Norwegian Medical
Products Agency

Date; Meeting; Location

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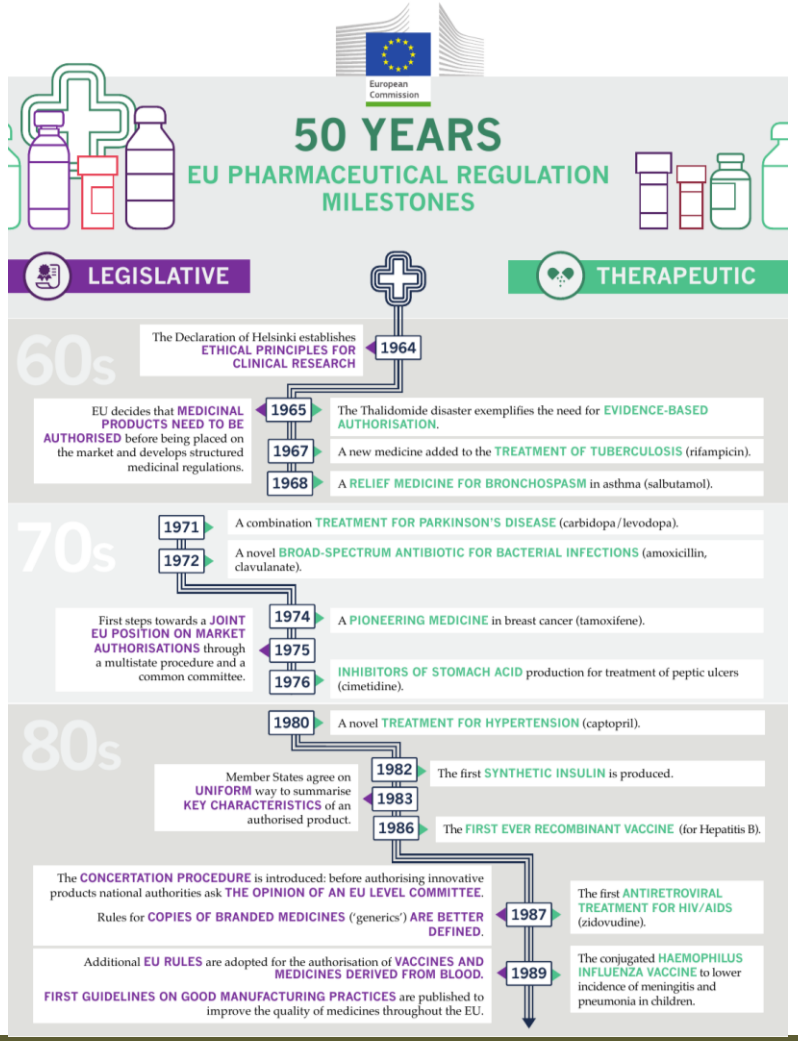
- Scientific Advice Working Party member
- Methodology Working Party member

