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European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

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ENCePP Secretariat

Minutes - ENCePP Steering Group Meeting

11 October 2013, 09.30-16.30 – chaired by Peter Arlett

List of Participants	
Present:	Morten Andersen (MA), Peter Arlett (PAR), Alfonso Carvajal (AC), Henry Fitt (HF), David Haerry (DH), Xavier Kurz (XK – *partly, via TC*), Nicholas Moore (NM), Yola Moride (YM), Ana Corrêa Nunes (ACN), Susana Perez-Gutthann (SPG), June Raine (JR), Miriam Sturkenboom (MS) *WG Chairs (via TC): Alejandro Arana, Nawab Qizilbash, François Meyer* *EFPIA Observer*: Laurent Auclert (LA) - *via TC* *ENCePP Secretariat*: Kevin Blake (KB), Thomas Goedecke (TG), Eeva Rossi (ER), Dagmar Vogl (DV)
Apologies:	Stella Blackburn, Nicola Magrini, Marcus Müllner, Hubert Leufkens

Agenda

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1. Welcome & Adoption of draft Agenda

PAR welcomed the group to this last meeting of the current Steering Group. He noted that an election will be taking place at the next Plenary meeting on 12 November, and for this purpose a call for submission of applications for Steering Group membership had been sent to all ENCePP partners earlier in the week. Deadline for nominations is 4th November. As per the mandate of the Steering Group, a maximum of two of the 6 current SG members elected at a Plenary meeting may be re-elected.

The agenda was adopted without changes.

2. ENCePP Work Plan

2.1. Report from Working Groups

WG1 – Research Standards and Guidances

Alejandro Arana reported that the group would continue to develop the Methods Guide, which was the subject of a number of sessions at the ICPE conference in August of this year. A number of new chapters are currently under development or have been proposed for development, including on genetic data use in pharmacoepidemiology, paediatrics and drug exposure. The issue of whether the Guide should be enhanced by including additional specific pharmacovigilance guidance had been discussed at working group level, and it had been decided to escalate the issue to the Steering Group. The issue would be discussed by the Steering Group later today under agenda item 5.2. In this context Alejandro noted that an expansion of the Guide would have an impact on the composition of the working group as additional expertise might be needed.

On further evaluation of the pros and cons of introducing an accreditation system for ENCePP centres, the working group has proposed not to introduce a separate system, but instead to include new fields in the ENCePP Resources database which would allow partners to be transparent by entering information about existing accreditations and quality assurance.

WG2 – Independence and Transparency

On behalf of the WG Chair Laura Yates, Thomas Goedecke informed the Steering Group that earlier this week a link had been published on the ENCePP website to the listing of PRAC recommendations on safety signals which, from now on, will be published monthly on the EMA website. Thomas confirmed that Working Group 2 will look further into how this information may be put to best use by the ENCePP network during its face to face meeting scheduled to take place in the margins of the November plenary.

Thomas confirmed that the third revision of the ENCePP Code of Conduct is about to start, particularly relating to the concept of 'independence', and it is planned to launch a survey of ENCePP centres regarding the uptake of the ENCePP Study Seal to inform the said revision. In this activity industry input will be actively sought through the follow-up meeting with industry associations scheduled Q1 2014 (see 2.3).

The 'ENCePP – DIA Information Day' for industry - originally scheduled for 2013 in the current ENCePP workplan - has been postponed pending further engagement with industry (see 2.3) which will include discussion on the format and content of such an information day.

The working group will be discussing the ongoing issue of monitoring compliance with the obligations of the ENCePP Study Seal at its next meeting in November. Subsequently, a proposal will be submitted to the Steering Group for its consideration.

WG3 – Data Sources and Multi-source Studies

MS started her report by highlighting that to date 48 data sources had been registered in the ENCePP resources database, which is considered a very positive development.

