EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Real-World Evidence Policy: Is harmonization between Regulatory and HTA a help or hindrance?

A regulatory perspective

ISPOR Europe 2024

19 November 2024 | Barcelona, Spain

Patrice Verpillat

Head of Real-World Evidence, Data Analytics & Methods Task Force

An agency of the European Union

Disclaimer

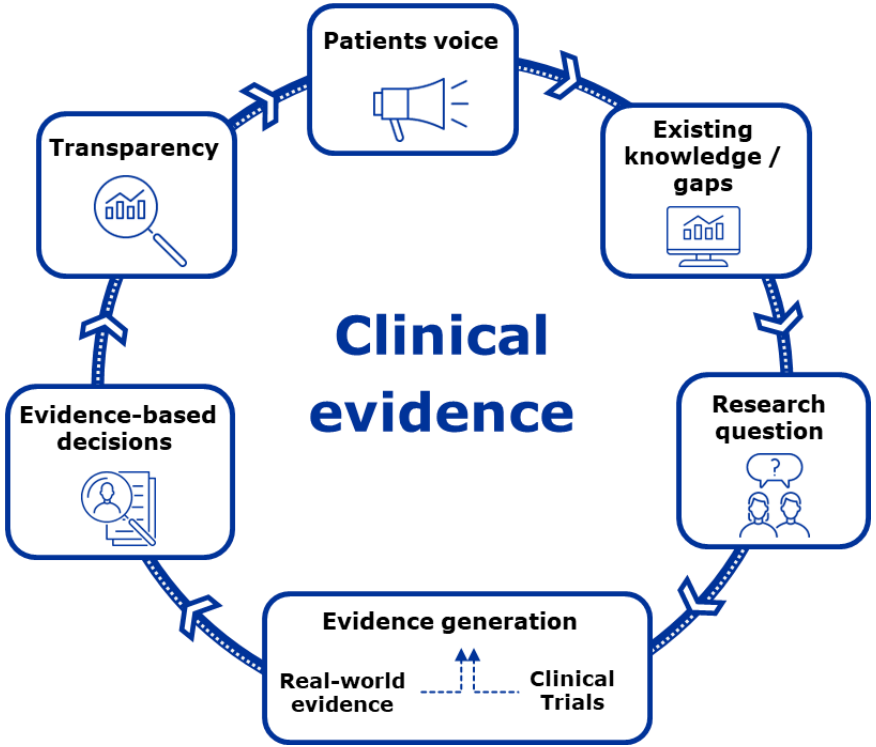
I have no conflict of interests

The views expressed in this presentation are mine and should not be understood or quoted as being made on behalf of or reflecting the position of EMA or one of its committees or working parties

Disclaimer It is acknowledged that EMA has no role in the development of HTA methodologies, as the remits are clearly separate

EU Regulatory Perspective on “Clinical Evidence”

- Patient voice guides every step of the way
- Evidence generation is planned and guided by purpose, data, knowledge and expertise
- Research question drives evidence choice and embraces spectrum of data and methods
- **Clinical trials remain core but are smarter, better and faster**
- **Real world evidence is enabled, and its value is established**
- High transparency level underpins societal trust



At the core of a successful MA dossier is excellent clinical evidence

Clinical evidence in action

Does it work?

Randomised Controlled Trials
vs. placebo to "control" the environment

Absolute assessment

Regulators

Does it work better?

Randomised Controlled Trials
vs. active comparator (SoC) to show an increased benefit

