The Data Analysis and Real-World Interrogation Network in the European Union (DARWIN EU)

ENCePP in the Time of Covid – Meeting 20th November 2020

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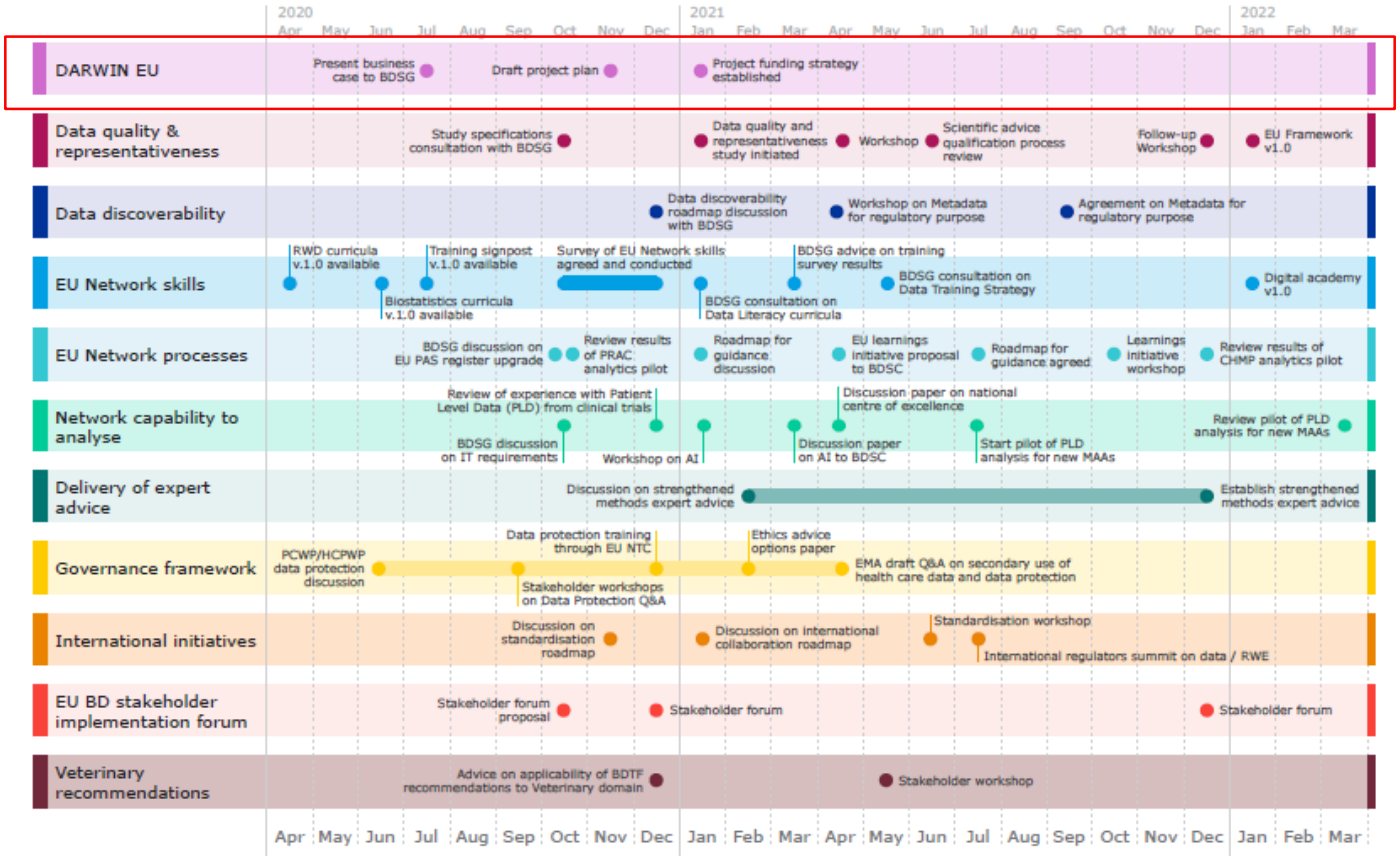
THE HMA-EMA JOINT BIG DATA STEERING GROUP WORKPLAN



Outline

- **DARWIN EU vision**
- Regulatory use cases
- Target operating model
- Evolving with the European Health Data Space
- Delivering DARWIN EU
- Conclusion

