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

16 December 2015, 09.30 to 16.30, chaired by Peter Arlett

List of participants	
Present:	Morten Andersen (*via TC*), Peter Arlett, Marieke de Bruin (*via TC*), Corinne de Vries, Dinah Duarte, Pierre Engel, David Haerry, Teresa Herdeiro, Tom MacDonald, Nicholas Moore, Susana Perez-Gutthann, Nawab Qizilbash (*via TC*), Patrice Verpillat Principal Scientific Adviser to SG: Xavier Kurz Statistical Adviser to SG: Jim Slattery ENCePP Secretariat: Thomas Goedecke, Cristina Sandu, Dagmar Vogl Others: Helen Dolk, Member of WG2 and SIG Pregnancy (partly, *via TC*)
Apologies:	Viola Macolić Šarinić

1. Welcome & Adoption of draft agenda

1.1. Welcome to new COMP representative

The Chair extended a special welcome to the new representative from the Committee for Orphan Medicinal Products (COMP) attending her first ENCePP Steering Group (SG) meeting. Dinah Duarte is the Head of the Evaluation Unit at the Portuguese Agency INFARMED.

1.2. Admin matter: Declaration of interest

Peter Arlett briefly explained that the Agency's declaration of interest and related visitor badge policy for experts attending meetings on non-product-specific discussions is undergoing review. Those SG members that have declared a current employment in industry or in CROs will be issued with 'red' visitor badges which provide access to the relevant meeting room only.

2. Implementation of ENCePP Work Plan – SG deliverables

2.1. Define an ENCePP mandate considering extension of scope beyond drug safety

The discussions under this agenda item were a brainstorming on how the link between ENCePP and regulatory decision-making might be strengthened further. This may be achieved by expanding the network's scope to explicitly include disease epidemiology, product effectiveness, and clinical use, in addition to product safety.

There was a discussion on whether or not to include cost effectiveness of medicines in the future scope of ENCePP. Overall, the SG members expressed their support for including within the ENCePP scope disease epidemiology, product effectiveness, and clinical use, in addition to product safety. The SG did not support to explicitly include cost effectiveness in scope.

In relation to the interface with EMA's Scientific Committees, the SG members supported a phased approach reviewing the interaction with each EMA committee in turn starting with PRAC and COMP.

As a first step, the following actions are proposed:

- Steering Group members representing PRAC and COMP to draft a reflection paper on optimisation of ENCePP impact on decision-making within that committee.
- Explore EMA Scientific Advice pathway for qualification of novel methodologies for drug development (EMA/CHMP/SAWP/72894/2008).
- Perform gap analysis of ENCePP Methods Guide with regard particularly to comparative effectiveness research.
- Review the ENCePP website to reflect extended scope.
- SG members to consider whether there are any barriers currently to delivering on the evidence generation mandate of ENCePP and if so, to identify the priorities.

3. Follow-up to Plenary discussions

3.1. Funding mechanisms for PAS

Peter Arlett highlighted that the purpose of this session was to summarise the key points of the recent ENCePP Plenary discussion on funding mechanisms, and to agree on next practical next steps.

Central mechanism for industry funded studies

Tom MacDonald provided a brief summary of the funding proposal he had presented at the Plenary which is based on a voluntary scheme for industry, with EMA acting as a portal to stream funding, and peer review being provided by an independent organisation. He stated that the ultimate goal should be to improve regulatory science through high quality peer-reviewed research.

The EFPIA observer on the SG suggested that the proposal might work well in the context of joint studies, as long as it was a voluntary scheme. He expressed reservations on the practicality of the peer review process.

The SG agreed that joint studies would benefit most from the proposed model, and it was suggested that a limited pilot could be performed to test the model.

The SG cautioned not to focus the discussions on industry sponsorship alone, and to also address the question of public funding. The Chair agreed that ENCePP does have a role in building the business cases for public funding, in particular for the period after Horizon 2020. He also noted that the

Innovative Medicines Initiative (IMI) has funding available funding up to 2020 that could go towards methodology research.

The SG supported that EMA consider the feasibility, including legal issues and particularly the interface with regulatory requirements, of a mechanism of industry funding via a third party, with a built-in peer review mechanism, and focusing on joint studies. The performance of a pilot was supported.

