EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

21 November 2016
EMA/666824/2016
ENCePP Secretariat

Minutes - ENCePP Steering Group Meeting

11 October 2016, 09.30 to 16.30, chaired by Peter Arlett

List of participants	
Present	Peter Arlett, Corinne de Vries, Dinah Duarte, Pierre Engel, David Haerry, Maria Teresa Herdeiro, Nicholas Moore, Yola Moride (partly – via TC), Susana Perez-Gutthann, Nawab Qizilbash (partly – via TC), Patrice Verpillat Principal Adviser to the SG: Xavier Kurz Statistical Adviser to the SG: Jim Slattery ENCePP Secretariat: Thomas Goedecke, Eeva Rossi, Dagmar Vogl Others: Alison Cave (EMA), Patricia McGettigan (EMA)
Apologies	Morten Andersen, Marieke de Bruin, Hans-Georg Eichler, Thomas MacDonald

1. Welcome & Adoption of draft agenda

The Chair welcomed the participants to this last meeting of the current Steering Group (SG), looking forward to fruitful discussions on a number of key topics.

The agenda was adopted without changes.

2. ENCePP delivering to the lifecycle of medicines

2.1. Real World Evidence

Xavier Kurz introduced this session, the aim of which would be to highlight current discussions about the use of real-world evidence (RWE) to support regulatory decision-making by scientific Committees, and to discuss how ENCePP could support the use of RWE for decision-making.

He elaborated that regulatory decision-making currently mostly relies on industry data, and it would be very desirable to complement this by enhancing the capability and capacity for the use of real world evidence, including from academia and via regulators.

The notion of common protocol models for quick access and access to wider sets of data was broadly welcomed by the Steering Group members, although it was highlighted that a strategic approach to data protection will be a key success factor in achieving this goal.

2.2. Inventory of longitudinal patient data sources & other initiatives to support RWE

Alison Cave introduced a landscaping process around existing data sources and European initiatives which aim to create a framework which delivers access to and analysis of multi-national real world data to optimise medicinal development, supervision and decision making.

Regarding the EMA analysis of EU data sources, and SG members were invited to discuss how ENCePP could possibly contribute to this work, be it through the identification of key data sources, or the identification of key initiatives.

The SG agreed that ENCePP will potentially be able to contribute with existing resources and expertise; to this end this topic will also be raised at the Plenary meeting in November. However, the group cautioned that clarification on the validity (including representativeness) and acceptability of data to regulatory decision-making would be a crucial element in this analysis.

The following areas were identified as requiring immediate attention:

- Clarification of what questions can be addressed with RWE.
- Identification of parameters for validity of data sources, their quality and robustness.
- Development of methodological guidance.

It was suggested that the EU PAS Register might be a good source for identifying existing multi-source studies.

The SG charged Working Group 'Research Standards and Guidances' with looking further into validation aspects, including potential revision of the existing ISPE Guidelines for good database selection and use in pharmacoepidemiology research (Pharmacoepidemiol Drug Saf. 2012 Jan;21(1)). To this end, Yola Moride, the ISPE representative on the Steering Group, agreed to liaise with the relevant ISPE special interest group to explore the need for a revision.

In concluding this topic, Xavier Kurz mentioned that the EMA will be hosting a workshop on registries on 28 October 2016. Attendees at this workshop will be registry custodians, scientists, regulators and industry representatives, and it is anticipated that the outcome of this workshop will be a set of useful recommendations and/or guidance. It was also noted that EMA will host a workshop on Big Data on 14 and 15 November 2016.

2.3. Interaction ENCePP/HTA

There is increasing interest among ENCePP members to integrate into ENCePP activities topics specifically related to HTA such as measurement of effectiveness, PRO or joint regulatory/HTA observational studies. The ENCePP Working Group on Research Standards and Guidances is due to discuss how to include more HTA topics into guidance documents, and SG members were therefore invited to reflect on whether/how ENCePP should have additional interactions with HTA.