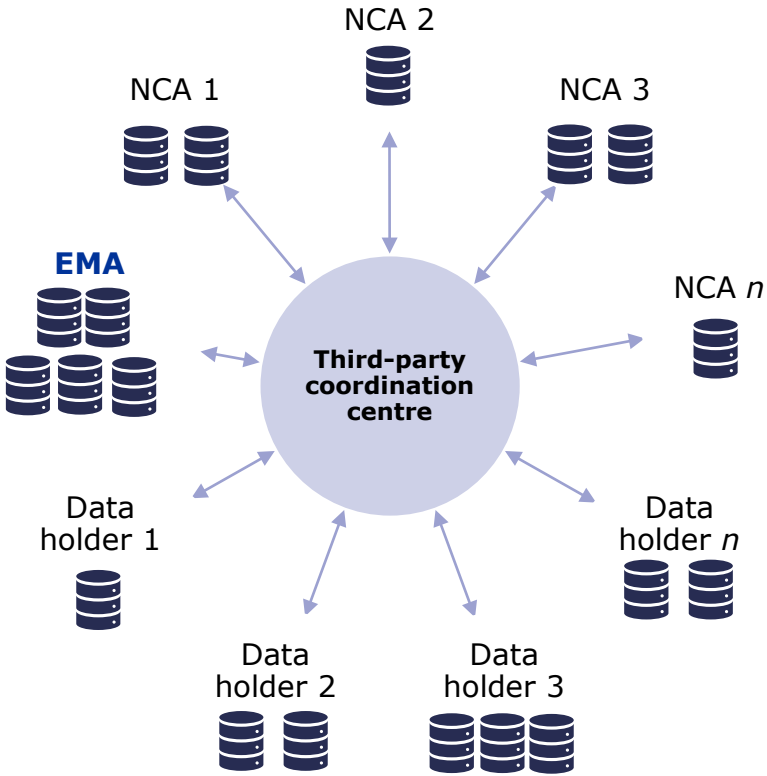
DARWIN EU scope

- Establish a **network of data, expertise, and services to support better decision-making by EMA and NCA scientific committees** on the benefits and risks of products via rapid access and analysis and increased reliability, validity and representativeness of EU health data in order to:
  - complement clinical trials and support the development, authorisation and supervision of medicines: supports patient access and, safe and effective use;
  - support the development of innovated medicines, deliver life-saving treatments to patients more quickly and optimise the safe and effective use of medicines through monitoring of a products performance on the market;
  - support early access to medicines thereby fulfilling the unmet medical needs of EU citizens,
  - support a learning healthcare system for marketed products enabling safe and effective use of medicines; and
  - establish evidentiary value of real-world evidence.

- Published business case for DARWIN

What is DARWIN EU?

- DARWIN EU is a network of data, expertise and services, not a database
- Main characteristics:
  - Distributed network for fast access and analysis
  - Federated data access
    - Data stays local
    - Data exchanged within the network is anonymous
    - Queried remotely
    - Includes use of a common data model for fast analysis
  - Include a Third party coordination centre :
    - **Data management and data quality activities**: Identification of the relevant databases , standards, individual agreements with data holders, transformation to a CDM, data quality
    - **Study analysis activities**: for running analyses to support EMA/NCAs/Committees
- EMA will have responsibility for managing the network and act as a data holder within it



Published business case for DARWIN

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DARWIN EU operating model (1/2)

- The Coordination Centre is envisaged as an outsourced service.
- Once established, it will provide and operate the service on behalf of the EU Regulatory Network.
- It will be responsible to:
  - Establish and operate a service centre handling and processing requests to support:
    - Data management and data quality activities: Identification of the relevant databases , standards, individual agreements with data holders, transformation to a CDM, data quality
    - Study analysis activities: for running analyses to support EMA/NCAs/Committees
    - In addition to training, governance, contract management, support of business services.

DARWIN EU operating model (2/2)

- Coordinating centre establishes and operates the necessary **IT & communications infrastructure**:
  - Software and tools for managing the data, analyse and visualise
  - Software for converting the data to a CDM and a common software to run the analyses distributed through the network
  - Platform to safely share scripts, analysis results and visualisations between the different data sources
  - Collaboration and support services, e.g. service request / ticketing systems, telephone, chat or email based service for queries

- EMA/Network will retain strategic and decisional activities and essential operations, e.g. interface with EMA committees, EMA own analysis including essential data management, driving standards, specifications, guidelines, management of third party.

