22 May 2018
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ENCePP Secretariat

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

Minutes - ENCePP Steering Group Teleconference

2 May 2018, 13.00-15.00 UK time

List of participants	
Present	Corinne de Vries, Dinah Duarte, Vera Ehrenstein, Rosa Gini, Teresa Herdeiro, Hans Hillege, Xavier Kurz, Tom MacDonald, Yola Moride, Patrice Verpillat Statistical Adviser to the SG: Jim Slattery ENCePP Secretariat: Thomas Goedecke, Eeva Rossi, Dagmar Vogl EMA: Patricia McGettigan
Apologies	Kathi Apostolidis, Peter Arlett, Marieke De Bruin, Hans-Georg Eichler, Olaf Klungel, Hervé Le Louet, Giampiero Mazzaglia, Gianluca Trifirò

1. Welcome & Adoption of draft agenda

The agenda was adopted with the addition of one item under 'AOB' relating to the annual revision of the ENCePP Methods Guide.

The pending action points from previous meetings were reviewed.

Xavier Kurz informed the Steering Group (SG) that following bilateral discussions with Hans Hillege it was agreed that a proposal for the objectives of further activities (incl. establishment of a potential special interest group) on use of effect tables for benefit risk analysis will be presented at the next SG meeting in July 2018.

Xavier reminded the group that once the ADVANCE governance model proposal has been finalised this will be circulated to the SG for discussion. The ADVANCE proposal should be used as a basis to develop a practical ENCePP proposal that also takes into consideration the aspects already included in the draft proposal on the governance of studies by Tom MacDonald.

Furthermore, it was confirmed that Gianluca Trifirò has been invited to provide a progress update at the next SG meeting (July 2018) on the work relating to the common data protocol models.

2. ENCePP SIG on Measuring the Impact of Pharmacovigilance Activities & Impact related activities

Thomas Goedecke provided an update on the work of the ENCePP Special Interest Group on Measuring the Impact of Pharmacovigilance Activities (SIG Impact) and related activities.

He stated that the draft chapter on 'impact research' for inclusion in the ENCePP Methods Guide has been circulated to ENCePP WG1 and the PRAC Interest Group for comments. Since this new chapter is rather comprehensive, the current proposal is to include it as an annex to the existing Guide, rather than a separate chapter. Patrice Verpillat suggestedincluding the executive summary in the core document with reference to the annex for more in-depth information. This proposal will be forwarded to the editors of the Guide for consideration and discussion with WG1.

The SG members were informed about other impact-related activities, incl. the following two recent publications by SIG members:

- Lane S, Lynn E, Shakir S. Investigation assessing the publicly available evidence supporting postmarketing withdrawals, revocations and suspensions of marketing authorisations in the EU since 2012. BMJ Open 2018;8:e019759. doi: 10.1136/bmjopen-2017-019759

- Vora P, Artime E, Soriano-Gabarró M, Qizilbash N, Singh V, Asiimwe A. A review of studies evaluating the effectiveness of risk minimisation measures in Europe using the European Union electronic Register of Post-Authorization Studies. Pharmacoepidemiology and Drug Safety [Internet]. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/pds.4434

The first publication is part of a project which will also include the development of statistical models for modelling the public health impact of regulatory actions based on supporting evidence and utilisation data. It is expected that the work will feed into future updates of the Methods Guide impact chapter.

Xavier Kurz attended the recent DIA Europe meeting in Basel and provided feedback from the session 'Measuring Impact of Pharmacovigilance in the EU'. The session was very well attended which suggests that the topic is of great interest, and as such provided a great opportunity for exposure of the ENCePP SIG Impact. The presentations included the results of a study on withdrawals of drugs, including the plan for a phase II study on modelling of health outcomes (Saad Shakir), a conceptual model done at the Dutch Medicines Evaluation Board (Agnes Kant), and the PRAC impact strategy (Xavier Kurz). Xavier further stated that EFPIA are planning to create a group with the aim to do some methodological work on this topic. Patient representatives have expressed the wish that the patients' perspective is also taken into account. It was agreed that the ENCePP Secretariat would circulate the three presentations to the Steering Group.

The Steering Group raised no objections to the suggestion of maintaining the ENCePP SIG Impact which will require a revision of its mandate. This revision will be a good opportunity to issue a call for expression of interests from ENCePP partners who are doing impact work and may be interested in joining the group.

3. ENCePP SIG Drug Safety in Pregnancy

Corinne de Vries reminded the Steering Group that the mandate of the SIG is to provide input on issues relating to drug safety in pregnancy and breastfeeding. A further objective of the group is the periodic review of the document "Overview of data sources for drug safety in pregnancy research" which is available on the ENCePP website.

The EMA has funded a study to identify, across all member states, all data sources that are or can potentially be used for evaluating associations between in utero exposure and adverse pregnancy outcomes that do not become apparent until long after exposure or marketing. This should include

details of the data sources in terms of research governance hurdles to be overcome relating to the use of the data sources for this kind of research, strengths and limitations regarding e.g. accuracy & completeness on outcome, exposure, confounders, selection etc. The study results will be integrated in the existing data source document.

