HMA
Heads of Medicines Agencies

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

PCWP/HCPWP joint meeting

3 March 2021

Peter Arlett (EMA), Nikolai Brun (DKMA)
Co-chairs HMA-EMA Big Data Steering Group

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BDSG 2020 REPORT

WHAT WILL BE DELIVERED IN 2021

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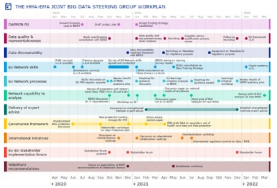
DARWIN EU UPDATE

Launching the Big Data Steering Group in 2020



Jan. 2020

'Ten recommendations to unlock the potential of big data for public health in the EU'

Sep. 2020

Making best use of big data for public health: publication of the Big Data Steering Group workplan for 2020-21

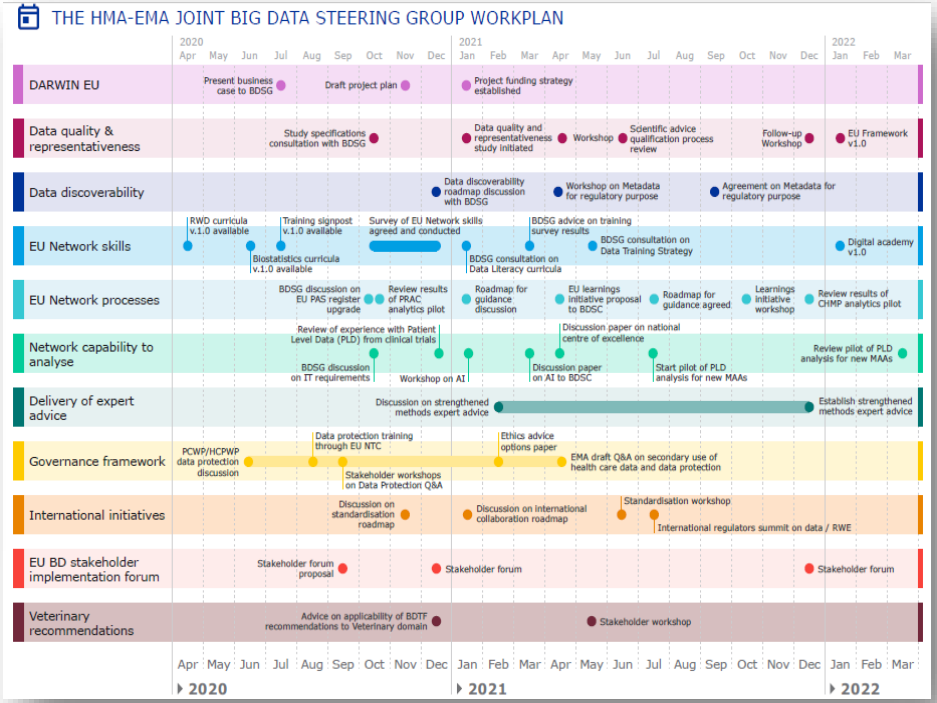
1st Big data steering group meeting in May 2020

May 2020

1st big data stakeholder forum

Dec. 2020

BDSG workplan publication



[Making best use of big data for public health: publication of the Big Data Steering Group workplan for 2020-21]

Big Data Steering Group: 2020 Report

1. **DARWIN EU:** Established project, funding and operating model + initiated planning for pilot of European Health Data Space
2. **Data Quality:** Defined scope for a study on a data quality framework for medicines regulation
3. **Discoverability:** Initiated a study to establish 'meta-data for real world data (RWD)'
4. **Skills:** Delivered a training signpost, a real-world evidence (RWE) curriculum and biostatistics curriculum
5. **Processes:** Progressed a PRAC RWE analysis pilot + initiated a CHMP review of RWE in MA submissions
6. **Analytics capability:** Initiated a CHMP pre-pilot of CT raw data analysis + selected software for RWD analytics
7. **Expert advice:** Initiated review of methods domain of EMA working parties
8. **Ethics and Security:** Delivered data protection workshops + initiated a data protection Q&A
9. **International:** Initiated analysis for an international collaboration roadmap on RWE
10. **Stakeholder engagement:** Delivered a multi-stakeholder forum in December 2020
11. **Veterinary:** Established a veterinary data workstream

