EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

15 June 2015
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ENCePP Secretariat

Minutes - ENCePP Steering Group Meeting

4 June 2015, 10.00 to 17.00, chaired by Peter Arlett

List of Participants	
Present:	Morten Andersen (MA), Peter Arlett (PAR), Marieke de Bruin (MdB), Corinne de Vries (CdV), Pierre Engel (PE), David Haerry (DH), Teresa Herdeira (TH), Tom MacDonald (TMcD), Viola Macolić Šarinić (VMS), Nicholas Moore (NM), Susana Perez-Gutthann (SPG), Nawab Qizilbash (NQ), Patrice Verpillat (PV) *Principal Scientific Adviser to SG*: Xavier Kurz (XK) *Statistical Adviser to SG*: Jim Slattery (JS) *Innovative Medicines Initiative (IMI)*: Hugh Laverty (*via TC*) *ENCePP Secretariat*: Thomas Goedecke (TG), Kevin Blake (KB), Eeva Rossi (ER), Dagmar Vogl (DV)
Apologies:	Ana Corrêa Nunes, Hubert Leufkens, Yola Moride, Hans-Georg Eichler

1. Welcome & Adoption of draft agenda

The agenda was adopted without changes.

2. Organisational matters

2.1. Working Group (WG) membership refresh

KB presented a draft revision of the ENCePP Plenary mandate. The proposal is to introduce the concept of a 'refresh' to allow new ENCePP partners to join working groups, and for existing members to periodically express their commitment to continue active participation. To this end it is proposed to link invitations to meetings to individual responsibilities for assigned deliverables in line with the ENCePP work plan.

A clarification will be included that WG Chairs shall be appointed by consensus from amongst its members, and that Chairs shall provide regular reports to the Steering Group in line with their group's work plan deliverables.

The Steering Group agreed the proposed changes in principle, with an additional proposal from SPG to add a clarification regarding the practicalities of inviting new members to join working groups.

TMcD suggested that ENCePP partners are reminded periodically of the underlying principles and aim of ENCePP with the proposal that the current text in the 'General considerations' section should be used as an ENCePP 'mission statement'.

For action:

- ENCePP Secretariat to add clarification regarding practicalities of inviting new members to join working groups; SG to adopt revised plenary mandate in writing.
- ENCePP Secretariat to inform WG chairs and members of changes to mandate, and highlight key changes to all ENCePP partners.
- Agenda item for November plenary: presentation of ENCePP mission statement and encouragement of ENCePP partners to register studies in the EU PAS Register.

2.2. Future approach to research including outcomes that support HTA

KB introduced a proposal relating to ENCePP's future approach to research including outcomes that support Health Technology Assessment (HTA). Since its establishment in 2012, the ENCePP working group on HTA has established that there is an important number of service providers within the network with experience in conducting studies with health outcomes. The group contributed to a number of guidance documents under development and conducted a survey of ENCePP partners on the experience with research outcomes directly relevant to HTA. The results of the survey were presented at ISPE, ISPOR and EUnetHTA, the European network of HTA bodies. Following further discussions between EUnetHTA and the European Medicines Agency it is now proposed to focus activities on methods for research with combined outcomes rather than continue with the stand-alone group.

It is therefore proposed to merge the existing working group on HTA with working group 1 (on research standards and guidances). Specifically, three individuals who have been particularly active in the past will be invited to join WG1. Other members of the existing HTA group will become 'associate members', forming a group for consultation on relevant matters.

In line with this proposal the mandate of the working group on research standards and guidances will be updated accordingly to reflect the need for work around assessing opportunities for methods and common protocols for research that combines outcomes relevant to medicines regulation and HTA.

XK emphasised that the present proposal does not represent a major change, but a step in the continuous evolvement of the scope of the ENCePP methods guide which already includes a chapter on comparative effectiveness. He proposed that the first step would be to discuss with the enlarged working group 1 the need for additional guidance and sections relevant to HTA and combined outcomes for future revisions of the Guide.

The Steering Group supported this proposal, and additionally proposed that experts from EUnetHTA should be invited to fulfil a liaison function and form part of the wider consultative group; additional expertise may be invited on an ad hoc basis and if the need arises.

For action:

- ENCePP Secretariat to communicate the changes to HTA and ENCePP communities.

2.3. Revised working group mandates

KB introduced this agenda item by stating that original working group mandates had not been updated substantially and remained very high-level and centred around putting into place the core principles of ENCePP. It was therefore felt that the mandates should be refined to more clearly align with ENCePP achievements to date taking into account key deliverables of the current work plan. He confirmed that all WG Chairs were consulted and had agreed to the proposed changes.

The proposed changes to the individual mandates were presented by the relevant EMA leads.

- ***WG1: Research standards and guidances***

The SG agreed the changes, subject to:

  - change of wording relating to accreditation
  - update of wording relating to HTA, based on proposal presented under agenda item 2.2.

- ***WG2: Independence and transparency***

The SG agreed the changes, subject to a minor editorial update.