Xavier Kurz mentioned that he presented the proposal for a central mechanism for industry-funded studies at the ADVANCE WP1 workshop on 10 December. ADVANCE held a preliminary view that this system could represent an extension of one of the governance models it is developing for vaccines (i.e. with a larger role for the trustee) which deserved to be considered for ADVANCE. The ADVANCE WP1 proposed that practicalities of the central system should be further developed to understand how it could work, for example criteria for the selection of the investigating centre. The ADVANCE WP1 expressed interest in further collaborations with ENCePP on governance for funding of studies.

The following actions were agreed:

- SG - under the lead of Tom MacDonald, and support by Xavier Kurz – to develop a short document elaborating further and the proposal and possible issues to address.
- EMA will look at related issues such as legalities, practicalities and financial aspects.
- EMA to liaise with industry to further discuss the feasibility and level of support of a pilot for joint studies.
- EMA to interact with ADVANCE to identify collaboration to agree on a system applicable in various situations.
- Exploration of opportunities for IMI funding of methodologies and capacity building to be explored further.
- SG to start to develop the business case for EU level public funding post Horizon 2020 of research into medicinal products on the market.

Proposal on research funding / medication safety in pregnancy

Helen Dolk reminded the SG of the proposal elaborated by the Working Group on Independence and Transparency, in collaboration with the Special Interest Group 'Pregnancy' that had been presented at the ENCePP plenary. The proposal foresees a common voluntary funding route for pharmaceutical companies to fund pharmacovigilance related to medication safety in pregnancy. She explained that a systematic approach is proposed, whereby funding would not be for any one safety study but would be used to maintain the capacity for monitoring, as well as for methods development and the conduct of ad-hoc studies.

The chair suggested that it could be challenging to aim for pure industry funding, and proposed to additionally explore public funding or private/public partnership.

In summary the Steering Group agreed that there is a public health need to support capacity and methods on studies on drug use in pregnancy. However, more work needs to be done on the scope of the proposal. The SIG 'Pregnancy' was mandated to further elaborate the proposal, in particular the administration of funds and possible funding models. Xavier Kurz will inform the SIG on the work done by the ECDC t on the different models and funding streams for vaccines.

The following actions were agreed:

- SIG Pregnancy to elaborate on details and funding sources, with a view to keeping the options open to different funding/governance options.
- Discuss the proposal with a wider industry group (e.g. industry stakeholder forum) before autumn 2016.

3.2. Better use of existing data and joint studies

Xavier Kurz provided a short summary of the presentations and discussions on this topic at the recent ENCePP Plenary meeting. He highlighted the approach adopted by the French OFSEP registry on multiple sclerosis where anonymised individual patient data are provided to researchers based on a study protocol. Discussions stressed the need to encourage approaches to sharing data, studies using common protocols, approaches for joint studies and multi-database studies.

The SG was informed that the Agency has recently been approached by a number of managers/owners of registries looking for ways of their data feeding into regulatory decision-making. The challenge is to make the different interests and stakeholders converge. There is also uncertainty of whether existing registries could answer questions relevant to regulatory authorities and health technology assessment bodies.

It was considered that ENCePP could play a role in encouraging use of common and valid standards and methods (e.g. through the ENCePP Guide), and in considering the establishment of a forum for exchange for existing registries.

3.3. Measuring impact of regulatory activities

Xavier Kurz summarised the key points from the plenary discussions emphasizing the fact that currently there are no broadly accepted methods for measuring how pharmacovigilance activities are translated into health outcomes. The Pharmacovigilance Risk Assessment Committee (PRAC) is working on developing a strategy to measure impact of regulatory action, and there is an opportunity for ENCePP to contribute to the development of methods in this field

The establishment of an ENCePP SIG to reflect on measures of impact of pharmacovigilance activities, and on the methodology for such measurement, was proposed at the plenary and supported by the SG.

To this end, EMA has drafted a mandate for the 'ENCePP Special Interest Group on Impact'; it was agreed that SG sponsors Marieke de Bruin and Susana Perez-Gutthann would review the draft mandate in the first instance.

For action:

- ENCePP Secretariat to revise draft mandate of SIG 'Impact' and submit for review by SG sponsors.

