ENCePP Plenary meeting 2025 Report

Monday, 1 December 2025

EMA, Amsterdam (hybrid)

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Agenda

Chairs: Helga Gardarsdottir (Utrecht University), Catherine Cohet (EMA)

Item	Topic	Speaker(s)	Time
1.	Arrival, connection to virtual room and technical checks		08:30-9:00
2.	Welcome	Peter Arlett (EMA)	09:00-9:10
3.	Meeting objectives	Helga Gardarsdottir (Utrecht University) Catherine Cohet (EMA)	09:10-9:15
SESSION 1: Where are we 2 years into the 2024-2026 mandate? **Chairs: *Laura Pizzi (ISPOR) & Patrice Verpillat (EMA)***			
4.	ENCePP workplan 2024-2026: progress update	Helga Gardarsdottir (Utrecht University) Catherine Cohet (EMA)	9:15-9:30
5.	New Working Groups and Special Interest Groups: mandate and progress so far	WGs/SIGs chairs	9:30-10:30
Coffee break and networking – 10:30 to 11:00			
6.	New Working Groups and Special Interest Groups: mandate and progress so far (ctn'd)	WGs/SIGs chairs	11:00-11:45
SESSION 2: ENCePP in the current RWD/RWE environment ***Chairs: Rosa Gini (ARS Toscana) & Daniel Morales (EMA)***			
7.	RWE generation at EMA: • DARWIN EU update • RWD studies: selected use cases	Andrej Segec (EMA)	11:45-12:15
8.	EHDS: latest news and testimony from Finland	Jaakko Lähteenmäki (VTT Technical Research Centre of Finland)	12:15-12:45
Lunch and networking – 12:45 to 13:30			
9.	EU/international guidance: what's new?	Catherine Cohet (EMA)	13:30-14:00
SESSION 3: 'Not so new' methodologies, new applications ***Chairs: Anna-Maija Tolppanen (University of Eastern Finland) & Alexandra Pacurariu (EMA)***			
10.	Target trial emulation and estimand frameworks: Current thinking and overview of the TARGET-EU project	Daniala Weir (Utrecht University)	14:00-14:45

Item	Topic	Speaker(s)	Time
11.	Interactive session on Pragmatic Clinical Trials	Panellists: • Isla Mackenzie (Dundee university) • Mira Zuidgeest (UMC Utrecht) • Patrice Verpillat (EMA)	14:45-15:45
Wrap-up			
12.	• Feedback from Plenary participants • Closing and next steps	Helga Gardarsdottir (Utrecht University) Catherine Cohet (EMA)	15:45-16:00
Adjournment – 16:00			

Welcome and meeting objectives

Catherine Cohet, the co-chair of the ENCePP Steering Group (SG), welcomed the participants. Peter Arlett, Head of the Data Analytics and Methods Task Force at EMA, opened the meeting; he highlighted some of the key achievements of the 3-year ENCePP workplan, including the creation of 6 new Working Groups and 4 Special Interest Groups aiming at addressing continued and new priority areas, such as artificial intelligence, pragmatic trials, diversity and equity in pharmacoepidemiology, and communications. The Plenary agenda was developed to address the high demand from ENCePP partners for topics such as updates from EMA on RWE-related matters, DARWIN EU and the EHDS; status of international guidance; the target trial and estimand frameworks; and pragmatic clinical trials. Peter reminded that the Plenary is not only about presentations but aims at fostering dialogue and listening to the views of the ENCePP partners, which are essential to continue supporting EMA's commitment to high-quality evidence generation for regulatory decision-making.

Helga Gardarsdottir (Utrecht University), the ENCePP Steering group co-chair, presented the objectives of the meeting:

- To reflect on the progress of the ENCePP Work plan since the 2024 Plenary;
- To present the new Working Groups and Special Interest Groups, and seek feedback from the ENCePP community on their objectives and completed/upcoming deliverables;
- To continue placing the work of ENCePP in the context of the ever-changing regulatory and real-world evidence (RWE) environment, by sharing updates on DARWIN EU[1], the EHDS, and new EU and international guidance relevant to ENCePP;
- Following up on methodological sessions in past years Plenary meetings[2], to dive deeper into topics of current interest.