- ***WG3: Inventory of EU data sources and methodological approaches for multi-source studies***

The SG proposed the following changes:

  - *EU inventory of data sources*: revise passive wording;
  - *Approaches & processes for interoperability and sharing of PhEpi data sources*: include reference to the new clinical trials regulation;
  - *Data Protection and PE/PV research*: broaden to include reference to national data protection legislation, and revise passive wording.

The revised mandate is to be adopted by written procedure following these further changes.

- ***WG Data Integration***

The SG agreed the changes.

- ***Joint Enpr-EMA – ENCePP Working Group on paediatric pharmacovigilance***

The SG agreed the mandate and noted the appointment of the ENCePP co-Chair.

- ***Special Interest Group 'pregnancy'***

The SG agreed the mandate subject to the following changes:

  - Include reference to relevant groups in ENTIS, ISPE and ISOP
  - Include input to ENCePP Methods Guide and consultation/input to development of GVP module on pregnancy.

For action:

- ENCePP Secretariat to publish revised mandates on ENCePP website.

3. Implementation of ENCePP Work Plan

3.1. EMA leads and SG sponsor per work plan deliverable

The individual deliverables in the ENCePP work plan usually also include the names of Steering Group sponsors who act as mentors for particular topics, based on their expertise and interest. There were no objections to the proposal prepared by the ENCePP Secretariat.

For action:

- ENCePP Secretariat to publish new version of the work plan including SG sponsors on the ENCePP website.

3.2. Update on the Guide on Data Integration

The current draft Guide was circulated to the Steering Group members in advance of the meeting, asking whether they considered the document would add value and fill any gaps. They were also invited to comment on the overall quality of the document.

During the ensuing discussion the Steering Group agreed that the Guide could potentially be a very useful document for researchers and should therefore be progressed. However, rather than having a stand-alone guide, the proposal is for the document to become an annex to the ENCePP Guide on Methodological Standards in Pharmacoepidemiology.

It was noted that in the current document the detail provided varied from chapter to chapter and this would need further revision. The SG members agreed to review the document and provide concrete proposals for revision within a relatively short deadline.

For action:

- ENCePP Secretariat to remind Steering Group to provide comments on the draft Guide by end June. Comments should focus on the detail provided rather than commenting on high-level conceptual issues at this stage.

3.3. Agency position on researchers sharing data prior to publication

The Agency's position document on researchers sharing data prior to publication was circulated to the Steering Group for information. KB explained that the document was a summary of principles that would apply in case researchers provided findings of potential health impact to the EMA, and that this document would be published on the EMA website in due course.

The Steering Group voiced concerns that the current wording of the document would discourage researchers from submitting findings prior to publication because they were of the view that scientific journals generally refuse to publish manuscripts if any of the information has been made public previously.

PAR said that the document is anticipated as a useful reference that captures current legal obligations on the EMA but it may require revision following more experience gained in practice and depending on to what extent the EMA wishes to actively encourage researchers to submit data prior to publication in peer-reviewed journals.

The group agreed that a clarification meeting with journal editors might be useful in this context.

3.4. Update on the revision of the paediatric pharmacovigilance guidance

An update on this was provided in the context of the agreed mandate of the Joint EnprEMA-ENCePP working group, the ENCePP members of which have actively contributed to the revision of the guidance, which is in a draft version.

3.5. Update on the revision of the ENCePP Methods Guide

XK provided a brief update on the latest revision (Revision 4) of the ENCePP Guide on Methodological Guidance in Pharmacoepidemiology which is on track for publication at the beginning of July. He stated that the Guide remains the most downloaded and viewed document on the ENCePP website.

All chapters of the Guide have been revised and improved with recent references and text amendments. Xavier provided a summary of highlights in the new revision which include much improved sections on the definition and validation of drug exposure (chapter 4.2.1.), methods on handling bias on confounding (chapter 4.2.3.), signal detection (Chapter 4.6.), amongst others. No new chapters are planned for this revision, but potential new topics for next year's revision include paediatrics, methods on studies with outcomes directly relevant for health technology assessment (HTA) and impact of new guidelines on post-authorisation efficacy studies (PAES).

In conclusion Xavier confirmed that a public announcement will be made once the new version of the Guide becomes available (July 2015).

It was confirmed that no SG consultation was required prior to publication of the new Guide.

3.6. Defining approaches to optimise EU public funding

Funding possibilities under IMI 2

Hugh Laverty, Senior Scientific Project Manager with the Innovative Medicines Initiative (IMI) joined the meeting via TC. He provided a brief introduction to IMI 2 and its key concepts. He confirmed that the aim of the IMI calls continues to be collaborative research, based on competitive calls for proposals from public/private partnerships. The major change under IMI 2 is that participation is no longer restricted to pharmaceutical industry, but that different industries are encouraged to participate, e.g. software, ICT. Further details can be found in the IMI 2 factsheet.