She further elaborated that the outcome of the survey on publicly funded multi-national collaborative studies which was conducted last year has been drafted into a manuscript for publication in a scientific journal and will be finalised with the continued involvement of the researchers targeted in the survey. Furthermore, the results of a survey of the former Pharmacovigilance Working Party on national data privacy requirements has recently been published on the ENCePP website.

Miriam noted that the working group's activities relating to the revision of the EU data protection rules have been put on hold for the moment pending the finalisation of the legislative process through the EU parliament and Council of Ministers. KB confirmed that the next European Parliament discussions are indicated as due to take place in March 2014. At this stage it is not possible to say when the revised legislation will come into force. Once the legislation has been adopted it may be possible for ENCePP contribute expert input to operational guidances/EC delegated acts considered relevant to the ENCePP mandate, in line with the current ENCePP work plan.

For action:

- KB to send a link to the European Commission website which tracks the progress of this draft legislation on data protection to SPG (for onward transmission to ISPE).
- WG3 to consult ENCePP WG on HTA on draft of multi-national studies paper.
- ENCePP Secretariat to relocate the survey on national data privacy requirements to a more prominent location on the ENCePP website.

WG Health Technology Assessment (HTA)

The Co-Chair of the group - François Meyer – started by saying that during its last meeting the working group had agreed on a revised work plan with a renewed focus on capacity building with a view to mapping existing resources within ENCePP to conduct studies that potentially bridge the requirements of medicines regulators and HTA bodies. For that purpose the WG will explore how the ENCePP resources database can be adapted to reflect the resources available to conduct research that may support HTA. In addition, a survey of ENCePP partners will be undertaken, enquiring about experience, available resources and specific training needs relating to the capacity to conduct such research. In the longer term, building on the results of the survey, the group could lead – subject to decision by the ENCePP Steering Group - on the development of a concept paper on practice in conducting post-authorisation studies (PAS) that might meet the needs of medicines regulators and HTA bodies.

The revised work plan of the group will be presented to EUnetHTA. A number of EUnetHTA institutions have already expressed interest in engaging with the ENCePP group and to provide input to its activities, which may impact on the composition of the WG.

François further reported that the group had successfully submitted two abstracts for a seminar and a poster at the next ISPOR meeting in Dublin in November 2013.

WG Data Integration

Nawab Qizilbash confirmed that the working group is working on a stand-alone guide for meta-analysis of pre-existing studies. For now a systematic search of the literature has been undertaken, a list of sections of a draft guidance agreed, and individual reviewers assigned to each

section. The review of sections is ongoing and the plan is to have a first draft of the guidance available for presentation at the ENCePP Plenary meeting in 2014.

Considering the possible regulatory implications of the guidance being developed by the working group, Nawab confirmed that the group includes regulatory expertise. In addition, the consultation of external experts belonging to various groups including regulators will be undertaken once a mature draft of the guidance has been developed. A more detailed proposal for external consultation will be elaborated and submitted to the Steering Group in due course.

SPG informed that the US FDA was working on a similar document, and that the working group is being kept informed on this so that duplication is avoided.

2.2. Progress Report: ENCePP Work Plan

KB presented slides listing achievements to date relating to the work plan and progress against its listed deliverables. The work plan is generally progressing well. In the context of the review of specific deliverables, the following **actions** were agreed:

- As a priority, the information on the ENCePP website relating to the registration of studies needs to be reviewed and updated to reflect the evolution of the study register's scope in its serving as the EU PAS register as cited in the GVP, and to take into account the feedback received from stakeholders including the ENCePP community and pharmaceutical industry. It needs to be highlighted that any non-interventional study can be registered and the requirements only relating to ENCePP Study Seal applications should be clarified.
- The deliverable 'Liaison with medical journal editors including submission of material for publication and possible a follow-up workshop with journal editors' is to be carried over to the next ENCePP work plan starting in 2015.
- The meeting heard that an EMA paper on disease-based registries in Europe is under development and would be shared with the ENCePP Steering Group at its next meeting.
- The current work plan published on the ENCePP website is to be updated with the amended work plan for the Working Group on HTA (see 2.4).