This report summarises the main topics and outcomes of the 2025 ENCePP Plenary meeting. For further detail, please refer to the presentations available on the ENCePP website.

[1] Real-world evidence | European Medicines Agency (EMA)
[2] Plenary Meetings - European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

Session 1: Where are we 2 years into the 2024-2026 mandate?

*Chairs: Laura Pizzi (ISPOR), Patrice Verpillat (EMA)*ENCePP workplan 2024-2026: progress update

Helga Gardarsdottir presented the status of the workplan at the end of the second year of the Steering Group (SG) mandate. Several deliverables have been achieved so far:

- Governance: new Working Groups and Special Interest Groups were established with corresponding Terms of Reference, and the mandates of ENCePP (see About us) and the Steering Group were reviewed and updated.
- Visibility: News items on the ENCePP website are published on a continuous basis; selected chapters of the ENCePP Guide have been published or are under development/submitted, as part of special series in *Pharmacoepidemiology and Drug Safety* and in *Value in Health*.
- Impact: qualitative research on ENCePP (report and webinar) was completed; co-branded events with learned societies (ISPE, ISPOR) were organised; ENCePP membership became open to public/regulatory bodies in EU candidate countries.

New Working Groups and Special Interest Groups: mandate and progress

The need for reorganising and/or creating new groups with the aim of contributing to the ENCePP work plan, and focus on new, important areas, was discussed in the 2024 Plenary, where new topics of interest were identified. The news groups were created after a call for interest among ENCePP partners. Following their respective kick-off meetings, the groups agreed on their draft mandate and objectives, which were reviewed and endorsed by the SG.

The co-chairs of the WGs and SIGs presented their objectives and deliverables in Plenary, provided a status update, and opened for comments. The objectives were published on the Working Groups and Special Interest Groups page of the ENCePP website after the meeting.

Refer to WGs/SIGs webpage and slides for the detailed objectives.

Working Groups:

- Communications and Outreach
- Revision of the ENCePP Guide on Methodological Standards in Pharmacoepidemiology
- Independence and Transparency
- Artificial Intelligence (AI) in Pharmacoepidemiology
- Diversity and Health Equity
- Real-World-Data (RWD) sources in non-interventional studies

Special Interest Groups:

- Pragmatism in Clinical Trials
- Update of the ENCePP Checklist for Study Protocols
- Supplement to the Good Practice Guide for the use of the HMA-EMA Catalogues of real-world data (RWD) sources and studies
- Publication of selected chapters of the ENCePP Guide in in *Pharmacoepidemiology and Drug Safety* and in *Value in Health*

Q&A/discussion

- Communications and Outreach
  - Q: Difference between internal and external communication? A: Internal refers to the communication with the various WGs and SIGs, and information gathering from these groups to support external communications.

- Q: How can the impact of communication be assessed? Any KPIs? A: under discussion; however, a tracking system, e.g., on number of website visits, or biannual checkpoints with the ENCePP network and the WGs/SIGs may be a more manageable approach.
- Q: How far is the WG in talking to the other groups? A: There have been some informal discussions, work for the WG is only starting.

