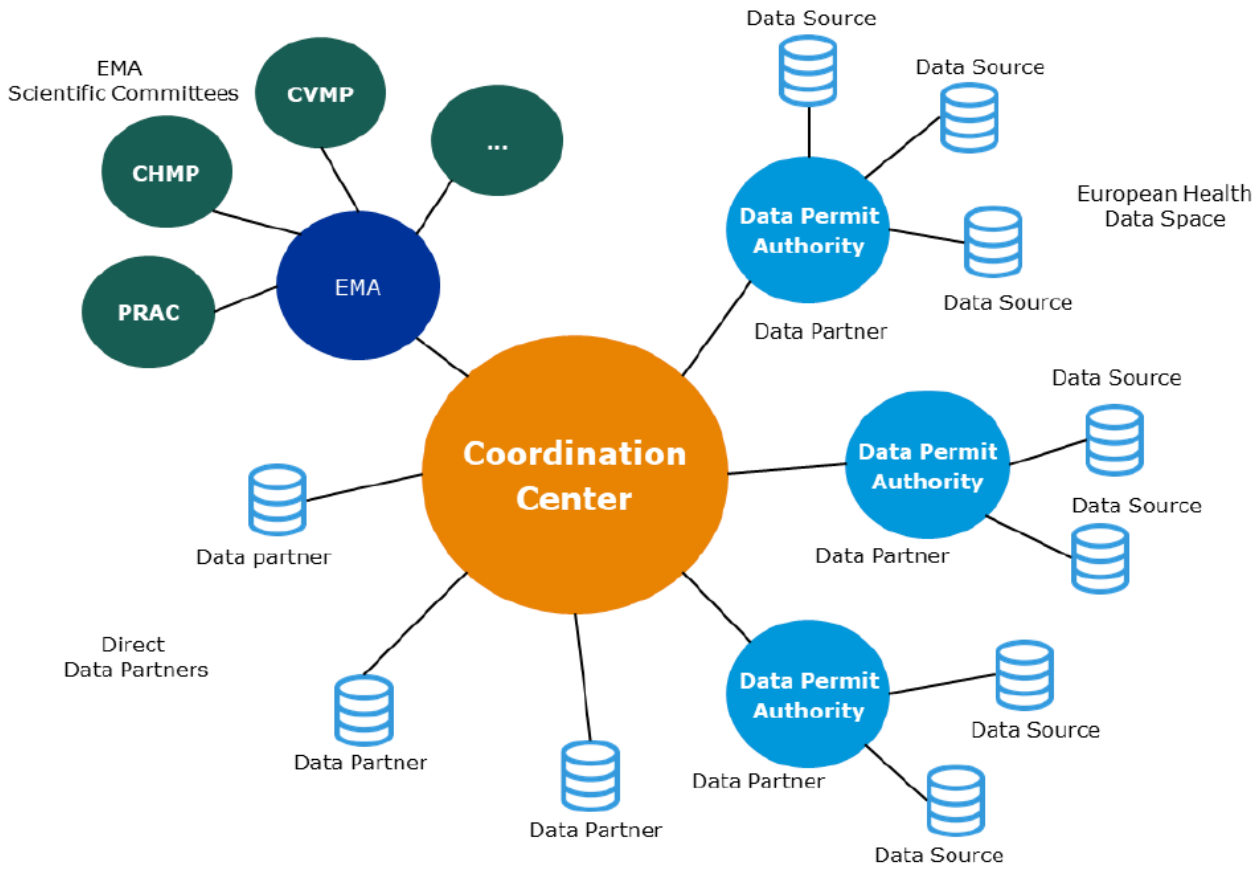
The Hyve

ODYSSEUS
DATA SERVICES INC

Establishment and Evolution of the Coordination Centre



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** to perform studies in a timely manner and increase consistency of results

Which data sources will DARWIN EU® use?

