European Network of Centres for Pharmacoepidemiology

Working Groups updates from 2024

Working Group 1

ENCePP research standards and guidance

Chair: Alejandro Arana

Objective

To address methodological aspects of pharmacoepidemiological research, including real-world evidence (RWE) research conducted to support decision-making by regulators and other relevant stakeholders

Updated Mandate (draft)

- Periodically update the ENCePP Guide on Methodological Standards in Pharmacoepidemiology to align with latest guidance and developments in the field [2024: deliver strategy for revamping of format/structure in view of 2025 update; explore publication in a scientific journal]
- Periodically review and propose updates, as applicable, to the ENCePP Checklist for Study Protocols [2024: embed elements of HARPER, EMA & FDA RWE draft guidance/reflections, and other relevant guidance]
- Monitor emerging research standards and guidance relevant for ENCePP activities and review as required to provide consolidated ENCePP WG1 feedback [e.g., public consultation for GVP VIII or ICH M14]
- Communicate on WG1 deliverables and support the other ENCePP Working Groups by delivering materials advocating the use of ENCePP standards and tools (such as webinars, slides, links to external trainings curricula, etc.)

Updates to the ENCePP Checklist for Study Protocols [2024: embed elements of HARPER…]

- Tool to promote transparency, reproducibility and harmonisation of non-interventional study protocols designed by academics, companies and regulators
- Will facilitate design and assessment of high-quality protocols by companies and regulators
- Compatible with legal format and content of GVP Module VIII on PASS and can be used in PASS protocols without change of structure
- Provides a structure for the evaluation of the suitability of RWD sources for a given research question based on the EMA metadata catalogue for data sources
- Provides a template for the development of generic protocols to be used in DARWIN EU® and other studies

Received: 7 February 2022 | Revised: 17 June 2022 | Accepted: 28 June 2022
DOI: 10.1002/pds.5507

ORIGINAL ARTICLE

WILEY

HARmonized Protocol Template to Enhance Reproducibility of hypothesis evaluating real-world evidence studies on treatment effects: A good practices report of a joint ISPE/ISPOR task force

Shirley V. Wang[1] | Anton Pottegård[2] | William Crown[3] | Peter Arlett[4] | Darren M. Ashcroft[5] | Eric I. Benchimol[6,7,8] | Marc L. Berger[9] | Gracy Crane[10] | Wim Goettsch[11,12] | Wei Hua[13] | Shaum Kabadi[14] | David M. Kern[15] | Xavier Kurz[4] | Sinead Langan[16] | Takahiro Nonaka[17] | Lucinda Orsini[18] | Susana Perez-Gutthann[19] | Simone Pinheiro[13] | Nicole Pratt[20] | Sebastian Schneeweiss[1] | Massoud Toussi[21] | Rebecca J. Williams[22]

Updates to the ENCePP Checklist for Study Protocols [2024: embed elements of HARPER…]

WG1 sub-team led by Katja Hakkarainen (Done)

ENCePP WG1 members to indicate additional guidance to consider, if any (Done)