Relative assessment

HTA bodies

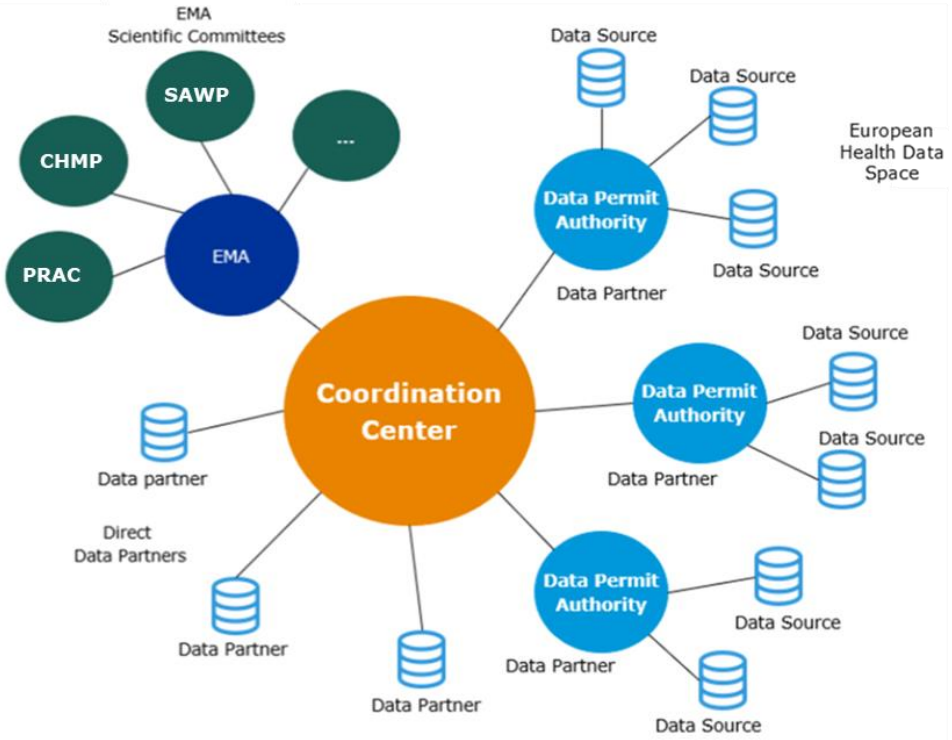
Uncertainty management

Regulatory/HTA collaboration (on a clinical level (i.e. not policy/economics)) is guided by the **ambition to enable the generation of evidence** that can answer different questions for benefit/risk assessment and relative effectiveness assessment, respectively

Despite the differences in scope, there are **overlapping commonalities** in what constitutes meaningful evidence generation and how **identified and quantified** (remaining) **uncertainties** at stage of decision making are managed across a product life cycle

DARWIN EU®: Key tool for EU regulators… only?

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**



Three main areas where RWD analyses support decision-making

★ Aligned with HTA need

1 Understand the clinical context

- Disease epidemiology ★
- Clinical management ★
- Drug utilisation ★

2 Support the planning and validity

- Design and feasibility of planned studies ★
- Representativeness and validity of completed studies ★

3 Investigate associations and impact

- (Comparative) Effectiveness and safety studies ★
- Impact of regulatory actions

DARWIN EU supporting HTA decision making
First Workshop – October 2022

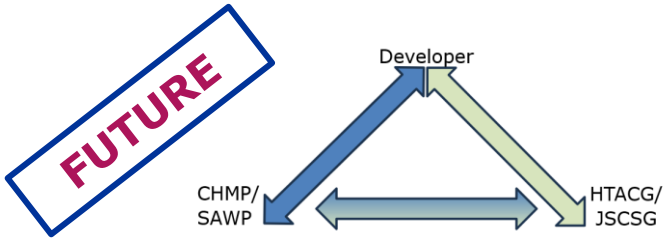
On topics to be addressed by studies

- **Effectiveness of medicines** is key to support HTA (/Payer) decision making
  - To bridge the gap in situations where authorisation is based on limited evidence
- **Natural disease history**
  - Provide a better understanding of standard of care, sequence of treatments…
  - External validation of patient population targeted in clinical trials

Two pilot studies agreed

- **Effectiveness study** to assess OS in patients with NSCL cancer treated with selected immunotherapies as first line
  - **Study on-going**
- **Natural history of multiple myeloma** to characterise MM patients, including treatments (sequences) received and overall survival
  - **Study completed**

EMA – HTA scientific consultation



"The EMA offers consultations in parallel with the European Network for Health Technology Assessment (EUnetHTA) 21 consortium, as of 2022. This aims to allow medicine developers to obtain feedback from regulators and HTA bodies in EU Member States on their evidence-generation plans to support decision-making on marketing authorisation and reimbursement of new medicines at the same time"

Joint Scientific Consultation for human medicines

Key principles

- Possibility for parallel process with EMA, subject to selection criteria under HTA Regulation
- Based on experience with Parallel Consultation (and precedents since 2010)
- Joint technical exchange on evidence planning including post-licensing/launch evidence

With synchronized timing and preserving separate remits!

