EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Comparing and Contrasting RWE Guidance: What Researchers Need to Know Considering the Global Picture

What researchers should consider in designing RWD studies?

ISPOR Europe 2024

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An agency of the European Union

Disclaimer

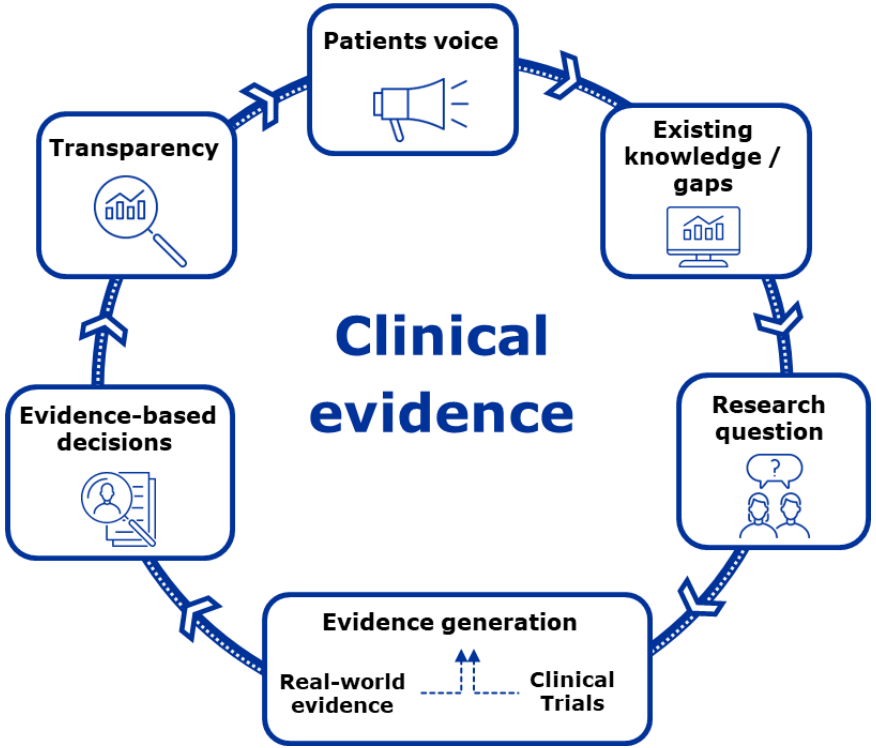
I have no conflict of interests

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

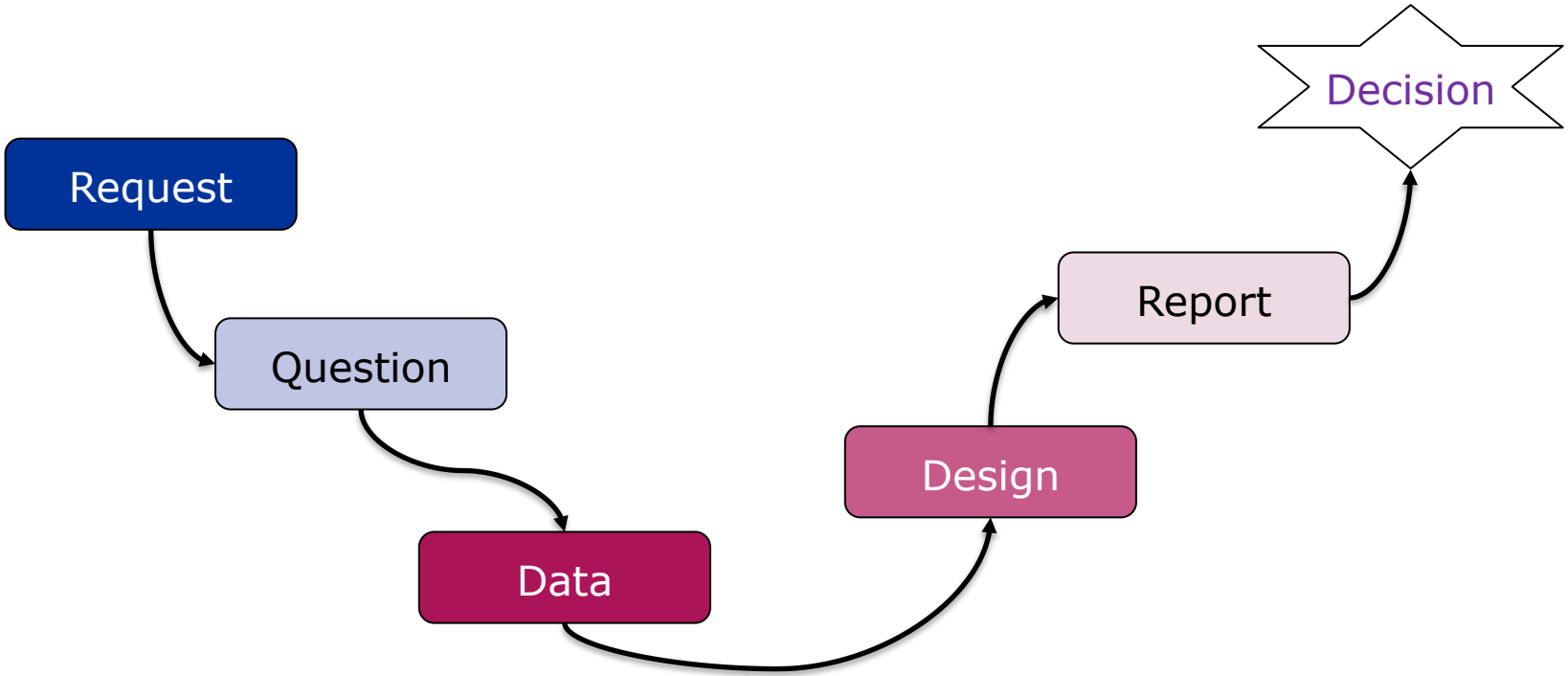
Disclaimer It is acknowledged that EMA has no role in the development of HTA methodologies, as the remits are clearly separate

EU Regulatory Perspective on “Clinical Evidence”

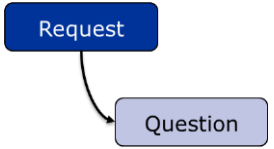
- Patient voice guides every step of the way
- Evidence generation is planned and guided by purpose, data, knowledge and expertise
- Research question drives evidence choice and embraces spectrum of data and methods
- **Clinical trials remain core but are smarter, better and faster**
