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SCIENCE MEDICINES HEALTH

Improving the generation of evidence: What is on the regulators' mind

EFSPI regulatory statistics workshop, 13 September 2021

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Disclaimer

The views expressed in this presentation are my personal views and may not be understood or quoted as being made on behalf of or reflecting the position of the European Medicines Agency or one of its committees or working parties.

Outline

- **Introduction** – what is on the regulators' mind
- **So far** – recent achievements on data and methods
- **Planning** – looking to 2022
- **How can you help?** – critical role of the statistician
- **Looking to the future** – what will change in the next 10 years?

What is on the EU regulators' mind

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COVID-19

COVID-19: latest updates Share

The latest updates on the COVID-19 pandemic from the European Medicines Agency (EMA) are available below.

HMA-EMA Joint Big Data Taskforce Phase II report:

'Evolving Data-Driven Regulation'

AT A GLANCE

Plenary – July 2021

European Parliament

European Medicines Agency mandate extension

Joint Action Towards the European Health Data Space – TEHDAS

The TEHDAS Joint Action project develops European principles for the secondary use of health data.

European Commission > Expert Groups > Details

Expert group on clinical trials (E01464)

ACTIVE

HMA-EMA joint Big Data Steering Group (BDSG)

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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

July 2021

EMA MB and HMA informed of BDGS workplan 2021/2023

1st Big data steering group meeting in May 2020

May 2020

BDSG workplan 2022/2023

May and June 2021

Publication of BDSG workplan 2021/2023

Aug. 2021

Big Data Steering Group: 2021 achievements – 2022 plans

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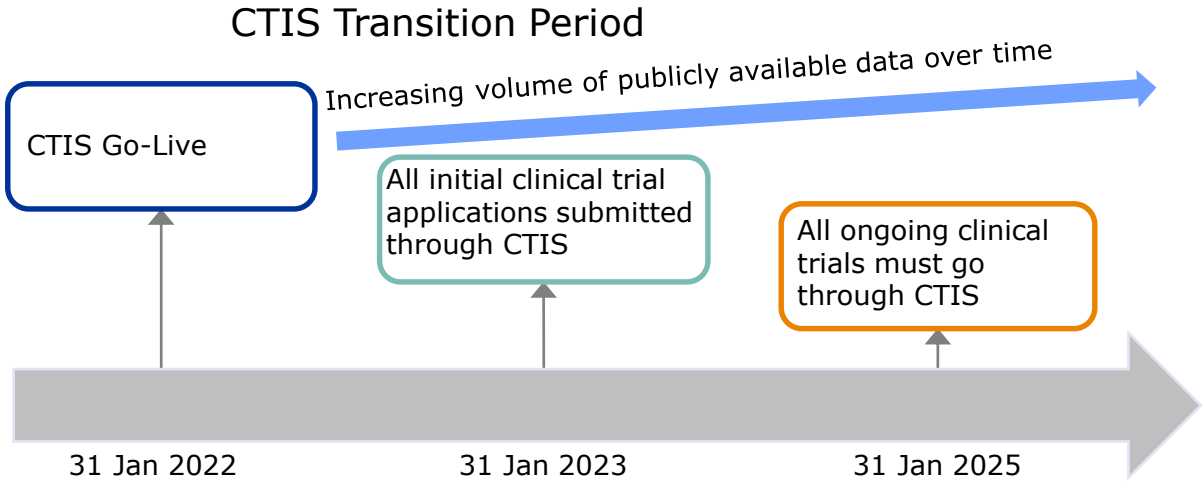
	2021	2022
DARWIN EU	**Procurement launched -** 1st meeting of the **Advisory board**	**Coordination Centre appointed** – Support EHDS2 pilot – **Start conducting pilot/studies** for decision making – explore role for **CT support**
Data quality & representativeness	**Procurement launched** for an consortium to deliver a quality framework	**EU Data quality Framework v1.0 available** - Recommendations to **strengthen data qualification** – **2 workshops** on data quality and data qualification
Data discoverability	Progress on **selection of metadata for RW**	**Agreement on RW Metadata for regulatory purpose** (v.1.0) - **Launch of RWD public catalogue**
EU Network skills	**Data science curriculum** finalised – **Survey of skills** completed - **Training delivery outsourcing** initiated	**Roll out** of Big data curricula (Biostatistics, Pharmacoepidemiology, Data science)
EU Network processes	**Use cases further developed** with PRAC, PDCO, COMP	**Learnings initiative workshop** – **RWE integration pilots** (PDCO, COMP, SAWP, CAT, CHMP)
Network capability to analyse	1st discussion on **Cluster of Excellence** – **Advisory group on Patient-level data** established	**Workshop on Submission & Analysis of Raw Data in MAAs** (informed by 2 pilots) - **Draft guideline on AI** - BDSG discussion on **change management**
Delivery of expert advice	**ENcEPP methods guide published**	Publication of **registries guidance** - **Roadmap for RWE guidance agreed**
Governance framework	**BDSG recommendations on ethics advice**	**Q&A on data protection** for 2ndary use of RWD **- EHDS legal proposal and impact assessment study** discussion – 1st discussion on **data governance**
International initiatives	**Data standardisation strategy** adopted – Progress on **RWE Collaboration Roadmap** with FDA and HC	**Data Standardisation Strategy implementation** - International **regulators summit on data/ RWE**
EU BD stakeholder implementation forum	**Next multi stakeholder forum on Big Data**	Stakeholder forum
Veterinary recommendations	**Workshop on the** Veterinary **Data Strategy**	**International** cooperation **forum** and the **Vet Data Hub** established