Review of the 1st draft by the ENCePP WG1 members in Dec 2024

Working Group 2

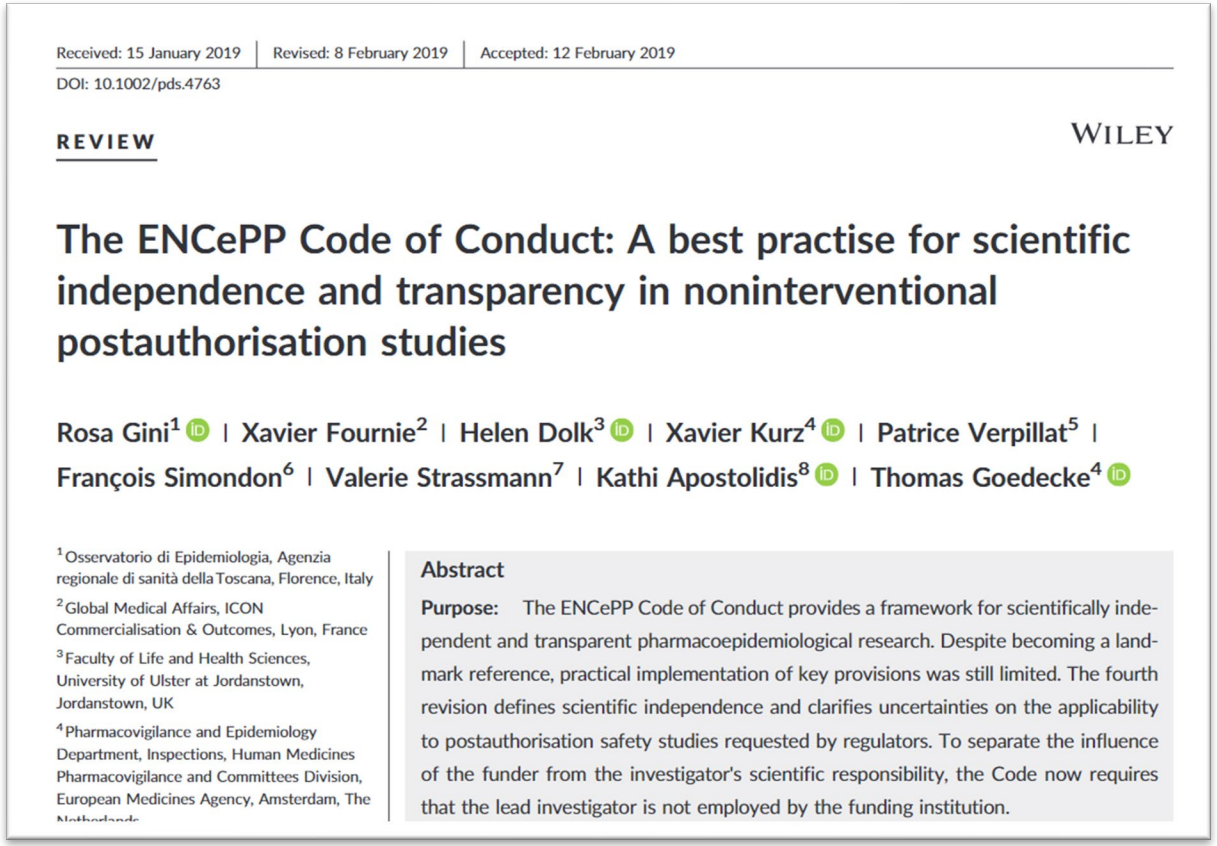
Independence and transparency

Chair: Rosa Gini

Mandate

- To periodically review the ENCePP Code of Conduct and propose updates, as applicable
- To support use of the Code of Conduct and explore ways of better monitoring its implementation for ENCePP Seal studies
- To promote registration of studies in the HMA-EMA Catalogues of real-world data studies and support EMA in the further development of the Catalogues with regards to transparency and use of the Code of Conduct

The ENCePP Code of Conduct



Received: 15 January 2019 | Revised: 8 February 2019 | Accepted: 12 February 2019
DOI: 10.1002/pds.4763

REVIEW

WILEY

The ENCePP Code of Conduct: A best practise for scientific independence and transparency in noninterventional postauthorisation studies

Rosa Gini[1] | Xavier Fournie[2] | Helen Dolk[3] | Xavier Kurz[4] | Patrice Verpillat[5] | François Simondon[6] | Valerie Strassmann[7] | Kathi Apostolidis[8] | Thomas Goedecke[4]

[1] Osservatorio di Epidemiologia, Agenzia regionale di sanità della Toscana, Florence, Italy
[2] Global Medical Affairs, ICON Commercialisation & Outcomes, Lyon, France
[3] Faculty of Life and Health Sciences, University of Ulster at Jordanstown, Jordanstown, UK
[4] Pharmacovigilance and Epidemiology Department, Inspections, Human Medicines Pharmacovigilance and Committees Division, European Medicines Agency, Amsterdam, The Netherlands