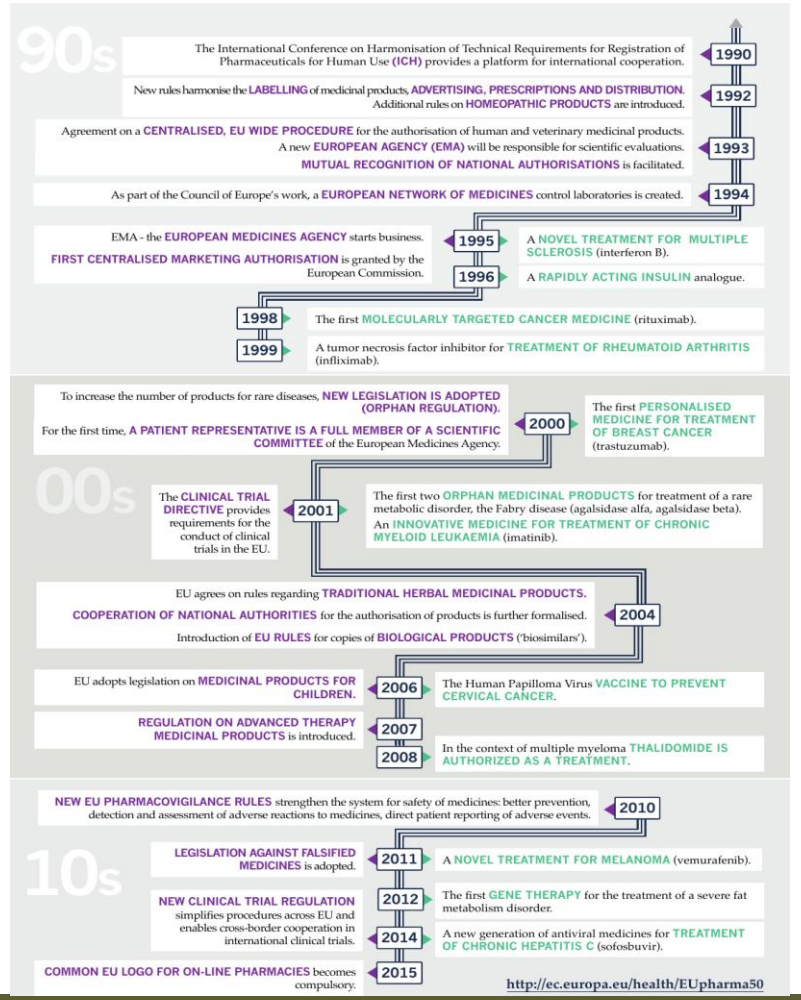
Disclaimer

The views expressed are those of the presenter and should not be understood or quoted as being made on behalf of:

- Norwegian Medical Products Agency (NOMA)
- The European Medicines Agency (EMA) or its scientific committees
- The HTA Coordination Group (HTA CG)

The history of Evidence generation requirements





There is more than one ‘Regulator’

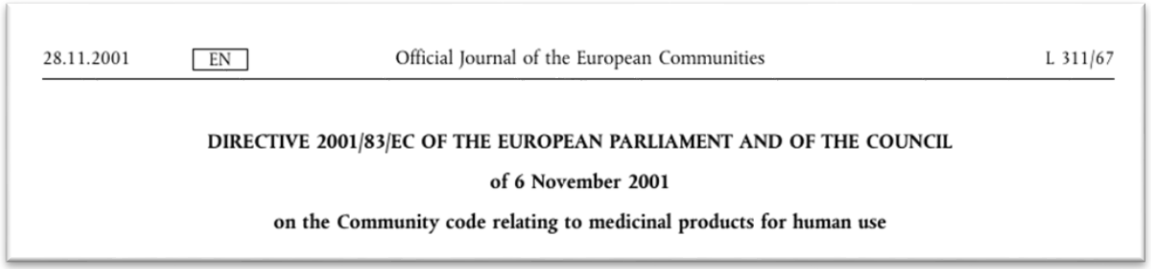
28.11.2001 EN Official Journal of the European Communities L 311/67

DIRECTIVE 2001/83/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 6 November 2001

on the Community code relating to medicinal products for human use

There is more than one ‘Regulator’



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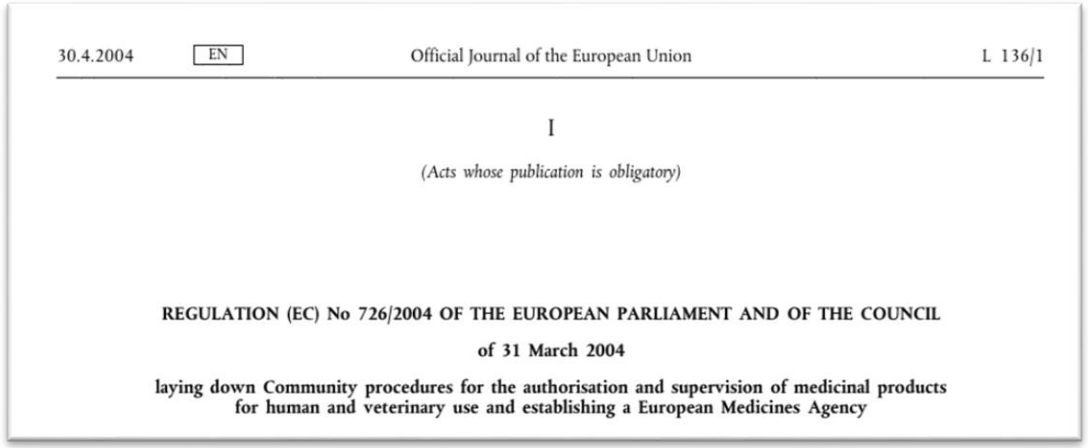