CTIS plan 2022-2025

The Clinical Trials Regulation has amongst its aims: the **harmonisation** of Clinical trials and Research in the Union and consequently easier upscaling to meet recruitment objectives.

CTIS will become the **single entry point** for clinical trial submission, authorisation and supervision in the EU and the EEA.

CTIS is the business tool of the **Clinical Trials Regulation**. It includes **Authority and Sponsor workspaces** and **public search functionality**.



CTIS future users

The **future users of CTIS** include:

Sponsors

Commercial: large pharmaceutical companies & CROs, SMEs

Academia

Will **input clinical trial data** in CTIS

Authorities

Member States (NCA & ethics committee)

EMA

European Commission

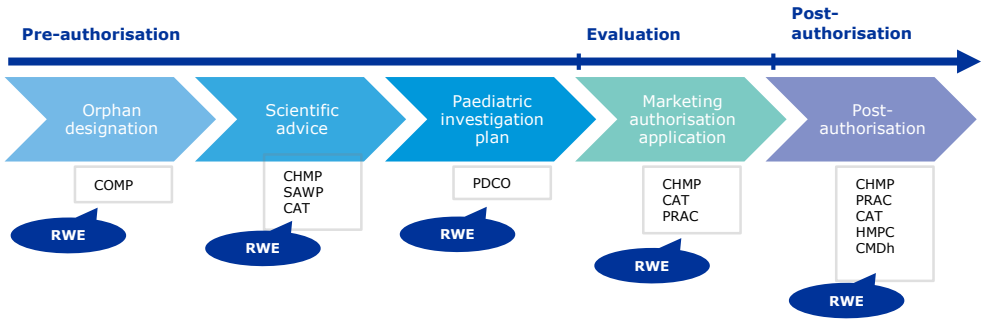
Will **review clinical trial data** (MS/EMA) and create **Union Control Reports** (COM)

Public

Public users (Healthcare professionals, patients, other)

Will **search for publicly available clinical trial data** in CTIS

Regulatory use cases of RWE are numerous



- Field of pharmacoepidemiology is mature and RWE has an established role to support safety evaluation of medicinal products
- Use of RWE for efficacy/effectiveness is more debated but is increasing to supplement, contextualise and, if needed, validate clinical trial results
  - Collaboration with DG Research, published call for the Horizon Europe Cluster 1 Health

What is DARWIN EU®

DARWIN EU is a federated network of data, expertise and services

EU Medicines Regulatory Network

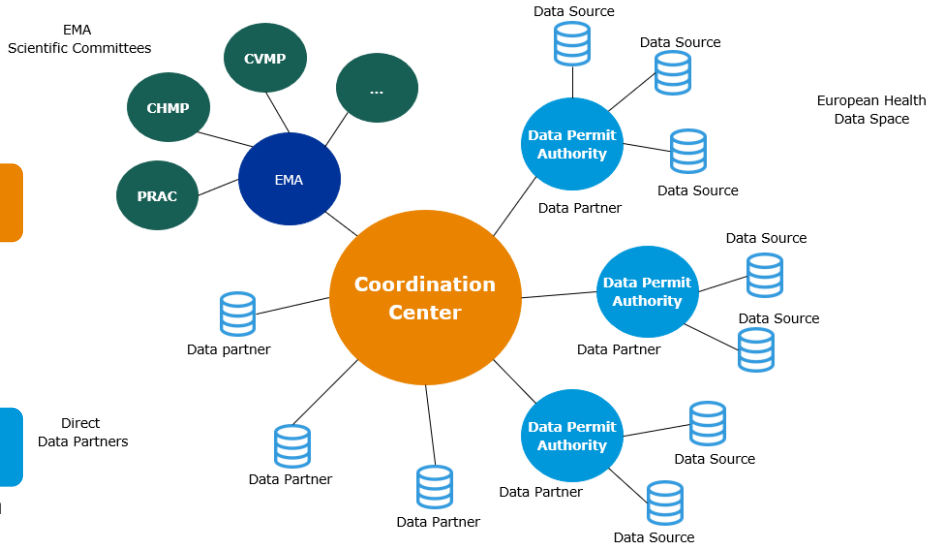
- **EMA** - provides leadership, setting standards, contracting studies,
- **EMRN –** including EMA scientific committees and working parties, national competent authorities (NCAs) and the European Commission: **request studies** via EMA