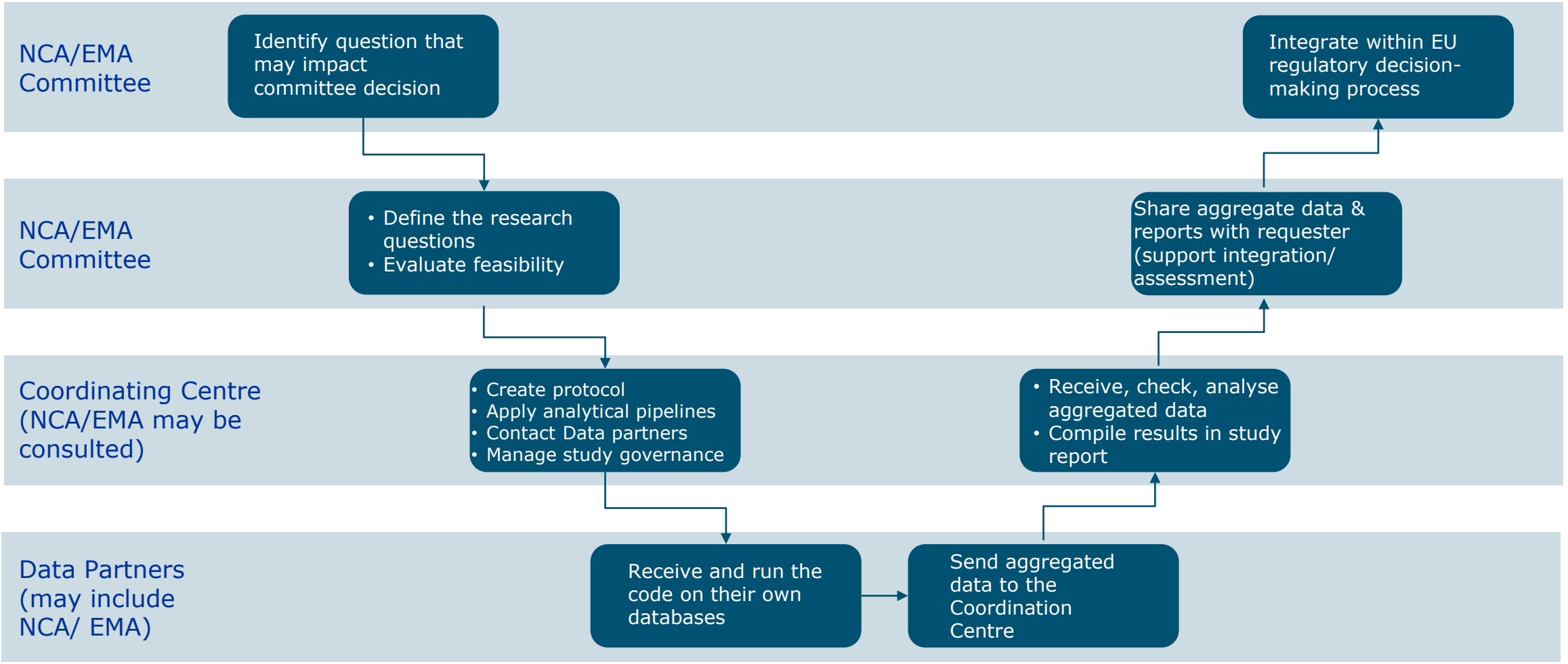
Data sources will be onboarded over time taking into account the following criteria:

- 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

What analyses and studies will DARWIN EU® deliver?

Category of observational analyses and studies	Description
Off-the-shelf studies	Studies for which a generic protocol is adapted to a research question
Complex Studies	Studies requiring development or customisation of specific study designs, protocols, phenotypes, etc
Routine repeated analyses	Routine analyses based on Off-The-Shelf or Complex Studies (see above), repeated periodically with a pre-specified regularity (e.g. yearly)
Very Complex Studies	Studies which cannot rely only on electronic health care databases, or which would require complex and/or novel methodological work

What is the DARWIN EU® process for conducting studies?



Draft Catalogue of Standard Analyses:
Off-the-shelf studies and examples

Standard Analysis	Regulatory example
Population-level disease epidemiology	• Prevalence of rare disease/s • Background rates of AESI or DMEs
Patient-level disease epidemiology	• Natural history/prognosis • Current practice/treatment patterns
Population-level DUS	• Incidence and prevalence of use of medicine/s over time
Patient-level DUS	• Describing indication/s for drug/s • Treatment duration, cumulative use

Draft Catalogue of Standard Analyses:
Complex studies and examples

Standard Analysis	Regulatory example
RMM Effectiveness	• Incidence of drug/s use before and after a regulatory action • Medicine/s user/s profile after new indication or contraindication
New user, active comparator, cohort studies	• Post-authorisation safety study • Comparative effectiveness
Self-controlled case series	• Vaccine safety surveillance

PROGRESS TO DATE AND NEXT STEPS

DEVELOPMENT

- New pipeline for population-level disease epidemiology
- Pipeline for DP onboarding
- Other tools upcoming, e.g. DUS

OPERATIONS

- Year 1 (n=10) DPs shortlisted and going through the onboarding process
- 4 studies requested, 3 ongoing

TECHNOLOGY

- Website being finalised
- Tools for federated execution
- Comms and Teams environment