30.4.2004 EN Official Journal of the European Union L 136/1

I

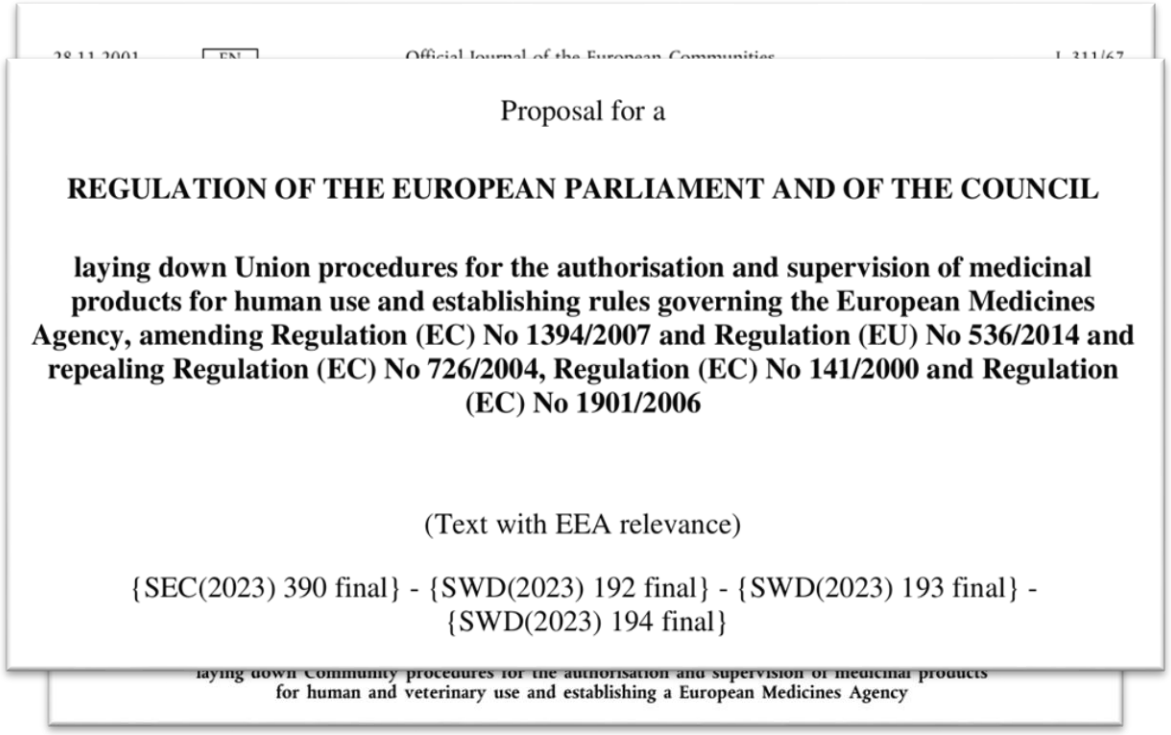
(Acts whose publication is obligatory)

REGULATION (EC) No 726/2004 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 31 March 2004

laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

There is more than one ‘Regulator’



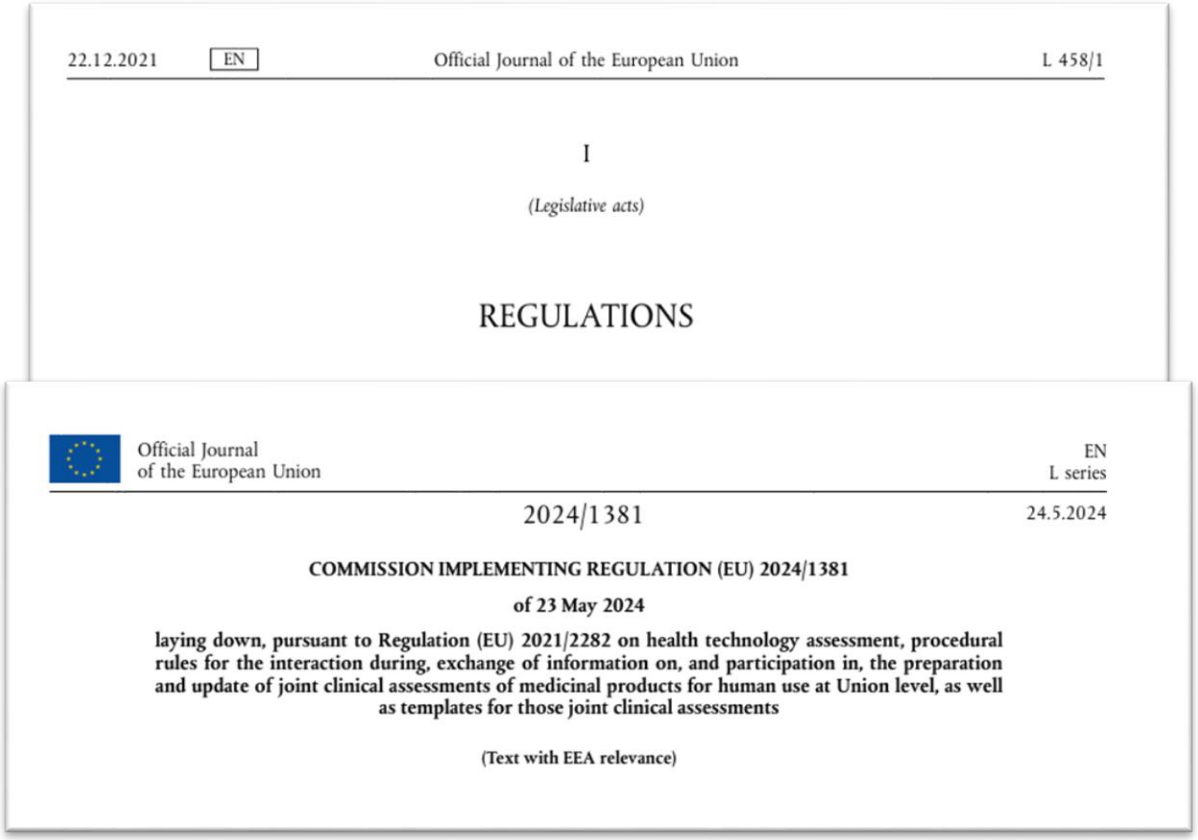
Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006