Xavier Kurz reminded the SG that the latest revision of the ENCePP Methods Guide had been reviewed for potential HTA amendments, and that the ENCePP Checklist for Study Protocols had also been amended to take account of HTA aspects. He invited the SG to reflect on the need of a specific HTA chapter in the next revision of the Guide.

The SG members agreed that with the increased use of multi-purpose studies there is also a need for developing further guidance on embedding effectiveness endpoints in observational PAS, and ENCePP could potentially be well placed to provide such guidance.

3. ENCePP 2007 to 2017

2017 will mark the 10th anniversary of ENCePP, and the Chair invited the SG members to an open discussion on the impact of ENCePP to date, its successes and where it fell short of expectations, including ideas on how ENCePP might be enhanced going forward.

3.1. ENCePP's impact to date, and enhancements going forward

In terms of impact, ENCePP has been the driving force for independence, transparency and collaboration in observational research over the past ten years. The SG agreed that ENCePP has increased the credibility and awareness of observational research in Europe - not just within regulatory bodies, but also within the pharmaceutical industry and among patients.

David Haerry stressed that - from a patient perspective – although ENCePP has had its impact on observational research in Europe, there is still room for improvement, particularly in the area of sustainable public funding for HIV cohort collaborations. Whilst the wealth of observational data collection experience in HIV should have been used as inspiration for other indications, current cohort models may have to be reviewed in the light of technical advances in data collection.

The methodological guidance developed by ENCePP has been influential in driving transparency, collaboration, and dealing with conflicts of interest. Sustainable method dissemination is a key aspect in collaborative research and together with FP7 funding in particular, it set in motion a research agenda driven by EMA and HMA that would not have happened otherwise.

ENCePP guidance documents are considered very valuable teaching tools in the area of epidemiology.

The following were named as potential areas of improvement:

- Low uptake of the ENCePP Seal;
- Communication and collaboration with other bodies (e.g. HTA and other initiatives, patient registries, full range of EMA committees);
- Supporting collaboration with patient cohorts;
- Lack of accreditation system or quality measure applied to ENCePP partners which makes it difficult for industry to identify suitable centres.

In terms of going forward, the SG supported the following suggestions to be taken into consideration:

- EMA committee representatives active in ENCePP governance;
- Nomination of an ENCePP representative at the ADVANCE workshop on governance (March 2017);
- Reflection on communication and use of social media, as a suitable replacement for the ENCePP partners' forum;
- Consider pros and cons of introducing a 'tiered' membership, e.g. based on numbers of studies registered in the EU PAS Register.

Xavier Kurz reminded the SG that discussions on the accreditation of ENCePP centres have been going on since the inception of the network. However, overall the network has never been favourable towards an accreditation of centres which would be difficult to administer and without having in place quality parameters for studies. Accreditations are available at national level and an additional section for the ENCePP database of research resources has been agreed, though not yet implemented, would include information on accreditations and other quality management in place. The upgrade of the resource database is subject to technical feasibility and EMA IT budget.

It was agreed that the 2017 ENCePP Plenary should be used to celebrate and take stock of 10-years of ENCePP.

3.2. Reflections from the outgoing ENCePP Steering Group

The Chair started by thanking the SG members for their time, support and expert contributions to ENCePP and invited them to share their thoughts on the workings of the Steering Group, its membership and any advice going forward.

The Steering Group agreed that it would be useful to more systematically include in future meeting agendas a review of action points and/or update on important issues discussed at the previous meeting.

In terms of topics for future meetings the group agreed that it would be useful to have an extended discussion on risk communication in ENCePP.

There was concern over the lack of engagement by some ENCePP centres, and it was suggested to work to get greater representation on the Steering Group of academic centres.