Corinne further explained that a scientific meeting is scheduled to take place at the European Medicines Agency at the end of June to which a number of ENCePP SIG members have been invited. The agenda of the meeting will focus on long-term outcomes and transferable learnings across products, diagnosing in utero, future outlook and prediction of risk with a focus on the EUROCAT database and pregnancy registries.

The outcome of the scientific meeting will feed into the drafting of the GVP guideline on pregnancy and breast-feeding. Feedback will also be provided to the European Commission in terms of potential future funding in this area. Following on from this scientific meeting the plan is to organise a meeting of the ENCePP SIG with the aim of receiving input to selected sections of the planned GVP module.

4. EMA Registries Initiative

Patricia McGettigan provided an update on the EMA Registries Initiative, including its core concepts, lessons learned from the EMA Registry workshops, strengths and limitations of disease registries and how regulators can support the use of disease registries.

Following the success of the first three workshops (*Cystic fibrosis*, *multiple sclerosis* and *CAR T-cell therapies*) a fourth workshop for *Haemophilia (Factor VIII) registries* will be taking place at the EMA on 8 June 2018. Anybody interested in following the workshop's broadcast is requested to contact emaregistries@ema.europa.eu.

In terms of regulatory support Patricia listed the qualification process through EMA scientific advice ('qualification opinion'), the development of methodological guidance, scientific advice on PASS/PAES study protocols, the inventory of disease registries (already available via the ENCePP resource database) and the facilitation of interactions between regulators, industry and registry holders.

Xavier Kurz added that it is planned to consult ENCePP partners to perform a peer review of the methodological guidance for disease registries. A draft of this guidance which will address methodological aspects from a regulatory perspective should be available by Q4 2018. In addition, he invited Steering Group members to reflect on how ENCePP partners might be involved further in supporting the development and better use of disease registries.

5. ENCePP Code of Conduct Rev.4

At its previous meeting the SG had supported the publication of the revised Code in a peer-reviewed journal, focusing on the background and objectives of the revision and the main changes, and describing the differences between the ENCePP and ADVANCE Codes. Thomas Goedecke confirmed that a number of authors from various stakeholder groups have been identified. He briefly presented the proposed outline of the publication which will include feedback from various stakeholder perspectives. To this end a survey will be distributed to industry, patient organisations, HCP organisations, public health institutions, HTA and ENCePP partners. The plan is to finalise the draft manuscript by Q3 2018.

Patrice Verpillat voiced concern that stakeholders may not yet be familiar with the revised code. In this context it was agreed that the ENCePP Secretariat would obtain and circulate statistics relating to visits/downloads ofo the revised Code of Conduct on the ENCePP website.

Yola Moride suggested that the authors take into consideration including in the list of guidance the ISPE Principles for Effective Academia-Industry Collaboration and also circulate the questionnaire to the ISPE public policy committee which could provide valuable input.

6. A.O.B

6.1. ENCePP Partners forum

The Steering Group was informed that the ENCePP Partners Forum will be removed from the ENCePP website in due course. This decision has been taken primarily for IT maintenance reasons related to this relatively outdated application, but also due to its underutilisation.

In the longer term it is envisaged to replace the forum with another, more user-friendly communication tool for ENCePP partners. The Steering Group will be kept up to date on any further developments in this regard.

6.2. ENCePP Symposium at ICPE

Xavier Kurz informed the Steering Group that the abstract for an ENCePP symposium at this year's ICPE meeting (under Alejandro Arana's leadership) has been accepted. The objective of the session will be to present the achievements of ENCePP after 10 years and discuss future ENCePP dynamic development, especially a greater participation of centres and data sources from Eastern European countries. The symposium will also be a good opportunity to promote the revised ENCePP Code of Conduct.

6.3. SG meeting in margins of ENCePP Plenary meeting

The SG was informed that it would be possible to organise a face to face meeting on the day prior to this year's ENCePP plenary. It was agreed that the meeting will be scheduled from 14h00 to 18h00 on Monday, 19 November 2018. The ENCePP Secretariat will circulate a placeholder to all SG members.

6.4. Revision of ENCePP Methods Guide

Xavier Kurz stated that the deadline for revision of individual chapters by their authors was Friday, 28 April, and a large number of good contributions has been received from many of the authors. The plan is to publish the revised Guide in early July 2018.

7. Action points

- ENCePP Secretariat to circulate to the SG the three presentations from the Euro DIA session 'Measuring Impact of Pharmacovigilance in the EU'.
- ENCePP Secretariat to circulate to the SG statistics relating to visits/downloads to the revised Code of Conduct on the ENCePP website.
- ENCePP Secretariat to circulate a placeholder for the face to face meeting on 19 November 2018.