(Text with EEA relevance)

{SEC(2023) 390 final} - {SWD(2023) 192 final} - {SWD(2023) 193 final} - {SWD(2023) 194 final}



22.12.2021 EN Official Journal of the European Union L 458/1

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(Legislative acts)

REGULATIONS

Official Journal of the European Union

EN
L series

2024/1381

24.5.2024

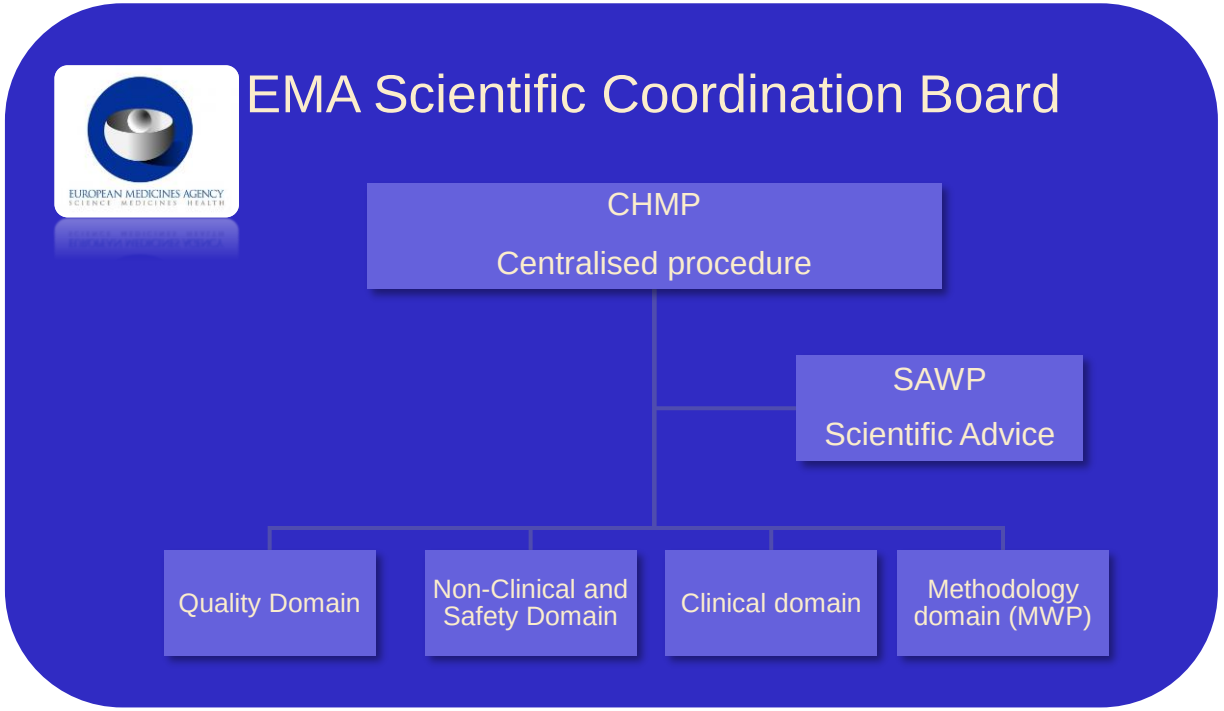
COMMISSION IMPLEMENTING REGULATION (EU) 2024/1381