3.3. Fresh approach to future Plenary meetings

The feedback from ENCePP partners in relation to Plenary meetings suggests that they appreciate most the networking aspect and discussions on scientific content (i.e. methods, PhV/PhEpi matters). The Steering Group was therefore invited to discuss what changes to the format of Plenary meetings would ensure optimisation of scientific and networking topics, and what synergies might be possible.

The engagement of ENCePP partners is crucial, and the SG was therefore in favour of having future scientific meetings centred around one topic, with clearly identified deliverables and meeting outcomes. It was agreed that whilst it is important to keep partners up-to-date on organisational and administrative matters, a more efficient way of delivering these updates should be explored, e.g. increased use of written updates and webinars.

To increase efficiency, the organisation of the ENCePP plenary back-to-back with other relevant EMA workshops could be a viable option.

In terms of scientific topics for discussion, one suggestion was to identify examples on particular research questions from the EU PAS Register and, thus, providing different stakeholders with a forum to discuss best methods and lessons learned, and to get feedback on the research from their peers.

4. ENCePP Plenary 2016

The Steering Group reviewed the preliminary draft agenda for the 2016 Plenary meeting which was agreed with some minor amendments.

This year's Plenary meeting will feature the election of the ENCePP members to the new Steering Group. In this context it was re-confirmed that in cases when the ENCePP centre is not represented at a Plenary meeting the proxy may be given to another ENCePP centre that will vote on its behalf. However, this needs to be notified to the ENCePP Secretariat in writing no later than one week before the meeting. A list of centres that have registered to attend the Plenary can be made available by the ENCePP Secretariat on request.

5. ENCePP Work Plan

With a view to presenting a more mature draft to the ENCePP Plenary in November, the Steering Group reviewed the first draft of the new three year work plan.

In addition to some minor amendments and a revision of timelines, the Steering Group agreed that the new work plan should include an item on effectiveness of risk minimisation measures (linked to pharmacovigilance impact), and an item on general communication (distribution of information in writing, and/or supplemented by webinars). Furthermore, a topic relating to the awareness and impact of regulatory policies and change will be added.

It was agreed that the communication with EMA committees on ENCePP should be enhanced further.

Further communication with stakeholders, including ISPE, was proposed in an effort to further raise awareness of the EU PAS Register. The possibility of organising an ENCePP Information Day in the margins of the 2017 ENCePP Plenary meeting should be explored.

On the occasion of the 10 year anniversary of ENCePP in 2017 it is proposed to publish an anniversary paper; the process of drafting this publication, including lead authors and contributing authors, will have to be agreed soon.

6. Measuring impact of regulatory activities

Following up on the discussions at the previous SG meeting, Thomas Goedecke presented the ENCePP SIG Impact work plan and introduced a reflection paper on the prioritisation criteria of PRAC regulatory decisions on safety topics which are relevant for collaborative impact research. The paper was adopted by PRAC in September 2016 as a deliverable of the PRAC Interest Group on Impact and the criteria will now be pilot tested.

He informed the group that a workshop on measuring the impact of pharmacovigilance activities will be taking place at the EMA on 5-6 December 2016 which will also be broadcast. It was confirmed that the ISPE special interest group on Benefit Risk Assessment, Communication, and Evaluation (BRACE) will present their white paper at the workshop, and this would be a good opportunity to collate all current activities in this area.

There will be an update on the ENCePP SIG Impact deliverables at the ENCePP Plenary in November. The SG suggested that ENCePP SIG Impact coordinators should consult the wider ENCePP community on the key deliverables reflecting the level of involvement in the impact work.

7. Issues raised / A.O.B.

Susana Perez-Gutthann informed the Steering Group about recent experiences where major objections were raised at national level to PRAC-endorsed protocols. She agreed to provide EMA with further background information.

8. Summary of discussions & next steps

In conclusion, and reiterating that this was the last meeting of the current SG, the Chair expressed his hope that the excellent collaboration would continue in the future, albeit in different fora for some of the current SG members.

He extended his special thanks for Susana Perez-Gutthann for her generous and able support as vice-chair during her tenure.