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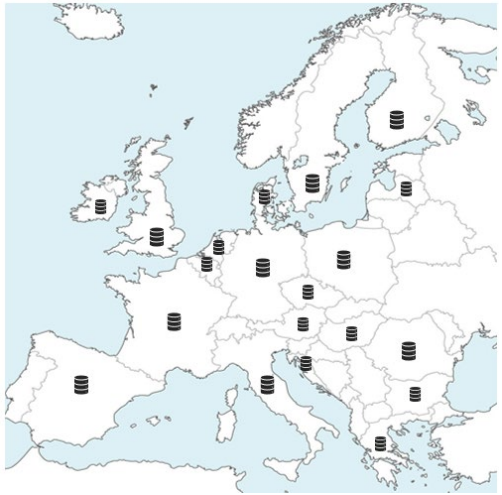
Evolution: DARWIN EU as pathfinder initiative in EU Health Data Space

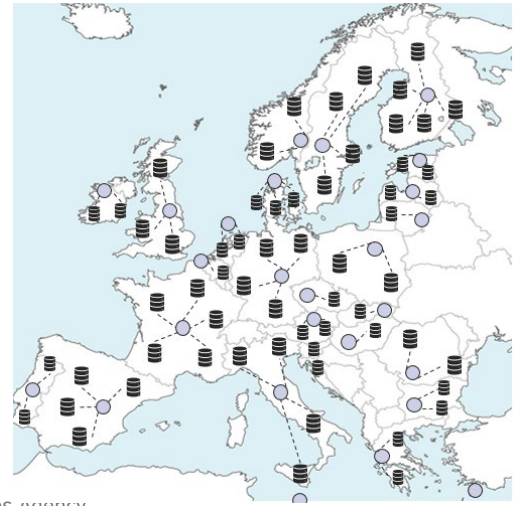
DARWIN EU **2023**

- Coalition of existing datasets with medicines regulators
- Federated access to data holders



DARWIN EU **evolution**

- Node in the EHDS
- Access including Data Permit Authorities (○ DPerA)



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Following an iterative approach

2021

EMA established as a node

- Rapidly generating evidence from electronic health data directly accessible in-house and embed it in core regulatory processes, piloting the federated network
- Focus on supporting 1st EMA committees

Network and Coordinating centre preparation

- Support pilot of the European Health Data Space
- Define governance, contract model, on-boarding and Coordinating center use processes
- Select 1st DARWIN EU data partners
- Data protection requirements established
- Support NCAs that may want to start establishing themselves as a node

2022

Collaboration with already established Data Permit Authorities (DK, FI and FR) and leverage work done by EHDEN

- Testing business process to collaborate with external nodes in term of accessing the data, data protection and ethical approval, and common analytics for data sources converted in the OMOP CDM
- Support other EMA committees

2023

DARWIN EU first version delivered

- Federated network established with a coalition of existing datasets with medicines regulators
- Use cases expanded to all committees

2025

Fully leverage the EU Health Data Space

- Leverage legislation on Data Permit Authorities to increase the number of nodes and access of the data in the network (increase geographical spread, type of healthcare delivery and type of data).

Main objectives for 2021

- Immediate: Securing project funding and agree for Fee regulation update
- Delivery/operating models finalised
- Sourcing strategy (service provider) progressed
- Pilot with the European Health Data Space initiated
- Change management initiated
  - Benefiting from DARWIN EU will require change management and need to ensure it meets the needs from the EU Network and is fully integrated into the EU regulatory system and decision making processes
  - Need strong engagement with the EMA committees and with stakeholders including ENCePP

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How the DARWIN network might operate: Data management and quality activities

Foundational activities – yearly frequency

EMA

Define and maintain specifications for metadata, quality, reporting format

EMA/Coordinating centre

Identify the relevant databases

Coordinating centre

Updating specifications

Individual agreements with data holders

At every database refresh

Data holders

Data quality activities

Coordinating centre

Check and sign-off on data quality results

Coordinating centre

Data & metadata characterisation

Information available on dashboards

How the DARWIN network might operate: NCA/EMA committee initiates an analysis

NCA/EMA Committee

Question that impacts committee opinion

NCA/EMA

Evaluates relevance and feasibility of RWD

Define the research questions

Coordinating centre

Create protocol and programming code

Contact relevant DBs holders

Manage specific study governance

Data holders (may include NCA/EMA)