- Revision of the ENCePP Guide on Methodological Standards in Pharmacoepidemiology
  - Revision of chapters selected by the WG based on current importance in the field is ongoing, aligning with the SIG on parallel publications in PDS/ViH; the strategy for further periodic revision is under discussion. There were no suggestions or questions from the meeting participants.
- Independence and Transparency
  - The WG co-chairs asked the ENCePP members to verify in the HMA-EMA Study Catalogue that their studies are compliant with the Code of Conduct (and if so, to be marked accordingly).
- Artificial Intelligence (AI) in Pharmacoepidemiology
  - Q: What does the WG mean by 'critically appraise AI tools relevant to pharmacoepidemiology'? A: The group aims to describe and evaluate AI tools in the context of pharmacoepidemiology, but also to analyse the impact of their implementation, including comparison with traditional approaches, assessing pros and cons, barriers for implementation etc.
  - Q: What does the group mean by 'collaborate with the other WGs to ensure alignment'? A: Alignment with existing initiatives, collaboration with the ENCePP groups to ensure outputs are useful. The WG also plans to coordinate with the SG for prioritisation of the deliverables.
  - Q: One of the objectives is 'Critically appraise AI tools relevant to pharmacoepidemiology'. Why not pharmacovigilance? A: In the WG there are experts in both areas, the same tools may be applied to both fields.
  - General suggestions to the WG: as the topic is broad, the WG is advised to carefully reflect on the scope. Focus should be more on users than on products/tools, as it's a fast-evolving area.
- Diversity and Health Equity

  Discussion points:
  - What is the importance of this topic in pharmacoepidemiology? Diversity (gender, ethnicity, etc.) is more a challenge in clinical trials than in pharmacoepidemiological studies, where consideration of socio-economic status, education, country of origin etc. is maybe more relevant due to impact on accessing treatments. Focus should be on how these population groups are accounted for in pharmacoepidemiological studies.
  - It would be valuable to understand what information is available and where, and what can be done with it in Europe. It would also be useful from a regulatory perspective.
  - Different trends in healthcare utilisation to be kept in mind: some patient groups are not using the healthcare system and may not be reflected in healthcare data. This also goes beyond the EU context. Disability would be relevant to explore, for example in simple drug utilisation studies, to illustrate possible obstacles to access to care.
  - The WG was advised to check the deliverables of the ISPE and ISPOR health equity SIGs.
- Real-World-Data (RWD) sources in non-interventional studies
  - Q: One of the objectives is on harmonisation and use of CDMs: is the aim really to harmonise CDMs? A: The intention is rather to identify all CDMs that the different data networks use and describe their limitations.
  - Q: Study feasibility is a critical aspect, and guidance would be welcome. A: The HMA-EMA Catalogue (studies and data sources) can address some feasibility aspects. The goal of the WG

is to provide guidance to facilitate feasibility assessments using a checklist to help identification of suitable data source(s) for a given research question.

  - In light of the ambitious workplan, the WG was advised to reflect on what is feasible to deliver and to consult the work of the ISPE/ISPOR feasibility taskforce for inspiration and avoiding redundancy. The WG co-chair clarified that sub-groups will be created to deliver the tasks.

- Pragmatism in Clinical Trials
  - The terminology - pragmatic clinical trials vs. pragmatism in clinical studies - was discussed in light of the broad context and continuum from exploratory to observational aspects (see PRECIS tools), and the limited number of PCTs conducted so far, or at least, identified as such (i.e., related to clinical regulation).
  - It was advised that focus should be on informing guidance development by the EMA Methodology Working Party (MWP) (see Methodology Working Party Workplan 2025-2027), as was done for the RWE Reflection paper, which contents were partly inspired by the ENCePP Guide. It was recommended that priority should be to support the future MWP concept paper on pragmatic trials.
  - The plan for the SIG is to start with the most relevant activities, and reassess timelines and deliverables as needed.
- Update of the ENCePP Checklist for Study Protocols
  - Q: question to EMA about the status of the revision of the Guideline on good pharmacovigilance practices (GVP) - Module VIII, which recommends use of the checklist for Post-authorisation safety studies. A: now that the ICH M14 guideline is published, work is ongoing to incorporate its contents in the revision. Finalisation is expected by Q2 2026.
  - The SIG co-chair confirmed that the checklist will be fully aligned with ICH M14.
- Supplement to the Good Practice Guide for the use of the HMA-EMA Catalogues
  - It was clarified by the chair that the main objective is to create a practical guide to show how to make best use of the Catalogues when working on specific studies.
- Publication of selected chapters of the ENCePP Guide in *PDS* and *Value in Health*
  - On the ENCePP Guide section of the ENCePP website, the publications will be linked in the corresponding chapters.