2.3. Draft Proposal for industry engagement

KB introduced a document capturing the conclusions and actions of the meeting with industry associations in May 2013 and subsequent discussions at SG level, including a proposal for further engagement with industry.

The SG agreed that the review of the Code of Conduct (particularly relating to the concept of 'independence') and review of the ENCePP website are to be prioritised.

Laurent Auclert – the industry observer on the Steering Group – confirmed his mandate to coordinate engagement with EFPIA and he agreed to coordinate a survey among industry partners to seek feedback on industry's needs for clarification. Logistics and how to best optimise the survey are yet to be agreed as there is a very real difficulty in identifying what 'industry' to target and who represents it in line with the diverse nature of the pharmaceutical industry. The Steering Group members agreed with the industry observer that ENCePP could be of particular benefit to small and medium-sized enterprises (SME) that may have less in-house pharmacoepidemiology resource, and that it was of utmost importance to include SMEs in the survey and to capture their feedback.

It was agreed that a follow-up meeting with industry representatives would be organised with a view to discussing the establishment of an ENCePP-industry platform. The mandate of this platform and a detailed action plan including goals and outputs are yet to be defined.

For action:

- ENCePP Secretariat to organise meeting with Laurent Auclert to plan the industry survey. SG to be consulted on draft survey.
- ENCePP Secretariat to organise follow-up meeting in 2014 with industry taking account of the results of the survey.
- ENCePP Secretariat to draft ENCePP-industry platform mandate and action plan further to this meeting with industry.
- The proposal for engagement with industry is to be revised taking account of the SG discussion and presented at the ENCePP Plenary meeting in November 2013.

2.4. Revised mandate of ENCePP HTA Working Group

KB presented the revised mandate of the working group which emphasises capacity building and the use of existing resources.

It was agreed that the Steering Group would decide in 2014 on initiating or otherwise a concept paper on practice in conducting post authorisation studies. The revised mandate was adopted.

For action:

- ENCePP Secretariat to update ENCePP work plan in line with the revised WG HTA mandate and publish both documents on the ENCePP website.

3. Non-EU ENCePP centres

KB introduced a document outlining options for extending ENCePP beyond the EEA/EFTA in light of the continued international interest in the network and its outputs. PAR clarified that the intention was not to come to an immediate decision, but to seek further orientation from the Steering Group on whether there was any interest in expanding ENCePP, whether the SG members saw any strategic advantages for ENCePP, and what would be the logistical aspects in the event of an expansion of ENCePP outside Europe.

During the ensuing discussions it became clear that whilst the Steering Group favours keeping ENCePP focussed on Europe, a certain degree of internationalisation – particularly relating to application for the ENCePP Study Seal - could be a welcome development. It was clarified that the requirement for the (primary) lead investigator for a study to qualify for a Seal that they belong to an entity that is included in the ENCePP Inventory of Research Centres should be subject to particular consideration. It was agreed that the ENCePP Secretariat would draft a proposal based on the discussions.

For action:

- ENCePP Secretariat to draft proposal for involvement of international partners separating the concepts of applying for an ENCePP Study Seal and participating in the network itself.

4. ENCePP mandates

4.1. Revision 4 of ENCePP Plenary mandate

DV presented slides summarising the proposed revision to the ENCePP plenary mandate. The revision was adopted by the Steering Group and will be published on the ENCePP website.

In this context the SG was informed that after careful consideration it has been decided to propose using the limited meeting budget available towards funding only one annual plenary meeting in 2014. The remaining funds would be used to finance face-to-face working group meetings. The Steering Group unanimously agreed this proposal.

NM suggested the use of supplementary webinars for Plenary meetings or the organisation of focussed webinar sessions; this was welcomed by the Steering Group members.