Receive and run the code on their own DBs

Aggregate data and results sent to the coordinating centre

Receive, check, analyse aggregate data

Compile the results in a study report

Share aggregate data and reports with committees (and support integration/assessment)

Integrate data and reports in the assessment report

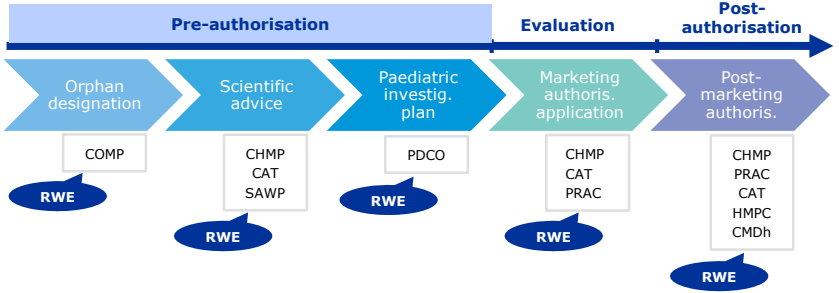
DARWIN EU: Benefits

- Principal benefits relate to the national and EU regulation of medicines
  - Drug development – disease epidemiology, unmet need, historical controls, planning
  - Authorisation – contribution to BR, controls, extrapolation to general & special populations
  - On market – benefit risk monitoring, extension of indication

- Additional benefits will come as EU partners participate and access the platform
  - European Commission – delivers on 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

Regulatory use cases are numerous

PRE-AUTHORISATION (1/3)

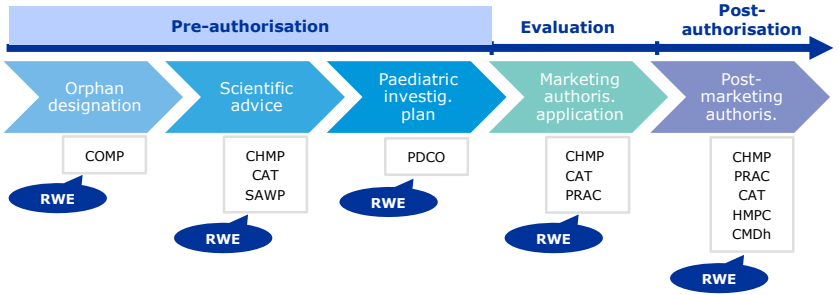


Committee for Orphan Medicinal Products (COMP)

- RWE to check prevalence of diseases to support orphan designation
  - A disease is defined as rare if it affects fewer than 5 in 10,000 people across the EU
  - An orphan designation allows a pharmaceutical company to benefit from incentives from the EU, such as reduced fees and protection from competition
  - For an orphan designation the company must demonstrate prevalence
  - RWE from DARWIN EU will provide data from multiple European countries to support the orphan designation

Regulatory use cases are numerous

PRE-AUTHORISATION (2/3)



Committee for Medicinal Products for Human Use (CHMP)

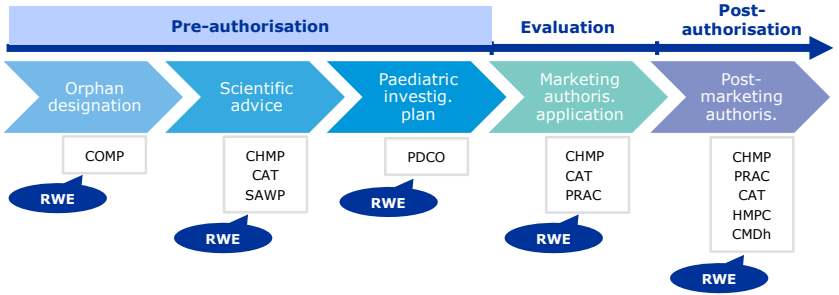
Committee for Advanced Therapies (CAT)

Scientific Advice Working Party (SAWP)

- Advising companies on use of RWE in product development based on feasibility and relevance of studies
  - Companies might want to use a new biomarker
  - Analysis of RWD can confirm the clinical outcome of short term surrogate markers

Regulatory use cases are numerous

PRE-AUTHORISATION (3/3)