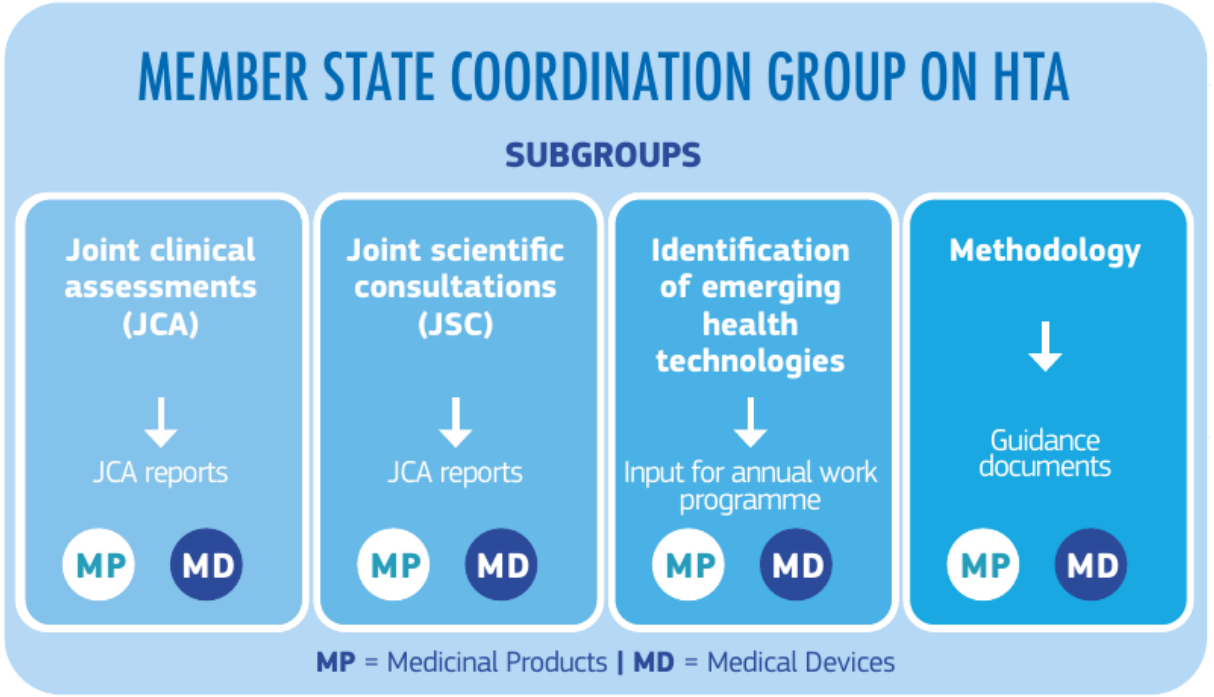
of 23 May 2024

laying down, pursuant to Regulation (EU) 2021/2282 on health technology assessment, procedural rules for the interaction during, exchange of information on, and participation in, the preparation and update of joint clinical assessments of medicinal products for human use at Union level, as well as templates for those joint clinical assessments

(Text with EEA relevance)

The Regulators structure





When did we start looking for real world data?

The history of Evidence generation requirements

- The 21st Century Cures Act (2016)

Public Law 114–255
114th Congress

An Act

To accelerate the discovery, development, and delivery of 21st century cures, and for other purposes.

Dec. 13, 2016
[H.R. 34]

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

21st Century Cures Act.
42 USC 201 note.

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the "21st Century Cures Act".

(b) TABLE OF CONTENTS.—The table of contents for this Act is as follows:

The history of Evidence generation requirements

- The 21st Century Cures Act (2016)