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Upcoming deliverables in 2021

1. DARWIN	**Coordinating centre** service establishment initiated | **DARWIN Network Coordination Group** established | Pilot of the **European Health Data Space** initiated
2. Data Quality	Initiate **Data quality and representativeness study** **Workshop on data quality**
3. Discoverability	Initiate enhancement of **EU catalogue of real world data resources | Best practice guide on Metadata for regulatory purposes** **Workshop on real world data meta-data 12 April**
4. Skills	Training curricula published | at least **one module delivered per curricula** (stats, epidemiology, data science)
5. Processes and transparency	Publish learnings from **review of RWE submissions** + learnings from **committee RWE analytics pilot | Roadmap for guidance** **Workshop on 'learnings initiative'**
6. Analytics capability	**Patient level data**: pre-pilot becomes **pilot.** **AI workshop 19-20 April**
7. Expert advice	**RWE and advanced analytics expert advice available** (even if full methods EWG not established)
8. Ethics and Security	**Publish EMA Q&A on secondary use of health care data and data protection** **Note: guidance expected from EDPB – our Q&A should await that**
9. International	**Publish international collaboration roadmap on RWE** **Workshop on data standards May 2021; international meeting Q4**
10. Stakeholder forum	**Stakeholder forum** **Likely in December**
11 Veterinary	**Agreement on applicability of the BDTF recommendations to the Veterinary domain** **Workshop 1 June**

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BDSG 2020 REPORT

WHAT WILL BE DELIVERED IN 2021

DARWIN EU UPDATE

What is DARWIN EU

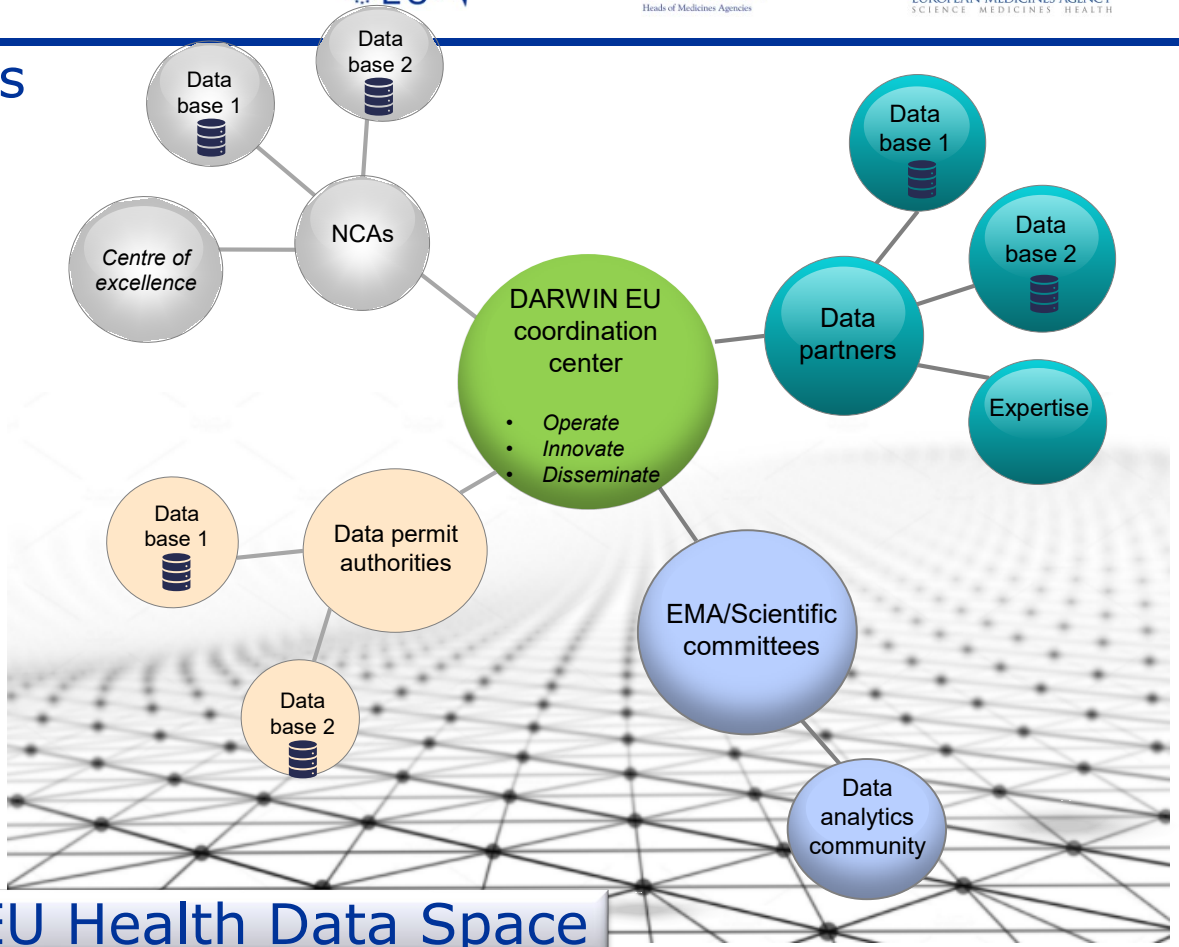
- Vision: Establish a network of data, expertise, and services, called **D**ata **A**nalysis and **R**eal-**W**orld **I**nterrogation **N**etwork (DARWIN EU), to support better decision-making by EMA and NCA scientific committees on the benefits and risks of products via rapid access and analysis and increased reliability, validity and representativeness of EU health data (Published business case for DARWIN)