For action:

- ENCePP Secretariat to publish Rev4 of the plenary mandate on the ENCePP website.
- ENCePP Secretariat to explore the organisation of ENCePP webinars.

4.2. Revision 3 of ENCePP Steering Group mandate

DV outlined the proposed changes to the ENCePP Steering Group mandate which include the extension of the SG's term of service from 2 to 3 years.

The revision was endorsed by the Steering Group. It was also agreed to seek to align the periodicity of future ENCePP work plans to the term of service of a given Steering Group.

For action:

- Revised SG mandate to be presented to the ENCePP Plenary on 12/11/2013.

5. A.O.B. / Issues raised

5.1. Evidence generation

The item was raised in the context of related deliverables in the current ENCePP work plan and was opened with a presentation by JR in her capacity as Chair of PRAC on possible approaches to further operationalise ENCePP for PRAC support. This is in light of PRAC now having been established for over a year and the various initiatives that have taken place over that time to operationalize the network to support regulatory decision making. These include calls to ENCePP for information in relation to EMA reviews of the benefit-risk ratio of certain drugs and the submission of manuscripts prior to publication coordinated by EMA best evidence activities. She invited feedback from the Steering Group colleagues on how to increase ENCePP familiarity with regulatory practice and to increase ENCePP support to evidence being considered by PRAC. She also proposed conducting a survey among ENCePP partners as a possible way of identifying the preferred mechanisms for interaction.

From the ensuing discussions it became evident that there is a clear need to raise the awareness amongst PRAC members of major ongoing research projects and existing research platforms. One option considered would be to keep an up-to-date inventory of such initiatives and make it publicly available on the ENCePP website. The timing of regulatory reviews and actions was also discussed. The need to identify mechanisms to disseminate focused information on important issues relating to drug safety while not flooding email inboxes was highlighted.

It was agreed that the item would be kept on the Steering Group agenda in terms of the impact analysis of ENCePP and the ongoing review of the work plan.

For action:

- Feedback from the discussion will be incorporated into a draft action plan for further reflection by the Steering Group. The action plan should include a proposal for a systematic approach to interaction between PRAC and ENCePP.

5.2. ENCePP Guide on methods for pharmacovigilance

XK stated that NM had proposed at the last ENCePP Plenary meeting that the ENCePP Guide on Methodological Standards could include more guidance on pharmacovigilance standards as currently the title of the Guide refers only to pharmacoepidemiology. Initial discussions had taken place at WG1 level on the need for such guidance and whether a new document was required, or whether the current Guide should be expanded. The working group also mooted that additional expertise would be needed, as most of the current group are experts on focussed pharmacoepidemiology.

NM informed the Steering Group that he was in the process of consulting ISoP, requesting feedback on the need for additional pharmacovigilance guidance.

It was agreed to await feedback from ISoP relating to gaps in the existing guidance. If gaps are identified, they will be included in the current guide. The need for additional expertise will be addressed if and when it arises.

5.3. Update on Enpr-EMA – ENCePP joint working group

KB informed the Steering Group that it had been agreed in principal that a joint Enpr-EMA-ENCePP group on paediatric pharmacovigilance should be established. Only a limited number of spaces were available, and a call for expressions of interest had been circulated to all ENCePP partners. The group will be consolidated and its mandate published once the necessary conflict of interest declarations have been received from all its members (in line with Enpr-EMA practices).

5.4. Pharmacogenomics – interface with ENCePP

PAR informed the Steering Group that three speakers had confirmed their availability to present to the ENCePP Plenary on 12 November on the subject of 'pharmacogenomics'. The intention was to follow the presentations by a discussion focusing on methodological aspects of pharmacogenomics, and also the interface between pharmacogenomics and the ENCePP network.

The Steering Group agreed that there is clear overlap between pharmacogenomics and PhEpi and PhV; it was proposed to invite a colleague from EMA's working party on pharmacogenomics to attend the meeting and join the discussions. The discussion at the Plenary meeting would determine the need for any further activities.