- **Real world evidence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



From question to decision

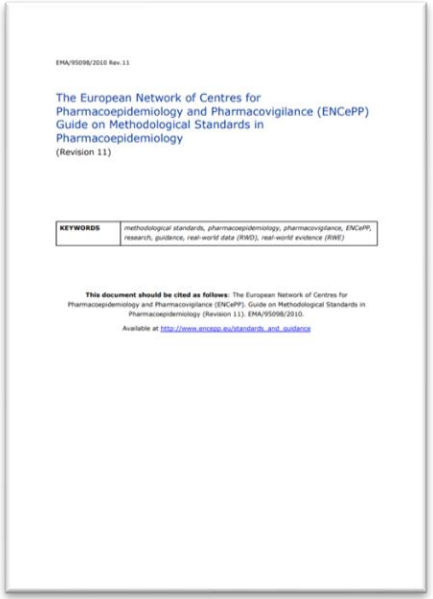


Initial first mandatory step…



- Transfer the request into a clear and precise research question
- Ensure the question fits the request
- Avoid to answer too many questions at the same time in one study

"It is essential that the research question is expressed with sufficient detail and attention to the regulatory question targeted"



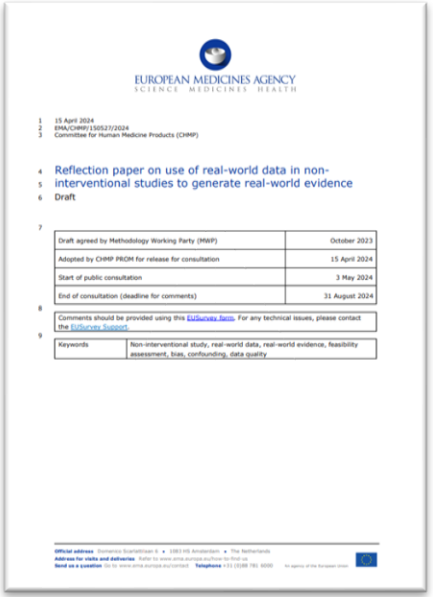
EMA/95098/2010 Rev.11

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) Guide on Methodological Standards in Pharmacoepidemiology
(Revision 11)

KEYWORDS	methodological standards, pharmacoepidemiology, pharmacovigilance, ENCePP, research, guidance, real-world data (RWD), real-world evidence (RWE)

This document should be cited as follows: The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP). Guide on Methodological Standards in Pharmacoepidemiology (Revision 11). EMA/95098/2010.

