EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

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ENCePP Secretariat

Minutes - ENCePP Steering Group meeting

12 May 2017, 9.30-16.30

List of participants	
Present	Kathi Apostolidis, Corinne de Vries, Vera Ehrenstein (*via TC*), Rosa Gini, Teresa Herdeiro, Johann Hillege, Olaf Klungel, Xavier Kurz (Chair), Hervé Le Louet, Janne Lehmann Knudsen, Tom MacDonald (Deputy Chair – *via TC*), Yola Moride (*via TC*), Gianluca Trifirò, Patrice Verpillat (*via TC*) Statistical Adviser to the SG: Jim Slattery ENCePP Secretariat: Thomas Goedecke, Eeva Rossi, Dagmar Vogl EMA: Sergio Bonini, Gianmario Candore, Alison Cave, Patricia McGettigan, Carla Alonso Olmo
Apologies	Marieke de Bruin, Dinah Duarte, Hans-Georg Eichler, Giampiero Mazzaglia

1. Welcome & Adoption of draft agenda

The meeting commenced with a brief tour de table and introduction of participants. The agenda was adopted without changes.

It was confirmed that all action points arising from the previous meeting held on 19/04/2017 had been addressed.

In his role as representative of the International Society for Pharmacovigilance (ISoP), Hervé Le Louet made an intervention saying that there is a perception that the focus of ENCePP is mainly on pharmacoepidemiology and not enough on pharmacovigilance. He expressed his wish to re-enforce the role of pharmacovigilance in ENCePP as an important source of real world data. He said that further discussions at the level of ISoP will be taking place with the aim of submitting a proposal to the Steering Group (SG) on how to better embed the principles of pharmacovigilance in ENCePP.

The SG agreed that this is an important initiative and further discussion on how to embed both sciences within ENCePP is needed. One practical suggestion was to refresh the composition of the working group on research standards and guidances (WG1) to include expertise in pharmacovigilance.

The Chair confirmed that there are ongoing discussions at the level of PRAC and PCWP on how to optimise the flow of information from patients and consumers to national regulators.

2. ENCePP SG contribution to minimise the impact of Brexit on post-authorisation studies in Europe

A draft communication from the ENCePP Steering Group to the Chair of the European Medicines Agency's (EMA) Operation and Relocation Preparedness (ORP) task force was reviewed. The intention of the document is to convey concerns expressed by the SG regarding possible consequences that Brexit may have on the contribution of UK researchers and UK data to PAS in Europe.

The Steering Group agreed that it would be important to raise awareness of potential negative effects of Brexit, and that the letter should be signed by the two Chairs on behalf of the whole group. SG members were invited to provide final comments on the draft letter within one week.

3. Governance of pharmacoepidemiology studies

Tom MacDonald presented a proposal on how to enhance the regulatory science of medicinal products through a third party funding system.

The Steering Group agreed that this is an important issue and putting the proposal on paper was seen as a first important step towards taking the discussions further in line with ongoing discussions on regulatory science within EMA and the ADVANCE project, amongst others. It was stressed that the proposal should be beneficial to all parties involved and for the governance model to be a success it will be important to also keep in mind the needs and concerns of industry in terms of peer review, quality, cost etc.

The importance of making disease registry data easily accessible as an additional data resource was highlighted.

In concluding a lively and very useful discussion, Xavier Kurz reiterated that there is a need to find a system that allows studies to be performed independently from the funder which represents a win-win situation for all parties involved. Whilst a number of projects on this topic are progressing in parallel, it would be beneficial to merge efforts and ultimately come up with a common proposal. He stated that the ADVANCE project is due to finalise a governance proposal in September 2017. His suggestion is to issue a concept paper building on both the ADVANCE and Tom MacDonald's proposals. He warned that a large number of practical aspects still have to be clarified, and consultation of the European Commission will have to take place.

4. Role of ENCePP in supporting collaborative studies

By way of introduction Alison Cave presented slides highlighting the multiple challenges in the use of real world data across the EU to support regulatory decision-making, focussing on potential mechanisms that would facilitate rapid access to and analysis of relevant data sources.

Her intervention was followed by presentations from Rosa Gini, Vera Ehrenstein and Olaf Klungel respectively in which they elaborated on their experiences with different approaches of common data and common protocol models.

The ensuing discussions highlighted that there is no 'one-size-fits-all' approach that can be applied to the multitude and variety of data sources in Europe. Whilst any new system should build on lessons learned from common data models such as OMOP, it should ultimately go further in terms of flexibility

and take into account other variables and new trends in EHR recording, such as social media for example.

Common data models are considered potentially very useful for simple questions on drug utilisation that require quick responses. With reference to the previous agenda item it was proposed that any new funding model should facilitate the putting in place of necessary infrastructure for addressing key questions that are to be explored systematically. Setting up and maintaining a CDM requires continuous update and for this reason dedicated funding should be allocated for it.

The Steering Group agreed that it would be useful to consult ENCePP on how to leverage the richness of data in Europe. In the longer term, and to take this topic forward, the establishment of a special interest group or task force on big data/CDM should be considered. Yola Moride and Vera Ehrenstein expressed their interest in participating in this group.

As a first step, and to get a better picture of what is already available in Europe in terms of algorithms, libraries etc., it will be useful to collect all relevant information to support a more informed discussion. Gianluca Trifirò and Rosa Gini volunteered to coordinate the collection of information on behalf of the Steering Group. A follow-up survey of ENCePP partners may be undertaken if considered necessary.