Subtitle B—Advancing Precision Medicine

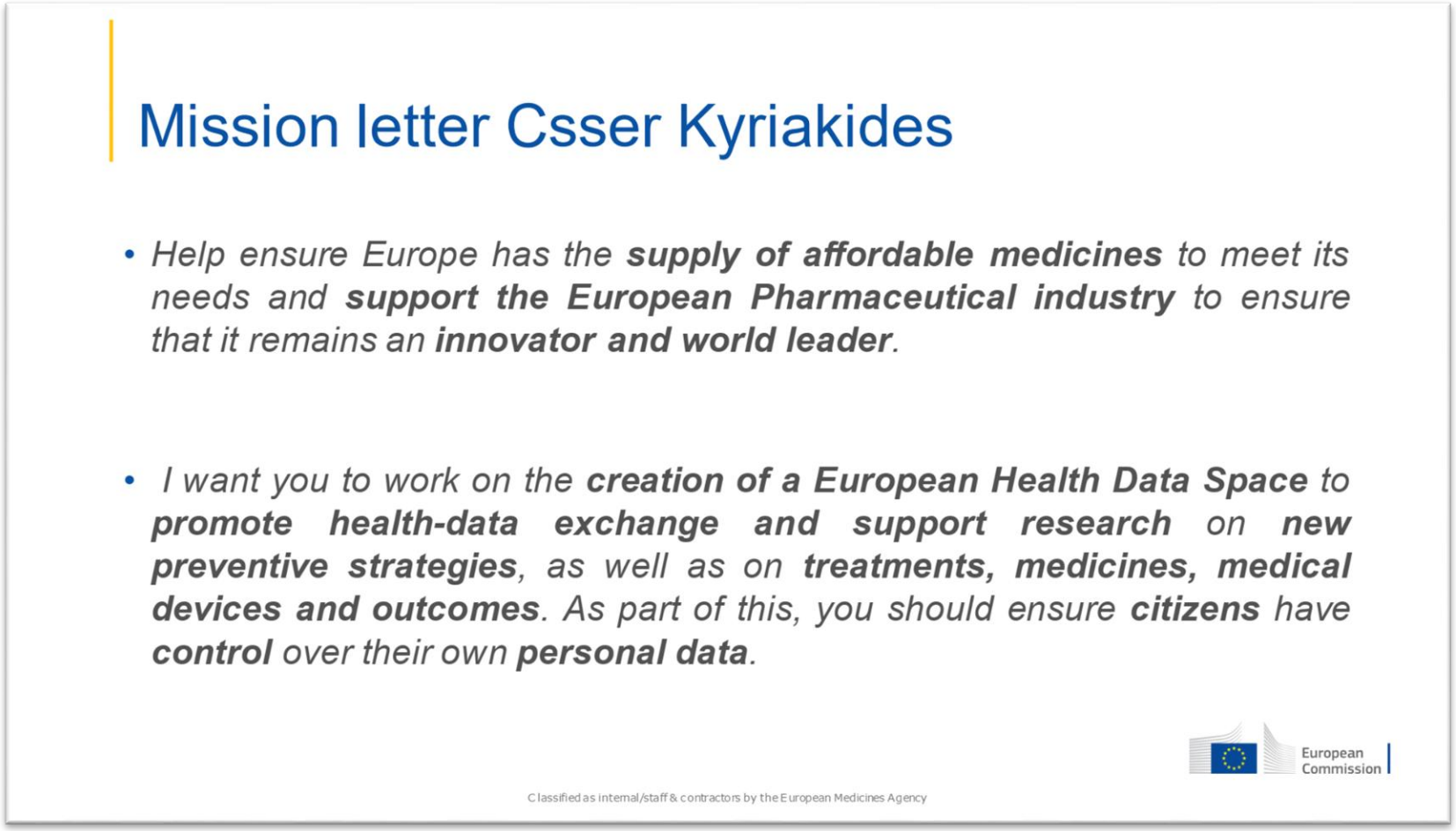
Sec. 2011. Precision Medicine Initiative.
Sec. 2012. Privacy protection for human research subjects.
Sec. 2013. Protection of identifiable and sensitive information.
Sec. 2014. Data sharing.

Subtitle C—Modern Trial Design and Evidence Development

Sec. 3021. Novel clinical trial designs.
Sec. 3022. Real world evidence.
Sec. 3023. Protection of human research subjects.
Sec. 3024. Informed consent waiver or alteration for clinical investigations.

The history of Evidence generation requirements

- The European Health data space (2020)



The history of Evidence generation requirements

- The European Health data space (2022)
- Reality in 2025

REGULATION (EU) 2024/…

OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of …

on the European Health Data Space and amending Directive 2011/24/EU and Regulation (EU) 2024/2847

(Text with EEA relevance)

Mission letter Csser Kyriakides

- *Help ensure Europe has the **supply of affordable medicines** to meet its needs and **support the European Pharmaceutical industry** to ensure that it remains an **innovator and world leader**.*

*…u to work on the **creation of a European Health Data Space** to … **health-data exchange and support research** on **new …ve strategies**, as well as on **treatments, medicines, medical …and outcomes**. As part of this, you should ensure **citizens** have …ver their own **personal data**.*

European Commission

The EHDS

- Thanks to the EHDS, people will have immediate, and easy access to the data in electronic form, free of charge.
- Citizens will be in full control of their data and will be able to add information, rectify wrong data, restrict access to others and obtain information on how their data are used and for which purpose.
- Interoperability and security will become mandatory requirements. Manufacturers of electronic health record systems will need to certify compliance with these standards.

Created by ChatGPT/Dall-e

The EHDS

- To ensure that citizens' rights are safeguarded, all Member States have to appoint digital health authorities.
- The EHDS creates a strong legal framework for the use of health data for research, innovation, public health, policy-making and regulatory purposes. Under strict conditions, researchers, innovators, public institutions or industry will have access to large amounts of high-quality health data.
- The access to such data by researchers, companies or institutions will require a permit from a health data access body, to be set up in all Member States.
- The health data access bodies will be connected to the new decentralised EU-infrastructure for secondary use (HealthData@EU) which will be set up to support cross-border projects.

Created by ChatGPT/Dall-e

Let’s start with some basics

- Does anyone know what RWD actually is?