Available at http://www.encepp.eu/standards_and_guidance



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15 April 2024
EMA/CHMP/130527/2024
Committee for Human Medicine Products (CHMP)

Reflection paper on use of real-world data in non-interventional studies to generate real-world evidence
Draft

Draft agreed by Methodology Working Party (MWP)	October 2023
Adopted by CHMP PROM for release for consultation	15 April 2024
Start of public consultation	3 May 2024
End of consultation (deadline for comments)	31 August 2024

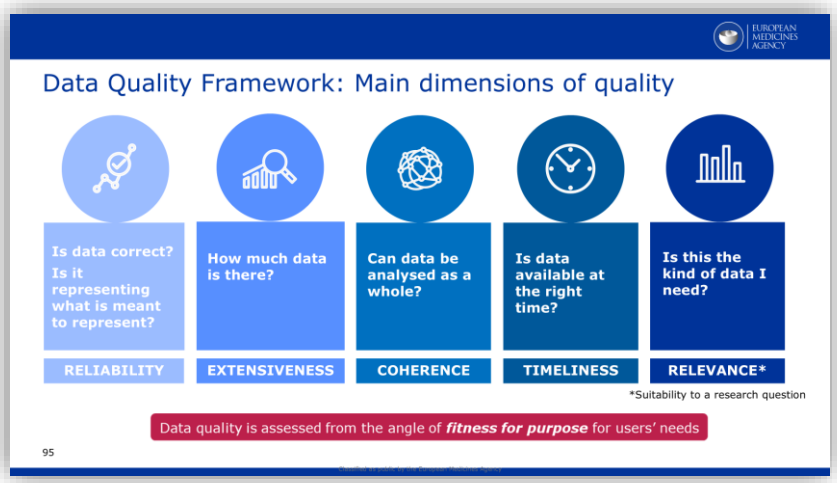
Comments should be provided using this EUSurvey form. For any technical issues, please contact the EUSurvey Support.

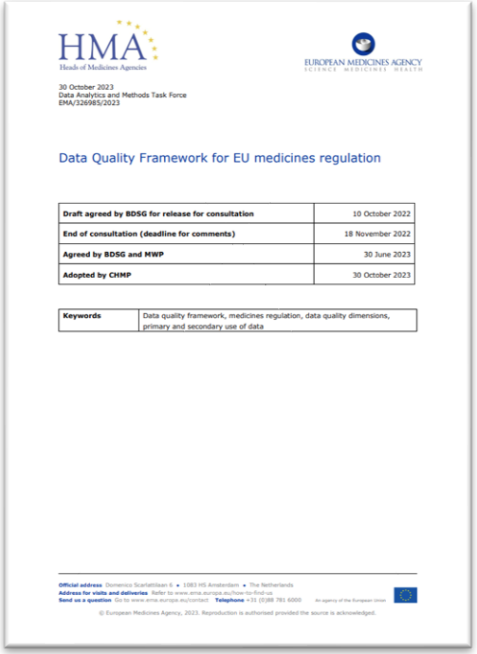
Keywords	Non-interventional study, real-world data, real-world evidence, feasibility assessment, bias, confounding, data quality

…Finding the appropriate data…

Data

- Sets out **quality criteria** for **data** to ensure they are **fit-for-purpose** for regulatory decision-making
- Definitions of **data dimensions**/ sub-dimensions as well as their characterisation and related **metrics**
- Further deep-dives to be developed: RWD deep-dive under preparation (first extension)




HMA
Heads of Medicines Agencies

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30 October 2023
Data Analytics and Methods Task Force
EMA/326985/2023