Alison Cave informed the group that the HMA/EMA Joint Big Data Task Force is working on mapping relevant sources of big data in Europe and suggested that ENCePP could potentially contribute to this work. She proposed to invite a representative from the Steering Group to attend the Task Force's workshop scheduled to take place in June 2017. Rosa Gini expressed her interest in attending the workshop on behalf of the SG.

5. EMA Patient Registries Initiative

Following on from the discussions that had already taken place at the SG meeting on 19/04/2017, Patricia McGettigan reminded the Steering Group about EMA's patient registry initiative. As agreed at the meeting in April, a number of questions were addressed to the Steering Group on ENCePP's role in the implementation of the recommendations from the Patients Registries Workshop.

Two disease specific workshops are scheduled to take place on 14 June and 7 July 2017 respectively. The aim is to develop guidance that will be relevant to a number of diseases; this guidance should be available for consultation in September 2017. It is proposed that the ENCePP plenary meeting in November should feature a presentation on the outcome of the two workshops and the consequent consultation.

The Steering Group expressed its full support of this important initiative and confirmed that it had no objection to hosting the inventory of Registries on the ENCePP database of research resources, and also agreed to the linking to other repositories of registry information, e.g. RD-Connect. The Steering Group supports close interaction with registries in terms of developing guidance on regulatory requirements.

In this context, Xavier Kurz added that the latest revision of the ENCePP Methods Guide due to be published in July 2017 will include a new chapter on patient registries and methodological considerations regarding definitions of registries and terminology.

6. Review of ENCePP Communication Plan

Thomas Goedecke informed the Steering Group that the ENCePP communication plan would have to be revised to take account of a proposed revision of the Code of Conduct, to better promote ENCePP at national level (i.e. to provide support to national networking initiatives), and to promote ENCePP with

patients and healthcare professionals (who are currently not one of its target audiences). Consequently, the key messages on ENCePP would also have to be re-defined.

He provided feedback from a recent meeting of the Working Group on Independence and Transparency (WG2) where a potential revision of the Code to overcome the perceived incompatibility of the Code's principle of scientific independence with any industry involvement in the study team had been discussed. As a potential solution to this problem the working group is proposing to separate and drop the concept of the ENCePP Seal from the provisions of the Code.

The SG agreed to proceed with the revision of the Code based on further information which is to be discussed at the next Steering Group teleconference:

- WG2 to provide a written justification for the removal of the Seal; and
- WG2 to outline the objectives of a revision of the Code with regard to dropping the Seal, adapting the Code's structure in line with the ADVANCE Code of Conduct to improve operability, and to further clarify the concept of scientific independence as appropriate.

7. Issues raised / A.O.B.

7.1. Letter from EUCROF

It was agreed that a TC would be organised with the European CRO Federation (EUCROF) to clarify the objectives listed in its recent letter addressed to the ENCePP Steering Group; Rosa Gini agreed to join the discussions.

7.2. Report to SG on need to revise ISPE Guidelines for good database selection and use in pharmacoepidemiology research

The Steering Group acknowledged a report from WG1 confirming that the ISPE Guidance provides comprehensive and clear recommendations to investigators on the selection and use of databases; there is no need to revise this text which is still up to date. However, it would be useful to provide investigators as complete information as possible, e.g. through publication in the ENCePP database, of the answers of each database holder to the questions included in the checklist. This could be done through a survey of database holders/owners or in the context of the inventory of EU electronic data sources performed by EMA. EMA is asked to investigate these options. ENCePP WG1 will re-discuss this topic based on additional information.

8. Summary of discussions & next steps

Xavier Kurz confirmed that the next TC meeting of the Steering Group will be organised in July. The discussions will specifically focus on the revision of the Code of Conduct, with a report from WG2 which will meet in June.

The SG members were reminded to take note of the dates of the next face-to-face meetings:

- 10 October 2017 (Steering Group meeting)
- 21 November 2017 (ENCePP plenary meeting)

9. Action points

- ISoP (via Hervé Le Louet) to submit a proposal to the ENCePP Steering Group on how to better embed the principles of pharmacovigilance in ENCePP for discussion at SG meeting in October 2017. Consequently, SG to issue recommendation on whether WG1 membership should be enriched with additional pharmacovigilance expertise.
- ENCePP Secretariat to circulate latest draft version of Brexit letter for final comments to SG members. Letter to be signed by both Chairs and sent to EMA Operation and Relocation Preparedness (ORP) task force.
- Once the ADVANCE proposal is available, Xavier Kurz will draft a concept paper on governance of PE studies, building on both the ADVANCE and Tom MacDonald's proposals (preliminary deadline: October 2017).
- To get a better picture of what is already available in Europe in terms of algorithms, libraries etc., Gianluca Trifirò and Rosa Gini to coordinate the collection of information on common data and common protocol models and report to the Steering Group at its October 2017 meeting. This exercise will also inform SG discussions on the need of establishing an ENCePP working group on common data models.
- Rosa Gini to be invited to represent the ENCePP SG at the big data task force meeting in June 2017.
- EMA to present the outcome of the two disease registry workshops and the consequent consultation on guidance to the November 2017 plenary meeting.
- WG2 to report to the Steering Group at one of its next meetings on the proposed removal of the ENCePP Seal, and revision of the ENCePP Code of Conduct.
- ENCePP Secretariat to organise a TC with EUCROF and invite Rosa Gini.
- WG1 to re-discuss the topic of how to make available information regarding the selection and use of databases once additional information is available from EMA in the context of its inventory of EU electronic data sources initiative.