Session 2: ENCePP in the current RWD/RWE environment

Chairs: Rosa Gini (ARS Toscana), Daniel Morales (EMA)

RWE generation at EMA

Andrej Segec (EMA) provided a recent update with a focus on the expansion of DARWIN EU and presented four selected use cases, highlighting the rationale for the studies, the analytical approaches, and the impact on regulatory decision-making.

Q&A/discussion

- Q: Considering the large network of data sources in DARWIN EU, why do the studies only use a limited number of data sources? A: The selection of data sources is based on relevance of the data, data granularity, and exposure and outcome counts.
- Q: In one of the use cases, 'lack of interpretation and or assessments of impact and limitations of results' was reported as limitations, why? A: It was to reinforce the importance of contextualising the study results with existing evidence such as from the available literature.

- Q: Two areas in which EMA is driving pharmacoepidemiology work relates to studies that EMA committees request to MAAs or MAHs; and helping to shape the programs of the Innovative Health Initiative. Can you comment on these branches and their directions? A: Regarding EMA studies, the framework contract pathway will remain, considering its importance to obtain specific data not available via DARWIN EU, such as from rare disease registries. Obligations on the MAAs/MAHs will remain, and DARWIN EU can support this process, for example by suggesting to the Rapporteurs suitable data sources that could be used by the MAAs/MAHs. In addition, EMA is also generating evidence about feasibility, that will not necessarily lead to an actual study but can inform evidence generation. Regarding IHI, EMA has indeed a role, via a dedicated group working on research needs of the regulatory network, also important in the context of the new pharma legislation.

EHDS: latest news and testimony from Finland

Jaakko Lähteenmäki (VTT) presented the VTT Technical Research Centre of Finland and provided an overview of the Finnish healthcare system. He then focused on secondary use of health and social data in Finland and provided his views about the EHDS implementation.

Q&A/discussion

- Q: Considering that Finland is well ahead with its infrastructure, can it be considered as a model for other countries? A: This is somehow already happening, since the regulation took many aspects from the Finnish model. Still, there are shortcomings in the Finnish system too.
- Q: Is there a place where lessons learned can be shared at EU level? A: There are two ways: one is through the data project in which Finland is participating, and another is the official working groups where representatives from Finland are bringing their knowledge.
- Q: Regarding the social services data that can be included in your dataset, are these being used to answer questions, or are just healthcare data? A: These data are mostly free-text data, and therefore more challenging to use. To some extent they are being used together with health data.
- Q: Can you comment on the aspect of limited involvement of Finnish and ENCePP experts in the process, and about delays in data preparation? This highlights a methodological risk: data minimisation might be performed before experts can access the data, introducing bias. A: This is an important aspect. Data minimisation needs to happen in the data access and in collaboration with the data user; it is extremely important that the data user has a clear role in the process.

EU/international guidance: what's new?

Catherine Cohet (EMA) presented on EU and international guidance aimed at supporting reliable and relevant RWE. She outlined the *Reflection paper on use of RWD in non-interventional studies to generate RWE for regulatory purposes*, the *RWD chapter of the Data Quality Framework for EU medicines regulation*, recent updates of the *HMA-EMA Catalogues*, the *Methodology Working Party workplan* and upcoming revisions of *GVP VIII* and the *EMA guideline on registry-based studies*. She concluded by highlighting some international initiatives on RWE harmonisation, such as the *ICH M14 Guideline* and the *Working Group on Real-World Evidence for Public Health Emergencies | International Coalition of Medicines Regulatory Authorities (ICMRA)*.

Q&A/discussion

- Q: Is Latin America involved in this kind of collaborations? A: Yes, Latin American countries are for example represented in ICH expert working groups and in ICMRA working groups.
- Q: The Reflection paper highlights the difference between descriptive and causal inference studies. Since the three elements of data science also include prediction studies, where do these fall? A: In the RWE reflection paper, prediction studies fall under the descriptive studies.
- Q: regarding the HMA-EMA Catalogues, are you considering including AI approaches, that could for example use natural language queries, rather than relying on traditional metadata search? A: feedback for improvement of the Catalogues is always welcome, this could be considered. In addition,

it should be noted that the metadata themselves can be downloaded, therefore AI tools can be applied.