Data Quality Framework for EU medicines regulation

Draft agreed by BDSG for release for consultation	10 October 2022
End of consultation (deadline for comments)	18 November 2022
Agreed by BDSG and MWP	30 June 2023
Adopted by CHMP	30 October 2023

Keywords	Data quality framework, medicines regulation, data quality dimensions, primary and secondary use of data

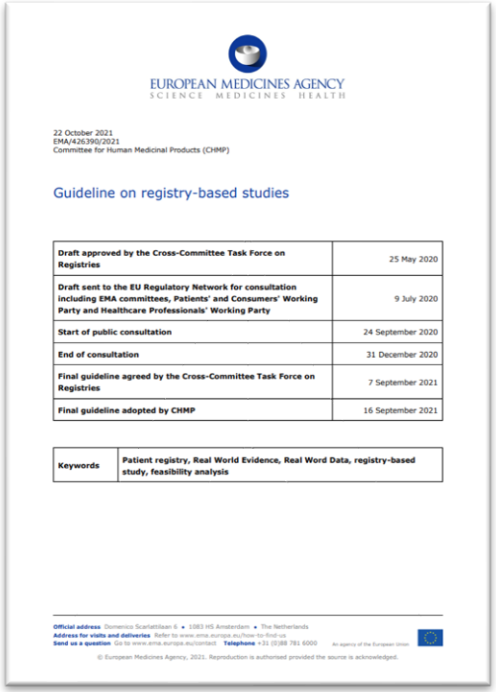
…Finding the appropriate data…

Data

Feasibility assessment

Recommended as a basis of early discussions with regulators

- Evaluation of fitness-for-purpose of the candidate data source(s) (e.g. data quality, availability of data elements, statistical power)
- Feasibility to implement the proposed study design, incl. choice of study populations, exposure(s), outcome(s), statistical parameters
- Reference to feasibility of target trial emulation approach if applicable
- Conclusion with a discussion of the relevance of the RWD sources and the study design to generate the required evidence, with a proposal of different options if applicable



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22 October 2021
EMA/426390/2021
Committee for Human Medicinal Products (CHMP)

Guideline on registry-based studies

Draft approved by the Cross-Committee Task Force on Registries	25 May 2020
Draft sent to the EU Regulatory Network for consultation including EMA committees, Patients' and Consumers' Working Party and Healthcare Professionals' Working Party	9 July 2020
Start of public consultation	24 September 2020
End of consultation	31 December 2020
Final guideline agreed by the Cross-Committee Task Force on Registries	7 September 2021
Final guideline adopted by CHMP	16 September 2021

Keywords	Patient registry, Real World Evidence, Real Word Data, registry-based study, feasibility analysis

…To fit the selected design…

Studies with causal objectives

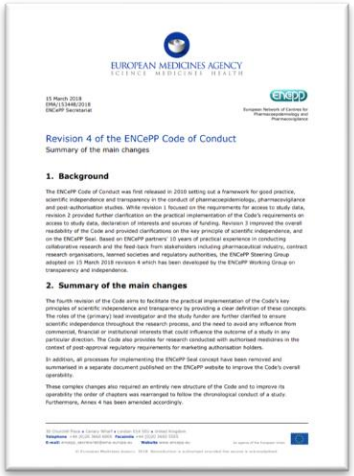
- Challenge is to deal with the risk of selection bias, information bias and confounding
- **Target trial emulation framework** should be considered as a strategy to formalise the design (and analysis)
  - Developed for NIS but similarities with CTs to facilitate evaluation of the contribution of the study to complement the evidence from CTs
  - Helps the investigators to consider potential bias and adequate methods to address them
  - Ensure high level of transparency on the study design as clear assumptions needed to emulate the trial and define causal effects, facilitating evaluation and replicability

Estimand framework may be considered for the design of the hypothetical target trial

…With an approriate governance…

Report

- Governance of the RWD sources used in a study to be made available in order to understand any restrictions related to the conditions of access, availability and publication of data
- Principles of the ENCePP Code of Conduct to be applied (ADVANCE CoC for vaccines)



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15 March 2018
EMA/153448/2018
ENCePP Secretariat