- Operating model:
  - A **Federated Network of Data Holders and expertise**, exposing data using a common data model and working under a common governance, set of standards and service levels with regards to studies and analysis of data.
  - A **Coordination Centre** that acts as the entry point into this federated network and manages the network on behalf of EMA and the EMRN.
  - **EMA with strategic control and oversight of operations**, e.g. interface with EMA committees, EMA own analysis, driving standards, specifications, guidelines, management of the coordination centre.

- Services that will be provided:
  - **Conduct scientific studies and analysis** on behalf of the EMRN and the EMA's scientific committees;
  - **Provide scientific expertise** in formulating and executing studies and analysis;
  - Maintain a **catalogue of known, relevant data holders**, continually ensuring/maintaining the **quality of the data** held by data holders and **conformance to metadata** (e.g. maintain the federated network); and
  - **Expand the federated network**, assisting potential new data holders in conforming the standards necessary for a data source to be used in the regulatory context.
  - Deliver **training, governance**, contract management, support of business services.

DARWIN EU characteristics

- Distributed data access for fast access and analysis
- Federated network
  - Data stays local, exchanged anonymous and queried remotely
  - Includes use of a common data model and common protocol for fast analysis
  - Use rapid analytics software
- Will leverage the EU Health data space initiative and fully integrated into EC Digital strategy.



EU Health Data Space

EC digital strategy and the European Health Data Space (EHDS): Commission to adopt legal proposal by end 2021

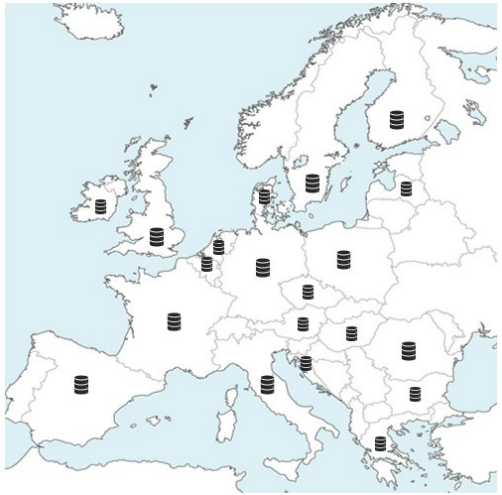
EHDS promotes health data exchange and supports research and innovation on new preventive treatments, medicines, medical devices