MANAGEMENT

- Multiple deliverables submitted and approved
- Progress to Phase 2

Data Partners – Phase I

UK

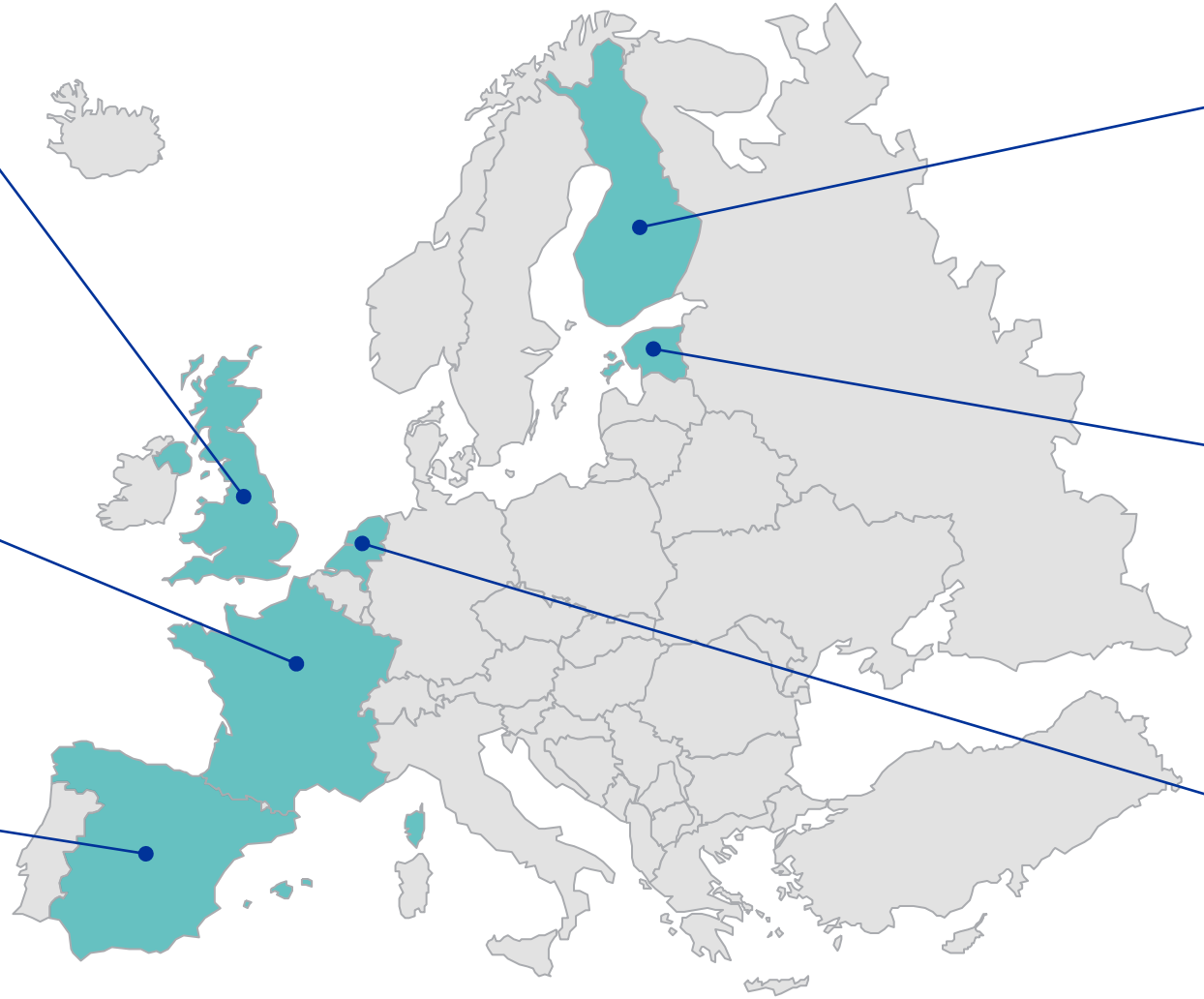
- Clinical Practice Research Datalink (CPRD GOLD)

France

- Bordeaux University Hospital

Spain

- IDIAPJGol
- Parc Salut Mar Barcelona, Hospital del Mar (IMIM)



Finland

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

Estonia

- University of Tartu (EE Biobank)

Netherlands

- Integrated Primary Care Information
- Netherlands Comprehensive Cancer Organisation

This slide has been edited for publication

DARWIN EU® Studies – Phase I

Type	Studies	Data Partners	Planned RWE use	Committee	
OTS	**Population level epidemiology** study on prevalence of **rare blood cancers** from 2010.	NL, ES, UK, BE, DE	Support COMP in orphan designation decision making	COMP	Ongoing
OTS	Patient level **drug utilisation** study of **valproate-containing medicinal products** in women of childbearing potential from 2010	NL, ES, UK, BE, DE, FI	Assess the use of valproate after safety referral	PRAC	
OTS	Patient level **drug utilisation** study of **antibiotics** on the Watch list of the WHO AWaRe classification, 2010-2021	NL, FR, ES, DE, UK	Inform PRAC/CHMP decision making	PRAC – CHMP AMR strategy	
Com plex	Background all-cause **mortality rates in patients with severe asthma aged ≥12 years** old		Support CHMP evaluation and post-authorisation informing future decision making	CHMP	Draft protocol

DARWIN and ENCePP

- **DARWIN EU CC registered as an ENCEPP Network**
- **ENCePP Centres** involved, including Erasmus MC HDS as Contractor
- **ENCePP Database/s** selected amongst first onboarded Data Partners:
  - IPCI (NL), CPRD (UK), SIDIAP (ES)
- **DARWIN EU Catalogue of Standard Analyses** and related methods inspired by *ENCePP Guide on Methodological Standards in Pharmacoepidemiology*
- **DARWIN EU DoI policy** based on *ENCePP Code of Conduct* and *CoI* form

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