Let’s start with some basics

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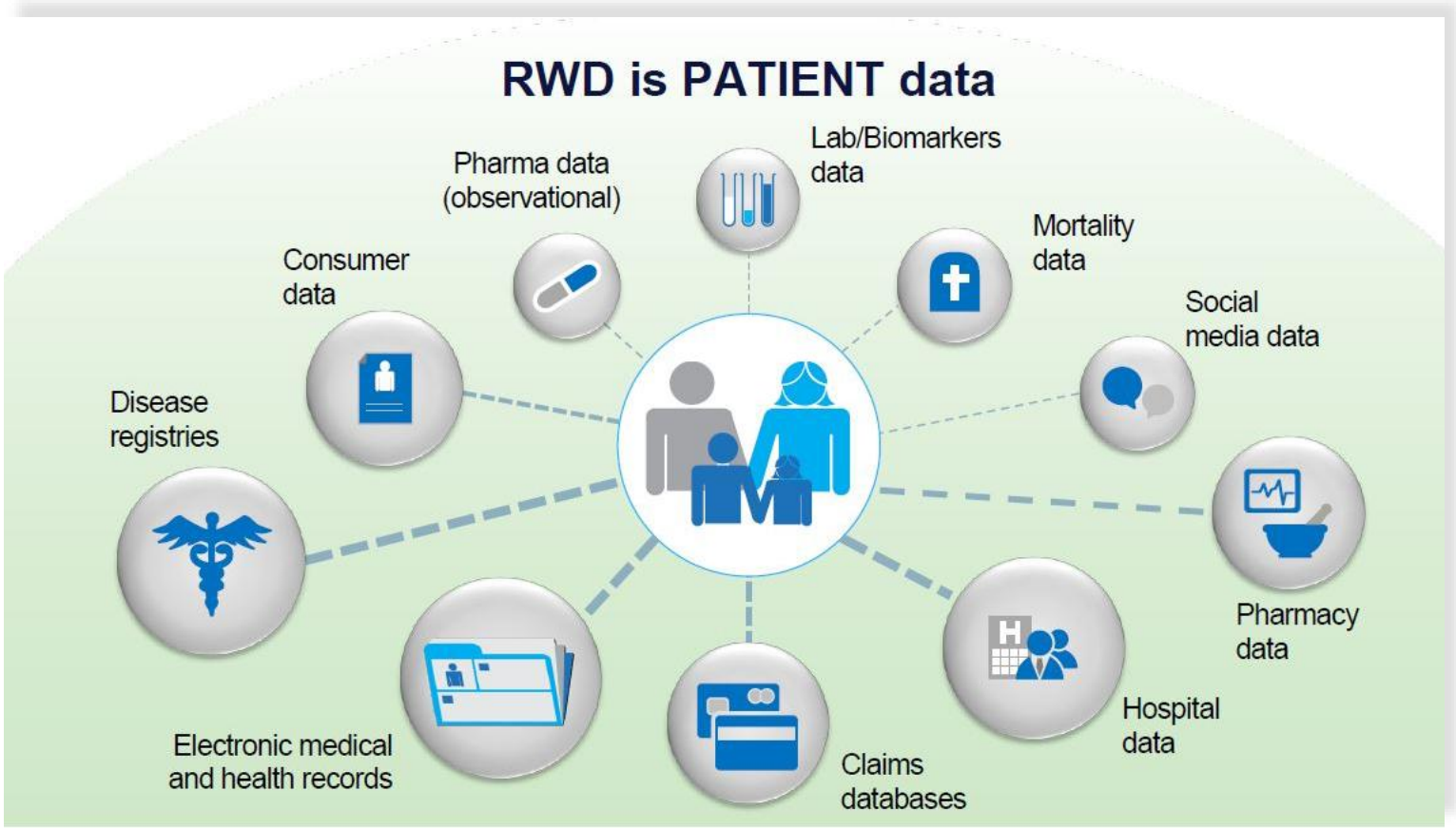
Trick questions....

- It makes more sense to look at data and then discuss how it can be used rather than put labels on it!



Source: IMS Health

If we can’t even agree on a definition……

innovative health initiative

IDERHA

101112135 - IDERHA

Integration of Heterogeneous Data and Evidence towards Regulatory and HTA Acceptance

WP6 Policy recommendations to enable Regulatory and HTA decision making

https://shorturl.at/COTpY

How to use RWD/RWE

Supporting trial design

- Assessing feasibility during the planning phase of a clinical study
- Generating hypotheses for clinical studies (e.g. estimating treatments effects or failure rates)
- Identifying relevant outcomes
- Identifying targets for the development of new therapies and design of the drug development pathway
- Estimating test accuracy or reproducibility of test results such as biomarkers
- Testing/validating surrogate endpoints