- Access of citizens to health data and portability of data
- Access of regulators to health data for policy making and regulatory purposes
- Study on regulatory gaps in cross border digital healthcare (eHealth, AI in health)
- Joint Action to provide rules, governance structures, guidelines, data quality framework, infrastructure

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

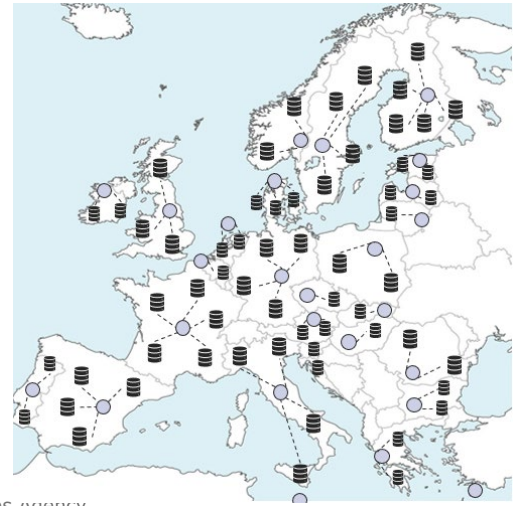
DARWIN EU **2023**

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



DARWIN EU **evolution**

- Fully connected to the EHDS, executing queries via the EHDS
- Access including Data Permit Authorities ( )



How the DARWIN EU network will operate: EMA committees initiates an analysis

EMA Committees

Question that impacts committee opinion

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 (ethics and scientific committees…)

Data holders

(may include NCA/EMA)