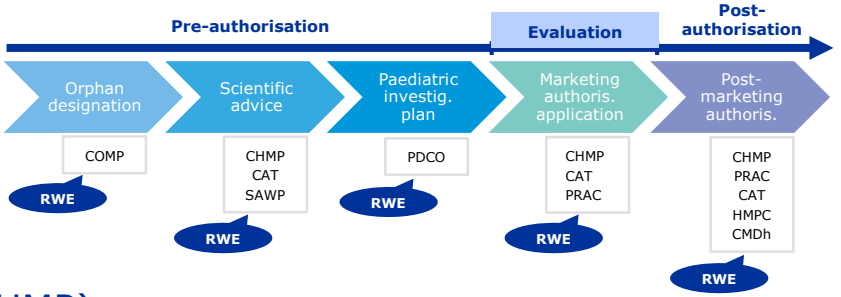


Paediatric Committee (PDCO)

- RWE to identify needs in children to support waivers and deferrals
  - Assessing applications for waiver and/or deferrals when development of a medicine in children can be delayed or it is not needed (i.e. for diseases that only affect the adult population)
  - Establishing and regularly updating an inventory of paediatric medicine needs

Regulatory use cases are numerous

EVALUATION (1/2)



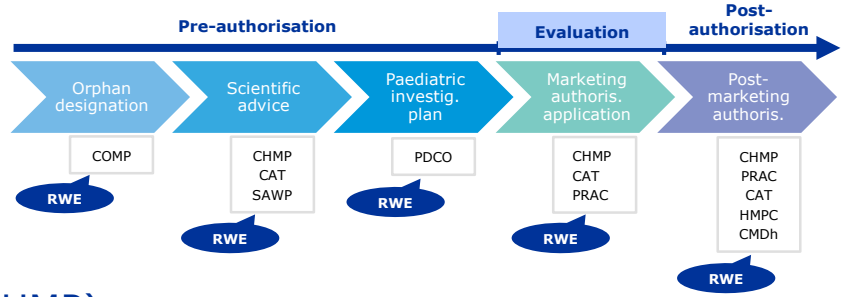
Committee for Medicinal Products for Human Use (CHMP)

Committee for Advanced Therapies (CAT)

- RWE to supplement, validate and contextualise clinical trial results to inform benefit-risk decision making
  - Use of external controls
  - Measure the representativeness of patients between the population studied in a CT and the target population of the new medicine
  - When appropriate validate study findings
  - Check that the standard of care used in the control arm of a CT is comparable with current real word standard of care

Regulatory use cases are numerous

EVALUATION (2/2)



Committee for Medicinal Products for Human Use (CHMP)

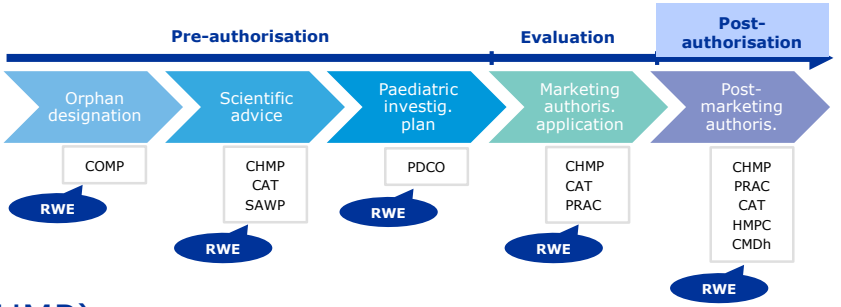
Committee for Advanced Therapies (CAT)

Pharmacovigilance Risk Assessment Committee (PRAC)

- RWE to inform decision-making on post-authorisation studies
  - Inform on the feasibility of imposed Post Authorisation Studies (e.g. number of incident patient per year to inform recruitment, data availability on specific diagnostic tests,…)

Regulatory use cases are numerous

POST-AUTHORISATION (1/2)



Committee for Medicinal Products for Human Use (CHMP)

Pharmacovigilance Risk Assessment Committee (PRAC)

Committee for Advanced Therapies (CAT)