Revision 4 of the ENCePP Code of Conduct
Summary of the main changes

1. Background

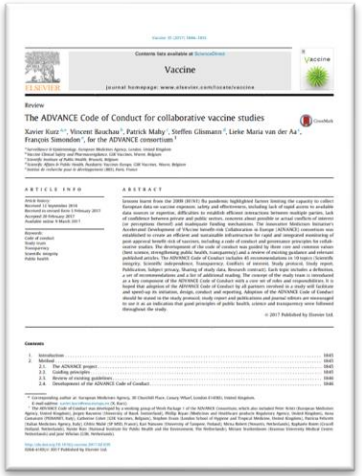
The ENCePP Code of Conduct was first released in 2010 setting out a framework for good practice, scientific independence and transparency in the conduct of pharmacoepidemiology, pharmacovigilance and post-authorisation studies. While revision 1 focused on the requirements for access to study data, revision 2 provided further clarification on the practical implementation of the Code's requirements on access to study data, declaration of interests and sources of funding. Revision 3 improved the overall readability of the Code and provided clarifications on the key principle of scientific independence, and on the ENCePP Seal. Based on ENCePP partners' 10 years of practical experience in conducting collaborative research and the feed-back from stakeholders including pharmaceutical industry, contract research organisations, learned societies and regulatory authorities, the ENCePP Steering Group adopted on 15 March 2018 revision 4 which has been developed by the ENCePP Working Group on transparency and independence.

2. Summary of the main changes

The fourth revision of the Code aims to facilitate the practical implementation of the Code's key principles of scientific independence and transparency by providing a clear definition of these concepts. The roles of the (primary) lead investigator and the study funder are further clarified to ensure scientific independence throughout the research process, and the need to avoid any influence from commercial, financial or institutional interests that could influence the outcome of a study in any particular direction. The Code also provides for research conducted with authorised medicines in the context of post-approval regulatory requirements for marketing authorisation holders.

In addition, all processes for implementing the ENCePP Seal concept have been removed and summarised in a separate document published on the ENCePP website to improve the Code's overall operability.

These complex changes also required an entirely new structure of the Code and to improve its operability the order of chapters was rearranged to follow the chronological conduct of a study. Furthermore, Annex 4 has been amended accordingly.



Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

The ADVANCE Code of Conduct for collaborative vaccine studies

Xavier Kurz, Vincent Bauchau, Patrick Mahy, Steffen Glismann, Lieke Maria van der Aa, François Simondon, for the ADVANCE consortium

ARTICLE INFO

ABSTRACT

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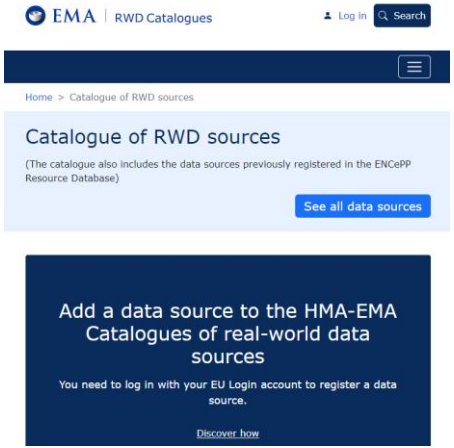
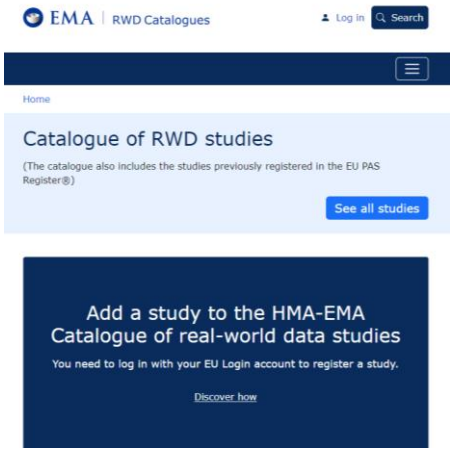
…And a high level of transparency.

Report





230
registered RWD sources

81.7% in the EU (n =188)

35
New data sources added since February 2024 (go-live)

2,929
registered RWD studies

65% conducted within the EU (n =1,905)

168
New studies added since February 2024 (go-live)

665
Studies linked to data sources in the RWD Catalogues

34
DARWIN EU® studies

As a conclusion…

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

Thank you!

Further information

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