The focus of IMI 2 includes projects relating to real life medical practice. Specific goals in IMI 2 are outlined in the Strategic research agenda which may be consulted on the IMI website and which is aligned with the 2013 WHO report on priority medicines. Scientific priority themes identified under IMI 2 can be split into four major research axes: 1. target validation and biomarker research (efficacy and safety); 2. adoption of innovative clinical trial paradigms; 3. innovative disease prevention, interception and treatment solutions; 4. patient-tailored adherence programmes. A wide range of areas is to be covered, including topics not explicitly covered by the above.

Some clarifications were provided during a brief Q&A session.

In conclusion it was confirmed that calls and topics can only be set within the framework of the strategic research agenda, but researchers are invited to submit suggestions for consideration by IMI's strategic governing group (infodesk@imi.europa.eu). Topic ideas may also be submitted via the EFPIA website portal. Call 6 is scheduled to be launched in October 2015.

Brainstorming

Hugh Laverty's presentation was followed by a brief brainstorming on funding options for pharmacovigilance research.

The take-home messages from these discussions are as follows:

- There is no more earmarked funding as had been under FP7.
- There are opportunities under IMI 2 including for networks, infrastructure and methods.
- There is a need to consider innovative approaches including new governance models and funding paradigms.
- Steering Group to return to this topic, particularly as governance projects, like ADVANCE, started to deliver.

The SG suggested that there would be numerous benefits of having study funding independently from industry at European level and suggested that further exploration of possible mechanisms may be worthwhile. One of the drivers for independent funding is the presence of a perceived conflict of interest arising from industry-funded studies.

Draft WG2 proposal on research funding for industry

The Steering Group was asked to discuss a draft proposal from working group 2 (Helen Dolk) regarding the potential model for creation of an independent centralised funding mechanism for pregnancy pharmacovigilance research.

The Steering Group agreed that surveillance in pregnancy is important and that there is a need to improve mechanisms/platforms for collecting data regarding drug safety in pregnancy. It would be desirable to raise industry interest in this topic - potentially via IMI 2. The group welcomed the draft paper and suggested to seek further advice from the special interest group on pregnancy to feed into follow-up discussions by the Steering Group.

For action:

- SIG pregnancy to be consulted on WG2 draft proposal.

3.7. Scope of potential changes to E-Register/EU PAS Register

TG presented a summary of proposed business and technical requirements for the upgrade of the EU PAS Register. He cautioned that currently this is at the stage of gathering the requirements for a business case only and no budget has been allocated to the upgrade of the Register yet.

The Steering Group was requested to review the list of proposed changes with the aim to identify any obvious gaps and priority requirements. The group identified the improvement of the search tool and the availability of a static link as extremely important.

For action:

- Priority of requirements to be agreed by end June through consultation of working group 2.

3.8. Draft ENCePP Communication plan

TG presented a proposal for revised key messages on ENCePP and an events calendar and communication methods for agreement by the Steering Group.

In addition to minor editorial changes it was agreed to incorporate into the key messages the 'mission statement' from the general considerations section of the Plenary mandate. Furthermore, it was proposed to develop a sequence of key messages for selection by ENCePP partners for presentation to each of the three target groups, i.e. (1) academia and CROs, (2) regulators and (3) pharmaceutical industry. The SG is to be consulted on the proposal.

Regarding the events calendar, VMS proposed to also include communication with Heads of Medicines Authorities (HMA); two updates per year could be envisaged. Presentations to the Health Care Professionals' Working Party (HCPWP) should also be considered.

Regarding communication tools DH suggested that a set of different tools should be developed for the use by ENCePP partners, e.g. a summary slide for use at the end of a presentation, but also a bigger set of 2 – 3 slides for when a more expansive presentation on ENCePP is required.

For action:

- ENCePP Secretariat to update top-level key messages and develop key messages by target groups for SG consultation.
- ENCePP Secretariat to revise events calendar as per SG discussions.
- ENCePP Secretariat to develop slide(s) for use by ENCePP partners.

4. Issues raised / A.O.B.

4.1. Report from HMA meeting

VMS provided feedback to the group about her recent presentation on ENCePP to Heads of Medicines Agencies (HMA). She reported that her presentation was very well received and generated a lot of interest. The HMA delegates were informed about potential benefits for regulators and how ENCePP might help in their decision-making, including reference to the ENCePP Study Seal and ENCePP resource database. It was noted that, there is an opportunity for greater awareness about ENCePP at HMA level, . As a direct result it was agreed to put a link from the HMA website to ENCePP, including some introductory text.

She invited national competent authorities to directly engage with and promote ENCePP and the interaction with NCAs should be considered in the communications strategy

4.2. Key messages of DIA/EMA Info Day on post-authorisation studies (PAS)

A document summarising the key messages of the DIA/EMA Info Day on post-authorisation studies was circulated to the Steering Group in advance of the meeting for information. It was confirmed that the main audience of the info day - scheduled for the day following the Steering Group meeting - would be from industry.

4.3. Update on Agency framework contracts for 'Effectiveness & PheEpi Research'

DV provided a brief status report and summary of the Agency's procurement procedure relating to the provision of effectiveness and pharmacoepidemiology research.