- Q: how will MAHs be engaged in the revision of GVP VIII? A: the decision was to focus the update on the protocol section taken from ICH M14, which has already undergone public consultation.

Session 3: 'Not so new' methodologies, new applications

Chairs: Anna-Maija Tolppanen (University of Eastern Finland), Alexandra Pacurariu (EMA)

Target trial emulation and estimand frameworks: Current thinking and overview of the TARGET-EU project

Daniala Weir (Utrecht University) presented her work on bridging the target trial emulation and estimate frameworks. The presentation included the definition of the estimand (as reflected in the ICH E9(R1) addendum), intercurrent events and strategies to handle them, and an overview of the ongoing EMA funded TARGET-EU project.

Q&A/discussion

- Q: Which aspects should one consider when choosing a particular intercurrent events strategy? Also, is it possible to choose more than one strategy in a TTE study? A: The clinical and regulatory question of interest is what we are interested in, for example, it depends on whether it is a safety or an effectiveness question.
- Q: While-on-treatment and the Treatment policy approaches: you then go for each intercurrent event, and discuss whether the choice of each strategy is actually answering the regulatory question of interest: what should be in the drug label? A: The rationale for the choice of each strategy should always be reported. Supplementary analyses can be conducted where another strategy is chosen. It is important to highlight that these are not sensitivity analyses.
- Q: Is it important to involve patient organisations to support better design? Could it be useful? A: It is, especially ensuring that patient organisations have a good understanding of how the evidence is being generated and then being used to make treatment decisions.

Interactive session on Pragmatic Clinical Trials

Mira Zuidgeest (University Medical Center Utrecht) gave a presentation focusing on the following aspects: what we mean by Pragmatic clinical trial (PCT), the main design principles, opportunities and challenges, and some use cases. Isla Mackenzie (University of Dundee) talked about the experience from Dundee University with three large PCTs conducted over the last few years.

Q&A/discussion

- Q: Which are the operational and logistical encounters that you face? A: The most difficult part is to obtain all approvals in time; also, when conducting multi-country studies, different legislations and systems for each data source are in effect. Another challenge is receiving the data, for example to process all hospitalisations, death, and pharmacovigilance safety reporting.
- Q: Are there opportunities to consider for PCTs approaches to support increasing diversity in the trial population? A: An opportunity is when patients come to seek care and are randomised. Another example is community-based recruitment, but this is not necessarily specific to PCTs.
- Q: How to consider the different perspectives in PCTs, e.g., reducing the burden on the patients and physicians by decentralising might restrict the types of questions and endpoints that can be analysed and make approval harder or more time-consuming. A: This is an important point, as for example, shifting burden away from primary care practice might put more burden on the participants (like entering or collecting the data themselves). Therefore, it is still very important to see it from everyone's perspective and find solutions for all stakeholders involved.

- PCTs could also be seen as a topic that comes after the regulatory 'absolute' assessment, more to support HTAs relative safety and effectiveness assessment and choice of optimal treatment. A point was made that relative effectiveness may be considered by regulators as well.

- There is a shift at HTA level towards implementing innovation, including opportunity costs. Complex interventions especially might benefit from pragmatic trials.

- The trial regulation is a challenge for pragmatic trials which are still in the 'grey zone' from an operational perspective. Both industry and regulators are still conservative on this front and PCTs might be rejected early on. Sometimes companies are afraid to submit. Drug supply chain is an example of such a blocker.

Wrap-up

The co-chairs Helga Gardasdottir and Catherine Cohet thanked the attendees for their participation and summarised the meeting, from the work presented by the WGs and SIGs, to new international guidance, the EHDS, and methodologies such as TTE and PCTs.