Receive and run the code on their own DBs

Aggregate data and results sent to the coordinating centre

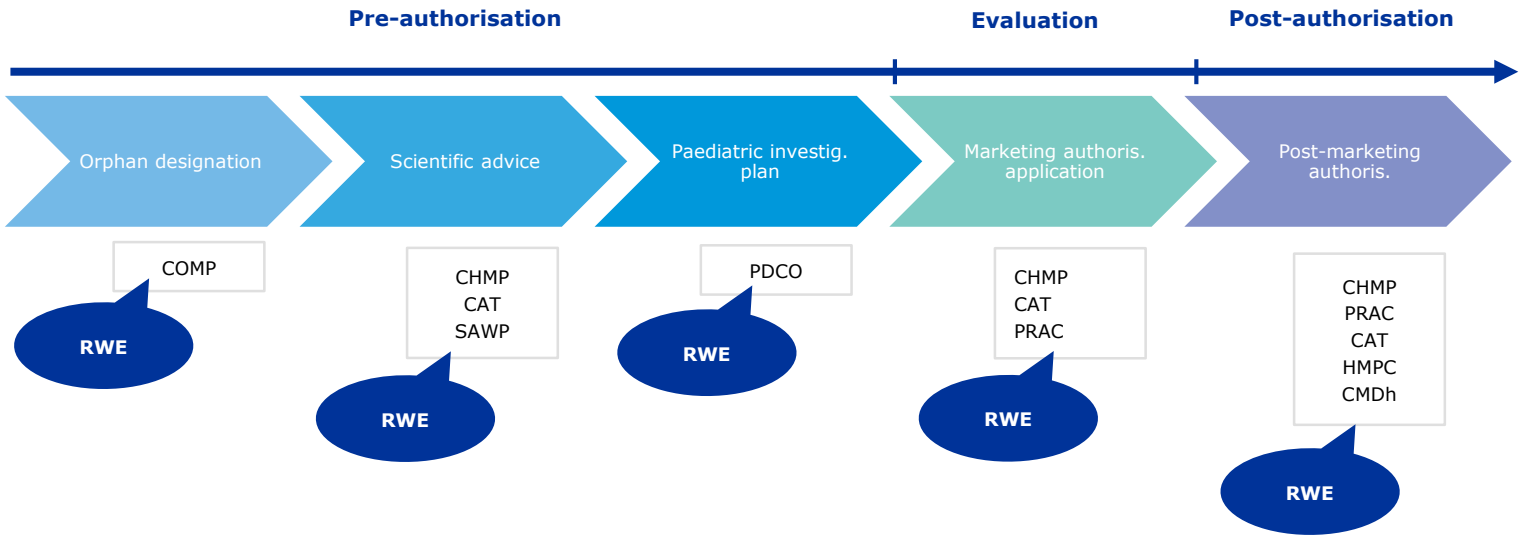
Receive, check, analyse aggregate data

Compile the results in a study report

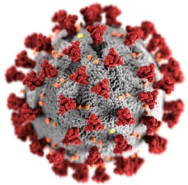
Share aggregate data and reports with committees (and support integration/assessment)

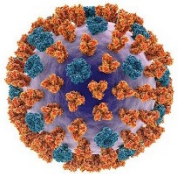
Integrate data and reports in the assessment report

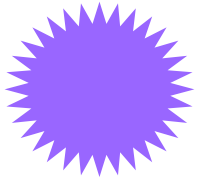
Regulatory use cases are numerous



DARWIN EU: central pillar for crisis planning and response







Use cases include:

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

DARWIN EU will support future crisis responses with an operational infrastructure for conducting rapid studies (change to EMA's mandate)

DARWIN EU benefits: bears fruit

- **Complements clinical trials**
- **Increase quality** of decision-making
- **Faster access** to safer, more effective and innovative medicines to patients
- Optimised **safe and effective use** on the market

- **Increase access** to data: GP, registry, claims and hospital data
- **Increase power, representativeness** and spectrum of **use cases** to support decision making
- **Rapid evidence generation**
- **Increased quality** of the evidence generated to a data quality framework tailored to EU data sources

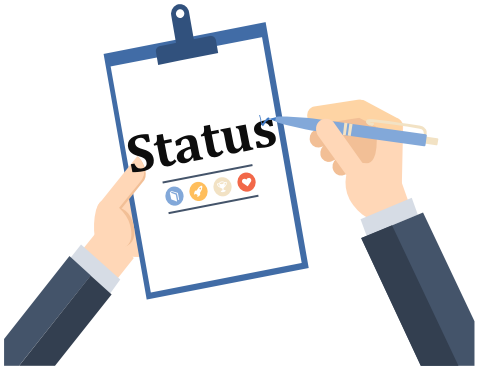
- **Enhanced support for industry through scientific advice and qualification procedures using RWE**
- DARWIN EU studies will replace studies done by companies when imposed, **reducing duplications** (e.g. generics, o questions affecting a class of products)

- Additional benefits as EU stakeholders participate:
  - European Commission – **delivers on European Health Data Space**
  - **National governments** supports health policy and delivery of healthcare
  - **HTA bodies and payers** supports decisions on cost-effectiveness
  - **EU health agencies** – e.g. health crisis preparation and response
  - Opportunities for **international collaboration**

DARWIN EU: Status

Achievements 2020

- [x] Project initiated
- [x] Funding identified including revised EMA fees regulation
- [x] Preliminary delivery model established
- [x] Support Commission to plan pilot with EU Health Data space



Key priorities in 2021

- [ ] Develop network use-cases and processes
- [ ] Initiate coordinating centre service establishment
- [ ] Governance: DARWIN Advisory Board established
- [ ] Pilot with EU Health Data space initiated

Full DARWIN EU services from 2023……..with pilots as early as Q4 2021

Conclusion

- Good progress on implementation of the Big Data recommendations in 2020 and a promising year in 2021!
- The BDSG workplan will deliver activities to enable access and analysis of RWD to support decision making and bring benefits for patients and public health.
- DARWIN is continuing to progress

"By delivering the vision of a regulatory system able to integrate Big Data into its assessment and decision making, we can support the development of innovated medicines, deliver life-saving treatments to patients more quickly and optimise the safe and effective use of medicines through measurement of a products performance on the market."