How to use RWD/RWE

Cohort characterization and contextualization of trial results

- Understanding natural history/disease progression/epidemiology
- Understanding care pathways
- Identifying relevant patient populations/population characteristics
- Identifying biomarkers or clinical characteristics relevant to the outcomes of interventional and non-interventional studies
- Identifying and characterising underserved/underrepresented audiences and areas of health inequalities against target population
- Assessing the applicability of trial results to patients in real life and/or a specific context /healthcare system
- To monitor use, adherence and experience of using health technologies
- Estimation of utility scores/mapping data to Quality of Life tools

How to use RWD/RWE

Estimating intervention effects (population-level estimation)

- Extrapolation of trial results
- Estimating comparative effects in countries in which the technology was available
- Estimating effects for combination therapies (including sequences) or decision strategies not examined in randomised controlled trials
- Allowing head-to-head comparisons between interventions in absence of head-to-head trials
- Filling evidence gaps in network meta-analysis
- External control arm for single arm trials
- Assessing long-term efficacy and safety
- Assessing effectiveness and safety in off-licence indications
- Exploring heterogeneity in intervention effects
- Estimating economic burden (e.g. resource use and costs)
- Measuring patient QoL

How to use RWD/RWE

Innovative technology and algorithm optimisation

- A mechanism for training and re-training artificial intelligence and machine learning-enabled medical devices
- Validating software as a medical device (SaMD) product
- Developing clinical prediction models

Who should use it and when?

Pre-marketing authorization

- Primary clinical evidence to support marketing authorization
- Supplementary evidence to support marketing authorization
- Conditional approvals
- Expedited approval pathways
- Expanding indications or assessing off-license efficacy

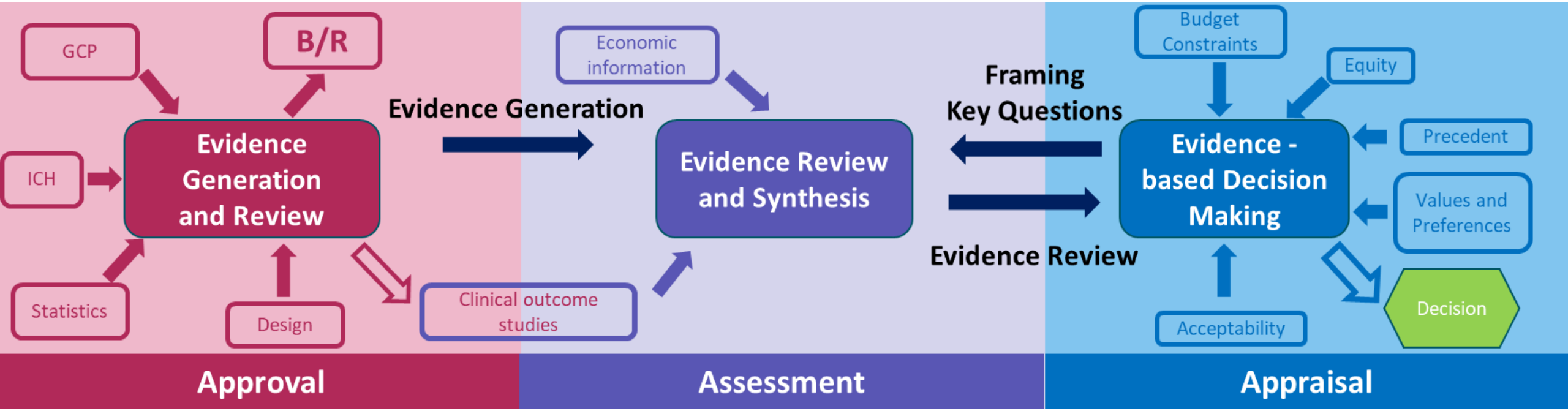
HTA

- Economic modelling
  - Providing inputs for modelling
  - Adapting models to local contexts
- Primary clinical evidence to support HTA and reimbursement decisions
- Supplementary clinical evidence to support HTA and reimbursement decisions

Post-marketing authorization/ reimbursement decision

- Regulatory
  - Pharmacovigilance (monitoring adverse events)
  - Postmarket clinical follow-up (PMCF) for medical devices
  - Vigilance for medical devices
  - Product reclassification
- HTA
  - Outcome-based contracting/managed entry agreements/ early value assessments
  - Reimbursement re-evaluations
  - Informing disinvestment decisions
  - Expanding indications or assessing off-license efficacy
  - Payer coverage decisions

Different mandates but same evidence



Adapted from Teutsch, S.; Berger, M. (2005) 'Evidence synthesis and evidence-based decision making: Related but distinct processes. *Medical Decision Making*, pp 487-489

dmp.no

helsenorge.no

Direktoratet for medisinske produkter

Norwegian Medical Products Agency