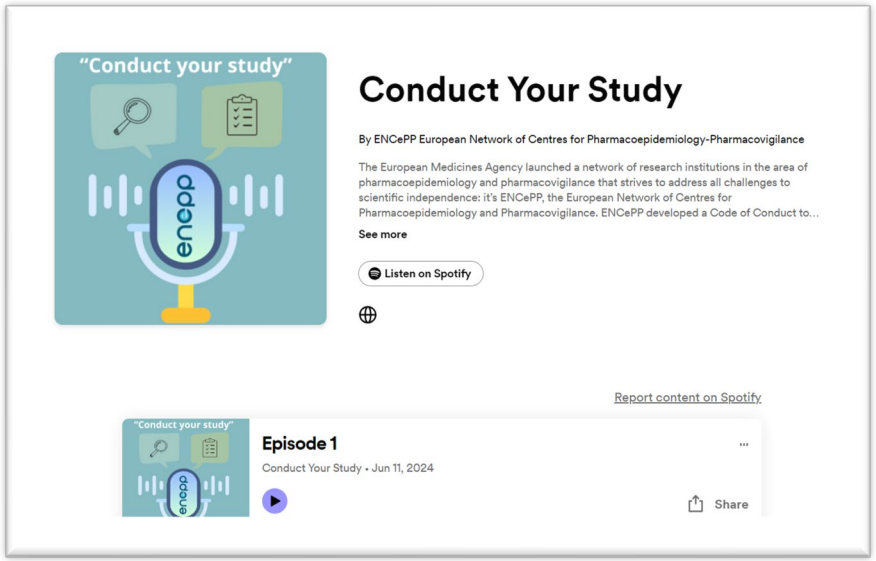
Abstract

Purpose: The ENCePP Code of Conduct provides a framework for scientifically independent and transparent pharmacoepidemiological research. Despite becoming a landmark reference, practical implementation of key provisions was still limited. The fourth revision defines scientific independence and clarifies uncertainties on the applicability to postauthorisation safety studies requested by regulators. To separate the influence of the funder from the investigator's scientific responsibility, the Code now requires that the lead investigator is not employed by the funding institution.

A revision is foreseen to

- Replace the EU PAS Register with the new HMA/EMA Catalogue
- Update the Checklist
- Update the transparency measures (e.g., reference to code sharing)

Conduct Your Study: a podcast on the Code of Conduct



Launched in June 2024

First episode: interview to Barbara Mintzes

Online **today**: second episode with **Shirley Wang** and **Anton Pottegård**

Upcoming episodes: perspective from investigators, regulators, researchers in pharmaceutical companies…

Next challenges

- Investigate barriers/enablers for adoption of the Code of Conduct
- Based on the EMA/HMA Catalogue: investigate the effect of compliance with the Code of Conduct on study quality and impact

We need you!

Working Group 3

Non-interventional studies in Europe

Chair: Gianluca Trifirò

Mandate

- Explore which type of data sources and study designs are used for which types of research questions in the HMA-EMA Catalogues of real-world data sources and studies
- Comparison of the HMA-EMA Catalogues of real-world data studies with other public registers of non-interventional studies (NIS)
- Understand the impact of the new clinical trial regulation on the conduct on NIS: explore the main designs reported in the HMA-EMA Catalogues of real-world data studies with a focus on hybrid designs (e.g., pragmatic clinical trials, clinical trials with real-world evidence components)
- Survey among ENCePP partners on definitions, use and challenges of hybrid designs
- Overview of the types, strengths, limitations, and application of Common Data Models (CDMs) in EU data sources
- To interact with ISOP Big data and RWE Special interest Group to explore the potential interplay of spontaneous reporting system databases and distributed database networks

List of suggestions/recommendations for EU-PAS Register improvement from ENCePP WG3

General comments:

1. To implement automatic quality checks as some data are not registered in accurate way and certain combinations of choices are not possible (e.g. scope of the study: disease epidemiology; type of study design: clinical trial - other example: study carried out with an established data source = No; sources of data = claims database); the use of natural language processing (NLP) to check discrepancies between what has been reported in the protocol and what have been recorded in the different fields.
2. To incorporate help text and the following guidance:
   - for those registering the study to facilitate accurate registration;
   - for data users;
   - on what fields have to be filled by the Principal Investigator.
   Such guidance may include a guided wizard, where, based on the answers given, some classifications are automatically generated. It could also be helpful to limit free-text fields by using drop down menus or other tools which limit options in data recording.
3. To make registration of the study protocol compulsory as the study protocol is currently available in less than 50% of the studies registered in the EUPAS register (suggestion: make PRAC assessment of a protocol conditional to having the study registered in the EU PAS). Since it is not legally possible to impose the registration of the study protocol, the only means would be to have a study registered only after the protocol is available and uploading of the protocol mandatory before registration is complete. Moreover, it could be helpful to create Policy/Procedure to automate data extraction from the study protocol.
4. To explore the possibility of linking the registration of the study to the PRAC minutes as well as ENCePP resource database or clinicaltrials.gov.
5. To compare date of already existing field on first registration of a regulatory required study (categories 1-2) and Marketing Authorisation (MA) date (initial MA, renewal, variation of MA), field that should be created, in order to monitor compliance with registration time frame required (within 6 months after MA according to GVP). More generally, a set of compliance checks (automated or semi-automated) should be defined.
6. To add new export functionalities to more easily extract data (.xls, .csv format etc…) including all fields available in the Register.
7. To implement metadata/API fields crosswalks for the EU PAS register like for clinicaltrial.gov (see https://clinicaltrials.gov/api/gui/ref/crosswalks).
8. A significant number of 'unknown' variables in EU PAS register form and they may not represent what was actually designed in study protocols.
9. Revise the list of mandatory fields – agreement has to be sought on what fields have to be mandatory.
10. Check whether there are MS or national competent authorities that have requirements for companies to register studies in catalogues and explore possibilities of link (reporting the ID of the study in the EU PAS Register?). A field could be included in the record to allow providing such links.

enepp

Different Strategies to Execute Multi-Database Studies for Medicines Surveillance in Real-World Setting: A Reflection on the European Model

Rona Gini[1,*], Miriam C. J. Sturkenboom[2], Janet Sultana[3], Alison Cave[4], Annalisa Landi[5,6], Alexandra Pacurariu[4], Giuseppe Roberto[1], Tania Schink[7], Gianmario Candore[4], Jim Slattery[4], and Gianluca Trifirò[8] on behalf of the Working Group 3 of ENCePP (Inventory of EU data sources and methodological approaches for multisource studies)

Drug Safety (2022) 45:333–344
https://doi.org/10.1007/s40264-022-01154-7

ORIGINAL RESEARCH ARTICLE

Check for updates

A Landscape Analysis of Post-Marketing Studies Registered in the EU PAS Register and ClinicalTrials.gov Focusing on Pregnancy Outcomes or Breastfeeding Effects: A Contribution from the ConcePTION Project

Leonardo Roque Pereira[1] · Carlos E. Durán[1] · Deborah Layton[2] · Georgios Poulentzas[3] · Panagiotis-Nikolaos Lalagkas[3] · Christos Kontogiorgis[3] · Miriam Sturkenboom[1]

Ongoing work

- Manuscript "*Identifying regulatory outcomes of non-interventional Post Authorisation Safety Studies in the European repository of studies using publicly available information*" submitted to the journal Pharmacoepidemiology and Drug Safety on 4th November 2024

- Manuscript "Descriptive Analysis of Pediatric Studies included in the European Union Post-Authorization Study Register from 2010 to 2023" finalized and to be submitted soon to the journal Pediatric Reports

- Manuscript “Evaluation of secondary data utilization in observational studies registered in the EU PAS Register” finalized and to be submitted soon

- Supplementation of use cases reported in the HMA-EMA Catalogues with some real-life practical examples (real-world studies already performed or fictional studies), demonstrating the use of the catalogues in the planning of the study and document the process

Thank you and thanks to all the members of WG3!

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