The Coordination Centre

- **Establishes** and **maintains the network** (including onboard/maintain data sources), manage the **execution of scientific studies**

Data Partners, incl. Data Permit Authorities

- **Partners** who have access to data, or who may request analyses in a data source and provide results to the Coordination Centre
- This includes **Data Permit Authorities** (DPAs), already existing or to be created as part for the EHDS



DARWIN EU® - milestones

2021

- Selection of the Coordination Centre provider

Phase I and II - 2022/2023

- Establish connectivity with EHDS and existing Data Permit Authorities
- Start recruiting and onboarding the data partners
- First catalogue of standard data analyses available
- Start running studies to support EMA committees - first benefits delivered

Phase III - 2024

- DARWIN EU® at full capacity and routinely supporting the scientific evaluation work of EMA and NCAs' scientific committees

Operation - 2025/2026

- DARWIN EU® continues at full capacity and continue to evolve
- Full integration with the EHDS

Review of activities of the Working Parties of the EMA

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- Effort to rationalise the structure of working parties
  - Proposed introduction of the concept of five Domains: quality, non-clinical safety, methodology, clinical and veterinary
  - New methodologies working party to being together different expertise (biostats, pharmacoepidemiology, modelling etc.)
- Domains will support implementation of the Network Strategy to 2025 and EMA RSS
  - Potential to deliver strategic priorities, being adaptable to future needs, being able to reach out to stakeholders
  - Support EU innovation in global drug development to benefit patients
  - Domains will continue supporting committees for product advice, assessment, etc.
- Communities of experts with special knowledge and interest in a specific area will be formed to be the source of expertise when constituting drafting or other groups

Guidelines in progress

- CTEG Question & Answer on decentralised trials
- CTEG Question & Answer on complex clinical trials
- EMA Reflection Paper on single-arm trials
- Revision of EMA Guideline on Data Monitoring Committees
- EMA Guideline on registry-based studies | European Medicines Agency (europa.eu)
- (i) Metadata for Data Discoverability and Study Replicability and (ii) Data Quality Framework
- International collaboration on Real World Evidence (e.g. FDA and Health Canada)

Where will statisticians play a critical role?

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- Newer ideas exacerbates the need for a **critical eye** (role of gatekeepers)… But keep also an **open mind** (role of enablers)!
- Stress test new concepts across a **multitude of factors**: estimands, design, data collection, analysis, data quality, interpretation of results, communication, etc.
- Statisticians will not become data scientists tomorrow! But they should **get trained** in a wider range of experimental design and statistical methods and learn from **other application areas** of statistics.
- Role of statistician is similar from the sponsor's or regulator's side: ensure that **quality information** can be collected to transform it into **relevant evidence** for both drug development and regulatory decision-making.

Looking to the future:
How would regulation look like in 2030?

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What will remain the same:

- ✓ A. Clinical trials remain the bedrock of clinical evidence generation
- ✓ B. Authorisation of medicines based on quality, safety and efficacy and positive benefit risk
- ✓ C. Decision-ready evidence relies on quality data and robust study methods

What will change:

- ➢ A. Role of real-world evidence established across spectrum of regulatory use cases
- ➢ B. Regulation more data driven: includes analysis of raw data from industry and RWD independent of industry
- ➢ C. Better evidence supports better decisions on medicines for patients

Conclusion

- Transformation to data-driven regulation in line with Network Strategy to 2025
- Ambitious work programme to deliver the change
- Deliver through collaboration: critical role for the biostatistician
- Patient focussed – in every thing we do

Big Data Task Force 2020 vision :"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 on the market."

Any questions?

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