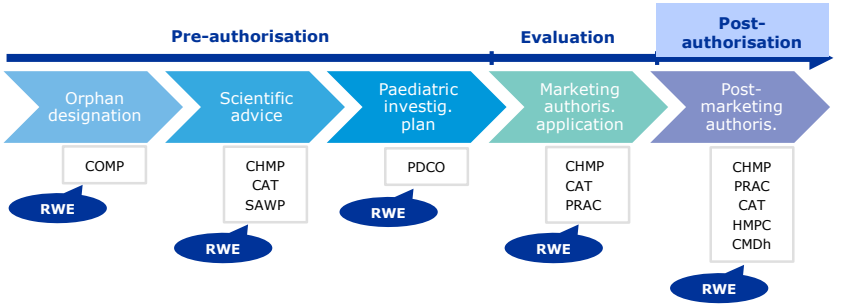
Committee on Herbal Medicinal Products (HMPC)

Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh)

- RWE to monitor the performance on the market and inform decision-making
  - Assessing benefit and risks on the market when imposing studies on specific companies is not appropriate
  - Assessing extension of indication and repurposing of medicines

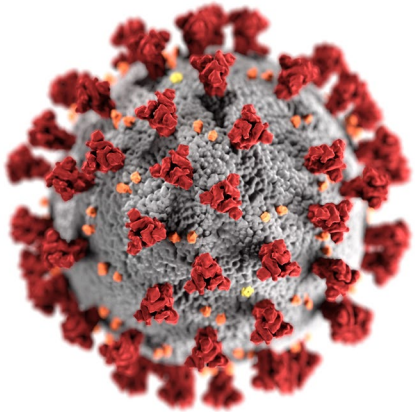
Regulatory use cases are numerous

POST-AUTHORISATION (2/2)



- RWE to monitor the performance on the market and inform decision-making
  - Safety and effectiveness in special populations especially of children and pregnant/lactating women
  - Identifying and monitor off label use
  - Characterisation of safety profile and monitor effectiveness of risk minimisation measures
  - Preparing a risk management plan

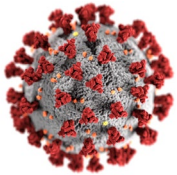
DARWIN EU: Central pillar for health crisis planning and response



Crisis response use cases include

- Understanding of the natural history of the disease to support drug development
- Provide evidence for repurposing existing medicines
- Monitor the safety of medicines and vaccines on the market
- Monitor use of medicines to predict demand and shortages

DARWIN EU: Central pillar for health crisis planning and response



The informed response to the pandemic brought an unprecedent interest and scrutiny in RWE

- Need to provide high-quality evidence focusing on strengthening all steps from data collection to assessment of evidence
- Need for timely answers

DARWIN EU will support future crisis responses with an operational infrastructure for conducting rapid studies

- EU wide network of data sources identified and characterised
- Quality framework and continuous quality monitoring
- Governance: prespecified agreements, processes and methods
- Availability of analytical tools with routine analyses already pre-specified

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Conclusion and interface with ENCePP

- DARWIN EU can deliver for better medicines regulation *and* be early deliverable for European Health Data Space
- DARWIN EU should be a central pillar of health crisis planning and response
- Interface with ENCePP
  - Access to data: supporting the identification and access to high quality data relevant to decision-making (e.g. promoting the use of FAIR principle)
  - Methods: update existing guidance on best practices, develop new guidance for new approaches (AI, pharmacogenomics), and use cases (beyond safety)
  - Governance principles: to strengthen collaboration with new networks
  - Network of excellence: ENCePP building capability and capacity through networking and best practice
  - Leverage ENCePP information tools (resources database + EU PAS Register)

Consulting ENCePP as foundation for European pharmacoepidemiology and RWE

Any questions?

Further information

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What the future could look like…

- **DARWIN EU network** will support better decision-making throughout the product lifecycle via its network of expertise/partnerships and databases
- **RWE will be a trusted and accepted source of evidence**
- **Data will be discoverable and of known quality and representativeness** allowing choice of optimal data source, enabling regulators to expertly assess study results
- **EMA and EU Network will have knowledge and experience** in data science, methods and analytics to advise companies developing products and to expertly assess application dossiers. **Committee decision-making will be enriched with expert advice** across the spectra of analytic and methodological approaches.
- **Learning initiative will allow to continue to** learn and evolve to rapidly be able to answer new regulatory needs, including response to future health crisis.
- **Suite of EU and international guidelines and standards available** to help industry and regulators develop and supervise medicines (built on learnings from submissions of Big Data and enhanced study transparency (EU PAS Register)
- **Full compliance with data protection and ethics** of data sharing
- **Collaboration** with all stakeholders, incl. patients and healthcare professionals
- Consulting ENCePP as foundation for European pharmacoepidemiology and real world evidence