Big Data Task Force final report December 2019

Any questions?

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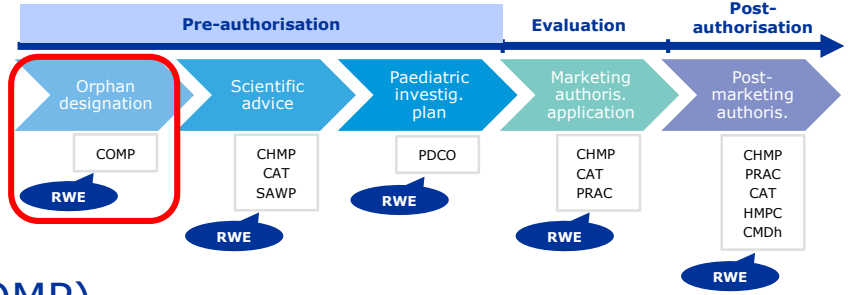
What the future will look like…

- **DARWIN EU network and the EU Health data space partners** 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

Regulatory use cases are numerous

PRE-AUTHORISATION (1/3)



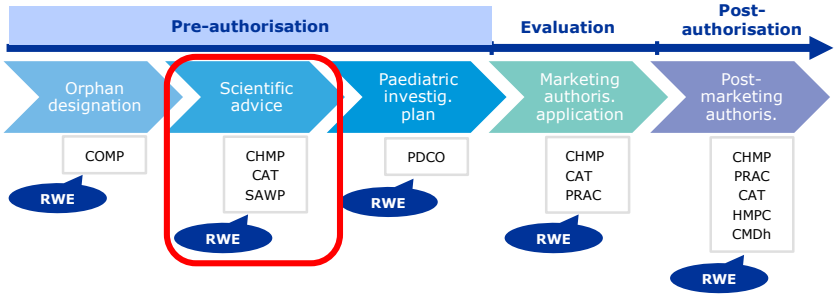
Committee for Orphan Medicinal Products (COMP)

- RWE to generate prevalence data to support orphan designation
- A disease is defined as rare if it affects <5/10,000 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 EU countries to support orphan designation

Regulatory use cases are numerous

PRE-AUTHORISATION (2/3)



Committee for Medicinal Products for Human Use (CHMP)

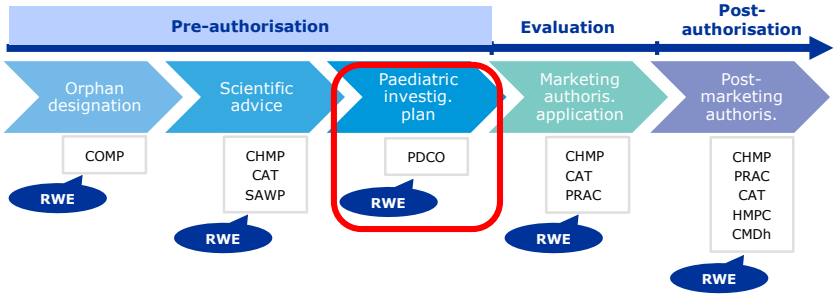
Committee for Advanced Therapies (CAT)

Scientific Advice Working Party (SAWP)

- Advising companies on use of RWE in product development based on feasibility and relevance of studies

Regulatory use cases are numerous

PRE-AUTHORISATION (3/3)

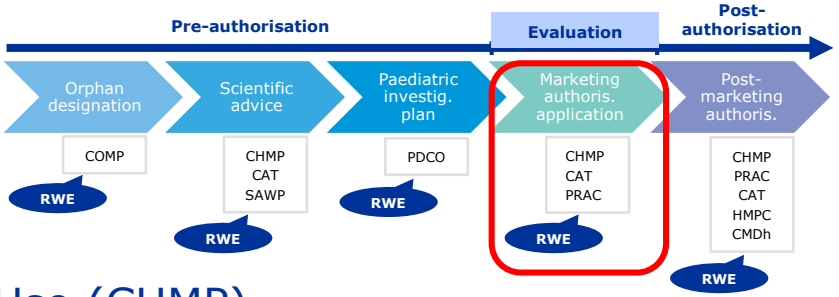


Paediatric Committee (PDCO)