Art 16-18, 20 of Reg (EU) 2021/2282

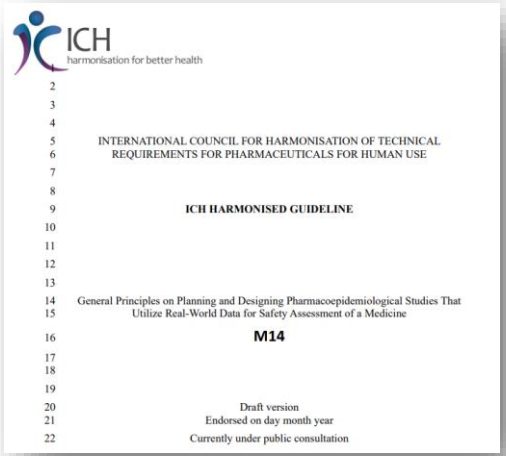
As a conclusion…

Is the aim really to "harmonise" or at least to "converge"?

Regulatory harmonisation Process by which guidelines are developed to be **uniform** across participating authorities

*Regulatory convergence P*rocess whereby regulatory requirements across countries become **more similar or "aligned"** over time

Harmonisation takes time!



ICH
harmonisation for better health

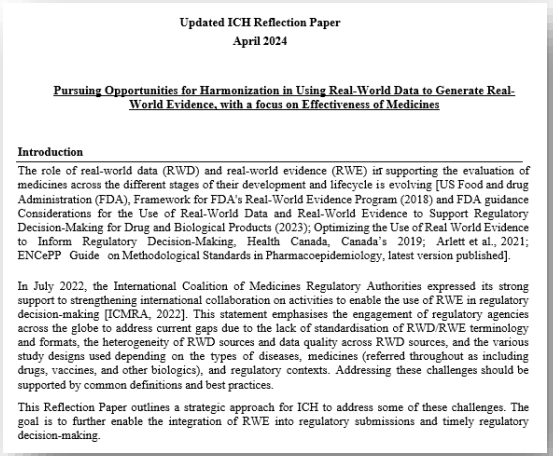
INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

General Principles on Planning and Designing Pharmacoepidemiological Studies That Utilize Real-World Data for Safety Assessment of a Medicine

M14

Draft version
Endorsed on day month year
Currently under public consultation



Updated ICH Reflection Paper
April 2024

Pursuing Opportunities for Harmonization in Using Real-World Data to Generate Real-World Evidence, with a focus on Effectiveness of Medicines

Introduction

The role of real-world data (RWD) and real-world evidence (RWE) in supporting the evaluation of medicines across the different stages of their development and lifecycle is evolving [US Food and drug Administration (FDA), Framework for FDA's Real-World Evidence Program (2018) and FDA guidance Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products (2023); Optimizing the Use of Real World Evidence to Inform Regulatory Decision-Making, Health Canada, Canada's 2019; Arlett et al., 2021; ENCePP Guide on Methodological Standards in Pharmacoepidemiology, latest version published].

In July 2022, the International Coalition of Medicines Regulatory Authorities expressed its strong support to strengthening international collaboration on activities to enable the use of RWE in regulatory decision-making [ICMRA, 2022]. This statement emphasises the engagement of regulatory agencies across the globe to address current gaps due to the lack of standardisation of RWD/RWE terminology and formats, the heterogeneity of RWD sources and data quality across RWD sources, and the various study designs used depending on the types of diseases, medicines (referred throughout as including drugs, vaccines, and other biologics), and regulatory contexts. Addressing these challenges should be supported by common definitions and best practices.

This Reflection Paper outlines a strategic approach for ICH to address some of these challenges. The goal is to further enable the integration of RWE into regulatory submissions and timely regulatory decision-making.

Thank you!

Further information

Contact me at patrice.verpillat@ema.europa.eu

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000

Follow us on **@EMA_News**