4. Update on issues discussed at previous meeting

4.1. WG1 Update

Interaction with EUnetHTA

Xavier Kurz informed the Steering Group that following the dissolution of the dedicated ENCePP working group on Health Technology Assessment (HTA) and integration of three of its members into the Working Group on Research Standards and Guidances, it had been agreed with EUnetHTA to consult the network as needed, e.g. on gaps in the ENCePP Guide to address methodological aspects of HTA and on guidelines currently developed by EUnetHTA, but that no members from EUnetHTA hav formally joined the working group. It was agreed that the interaction with HTA will be discussed at the next SG meeting.

ENCePP Methods Guide Rev.5

Xavier informed the SG that sections needing revision have been identified. Some of the existing sections need to be complemented with information regarding studies including HTA outcomes. In this context, EUnetHTA will be requested to review the Guide to flag any gaps.

In the long term, the working group is proposing a survey of users of the Guide; a first draft of the survey was tabled for information.

4.2. WG2 Update

Draft Revision ENCePP Q&A

The Working Group on Independence and Transparency has revised the Q&A on ENCePP based on the outcome of last year's survey of ENCePP centres and based on the key messages for communication on ENCePP adopted by the Steering Group. The draft Q&A had been tabled for information and final comments by the SG.

It was noted that the Q&A does not make any reference to GVP module VIII and this should be added.

It was agreed to update the text based on the SG comments and consequently to publish the revised Q&A on the ENCePP website.

Communication Plan

The communication plan was adopted, subject to final editorial review and minor amendments.

It was suggested that, in addition to circulating the communication plan to all ENCePP partners, a pdf version of the general slide set would be published on the ENCePP website.

4.3. Guide on Data Integration

At a previous SG meeting it had been agreed that, rather than being a stand-alone document, the guidance will become an Annex to the existing ENCePP Methods Guide.

Jim Slattery explained that the public consultation originally foreseen in the work plan for the stand-alone guide was no longer considered necessary given the status as Methods Guide annex and the ongoing review of that Guide. The current version was therefore presented to the Steering Group for adoption. He further explained that the document had undergone internal review at EMA and all comments had been agreed with the Drafting Group's Chair Nawab Qizilbash.

It was agreed that the research community, including all ENCePP partners, will be informed of the availability of this new annex to the Methods Guide, and will be encouraged to forward any comments or additional relevant guidance document to the ENCePP Secretariat.

In thanking Nawab Qizilbash and all contributors, the Steering Group adopted the '*Guidance on conducting systematic reviews and meta-analysis of completed comparative pharmacoepidemiological studies of safety outcomes*'.

For action:

- ENCePP Secretariat to publish Annex 1 to Methods Guide on ENCePP website.

4.4. Draft Agency policy on ENCePP researchers declaring interests

Xavier Kurz presented the key points of a draft concept paper by EMA that aims to address the different scenarios relating to declaration of interest by ENCePP researchers providing information and expert input to support EMA's regulatory decision-making. Specifically, the paper addresses the issue of ENCePP researchers submitting data and information to EMA in the context of ongoing procedures or providing input on methodologies on substance-specific (single drug or class) post-authorisation studies. Currently, members of the ENCePP SG complete declarations of interest (DoI) and any ENCePP partner contributing to a product meeting such as a scientific advisory group follows the normal DoI and scrutiny procedure. The concept paper proposed that a declaration, aligned with those used by journals, is introduced when study results are submitted by ENCePP partners outside the context of a normal DoI procedure.

The presentation prompted a discussion on the EMA declaration of interest procedure. Due to the complexity of the subject, Peter Arlett suggested to organise a detailed presentation on the EMA policy at a future SG meeting.

In conclusion it was agreed that this was an important topic and that the subject requires further discussion at SG level in 2016. The discussions should focus on definition of scope and common understanding.

5. Issues raised / A.O.B.

5.1. Lessons learnt on PASS

Pierre Engel presented an update on his research into PASS during the first three years of PRAC oversight between July 2012 and July 2015. He confirmed that the paper will be submitted for publication in January 2016.

Pierre stated that the effort it had taken to compile this work confirmed the complexity of measuring regulatory process.

The chair thanked Pierre for the very good and interesting work done so far and expressed interest in a long-term follow-up of the cohort of studies presented.

5.2. PAES guideline

It was agreed to circulate a link to the ongoing public consultation on the PAES guideline to all ENCePP partners.

For action:

- ENCePP Secretariat to circulate link to public consultation on the draft scientific guidance on post-authorisation efficacy studies.