- 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 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)



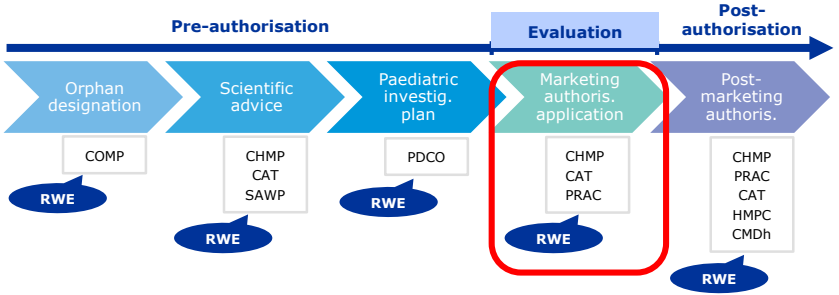
Committee for Medicinal Products for Human Use (CHMP)

Committee for Advanced Therapies (CAT)

- RWE to supplement, validate and contextualise clinical trial results to inform benefit-risk decision making
  - Use of external comparator
  - Measure 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)

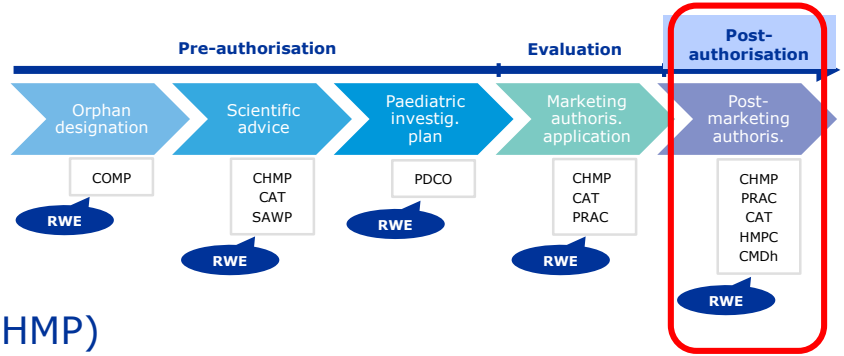
Committee for Advanced Therapies (CAT)

Pharmacovigilance Risk Assessment Committee (PRAC)

- RWE to inform decision-making on post-authorisation studies
  - Inform on the feasibility of imposed PASS (e.g. number of incident patients per year to inform recruitment, data availability on specific treatments or 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)

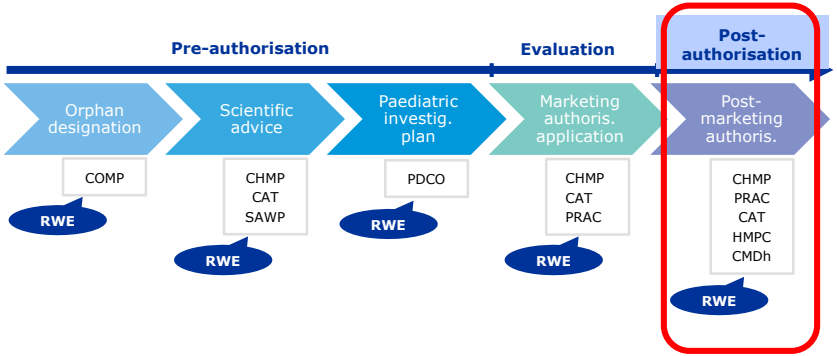
Committee on Herbal Medicinal Products (HMPC)

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 in real world when imposing studies on specific MAHs 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 (children, elderly, pregnant/lactating women, immunocompromised…)
  - Identifying and monitoring off-label use
  - Characterising the safety profile and monitoring the effectiveness of risk minimisation measures
  - Updating the Risk Management Plan