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European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

Meeting Report – 6th ENCePP Plenary Meeting

18 November 2010 – chaired by Noël Wathion & Peter Arlett

Agenda	
1	**General Matters** 1.1 Welcome and introductory remarks 1.2 Adoption of agenda
2	**Report from the Steering Group**
3	**ENCePP Studies** 3.1 Presentation from investigators of first ENCePP Study awarded 3.2 EMA-funded Study: Award of first tender 3.3 Lessons learned from first ENCePP studies 3.4 Q&A
4	**Highlights of the new Pharmacovigilance Legislation relevant to ENCePP** 4.1 Discussion
5	**Database of studies** 5.1 Presentation of Studies' database & feedback from pilot phase
6	**ENCePP Guide on Methodological Standards in Pharmacoepidemiology** 6.1 Presentation on new Guide
7	**Implementing rules for Code of Conduct: Access to data** 7.1 Presentation of Implementing rules adopted by SG 7.2 Discussion
8	**ENCePP Work Plan 2011-12** 8.1 Presentation of Work Plan 8.2 Next steps for ENCePP Working Groups
9	**Upcoming Events** 9.1 ENCePP Info Day
10	**Summary of discussions & next steps**
11	**A.O.B**

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1. General Matters

1.1. Welcome and introductory remarks

Thomas Lönngren, Executive Director of the European Medicines Agency, delivered the introductory remarks to the Plenary. He informed the delegates that this would be his last Plenary, as he finishes his second mandate at the end of the year. He considers ENCePP as one of the key achievements during his ten years at the helm of the Agency.

ENCePP was born out of the realisation of the need to build capacity for EU research by bringing together academic centres performing research in Europe and to coordinate the available expertise. Today the network is an integral part of the Agency road map with dedicated resources. ENCePP is unique in the world and its partners should be proud of what has been achieved so far.

He expressed his hope for the future that all information and knowledge generated through this network feeds into the regulatory decision making processes. He highlighted the fact that, as the complexity of medicines is increasing there is need to carefully monitor their real life and rational use, as well as the effectiveness of risk minimisation activities. With this in mind, he urged the centres to reflect on the real-world use of medicines when designing new studies.

In conclusion, Thomas Lönngren thanked the ENCePP partners for their achievements so far and assured everybody that he would continue to follow the network's progress.

1.2. Adoption of agenda

Noël Wathion briefly introduced the various agenda items. The agenda was adopted without changes or comments.

The Chair welcomed all delegates who attended their first Plenary, and introduced the following new ENCePP partners:

- Italian Paediatric Federation-Medicines for Children Research Network
- IADB/University of Groningen, Netherlands
- Prism, Switzerland
- Parexel, UK
- BIOBADASER Network, Spain
- Kappa Santé, France

He highlighted the fact that ENCePP is a fast growing scientific community, and that to date 75 centres, 11 networks and 11 data sources have been registered in the ENCePP database of research resources.

The Chair also extended a warm welcome to observers from Croatia, Serbia and FYROM, together with an observer from the Healthcare Professionals (HCP) Working Group.

2. Report from Steering Group

Ingemar Persson, Vice-Chair of the ENCePP Steering Group, gave a brief update on the activities of the Steering Group since the last Plenary, including a list of agreed deliverables and ENCePP Plenary meeting dates for 2011.

ENCePP partners were invited to participate in the drafting of the Work Plan by suggesting additional topics. The following discussion highlighted that the lack of consistent interpretation, as well as the

often restrictive interpretation of the definitions for interventional and non-interventional trials appears to be a major obstacle to the conduct of research. This often leads to the assumption that any non-database study is automatically considered an interventional trial. Moreover, it appears that implementation of the legislation varies in the different European States. To this end, the delegates agreed that it would be desirable to elaborate a formal ENCePP position. This should be done as rapidly as possible to feed into the Clinical Trials Facilitation Group, as well as the European Commission which is reviewing the Clinical Trials Directive.

Noël Wathion summarised that the Plenary had identified an issue which clearly needs to be addressed as a matter of importance. In the long term this will be done within the framework of the revision of clinical trials legislation. In the short term, the Plenary or one of its working groups is charged to come up with an official ENCePP statement clarifying this issue.

Furthermore, with regard to the work plan, it was agreed to delete the word "database" from the deliverable "Development of approaches to facilitate conduct of multi-national *database* studies in light of existing differences in data privacy laws across the EU".

3. ENCePP Studies

3.1. Presentation from investigators of first ENCePP Study awarded

Ursula Kirchmayer, representative from the Lazio Regional Health Service in Italy, presented on the first study to have been awarded the ENCePP seal. The seal was awarded in October 2010 to an observational study investigating the "long-term outcomes and adverse events of therapy with inhaled corticosteroids, long-acting beta-2-agonists and anticholinergic drugs in hospitalised patients with Chronic Obstructive Pulmonary Disease (COPD)". The presentation provided a brief history of the relevant study protocol and the registration and application process for the ENCePP seal. She concluded by assuring the Plenary that the application process was not as daunting and bureaucratic as it might seem.

Following a query from one of the delegates, it was reiterated that the ENCePP Secretariat checks adherence with the Code of Conduct and the checklists in administrative terms only. The current process does not foresee any peer review of the study protocol itself. It should be clear that the ENCePP seal stands for transparency, independence and adherence to certain standards, but does not guarantee the quality of the study. A study that has been awarded the seal will therefore not be beyond criticism.

Peter Arlett noted that there are ongoing discussions as to whether or not scientific peer review or some form of accreditation should be done through ENCePP. Although this is not part of the ENCePP study concept, the idea is not dead and it is foreseen to consider this issue further in one of the Working Groups and in the framework of the ENCePP Work Plan 2011-12.

3.2. EMA-funded Study: Award of first tender

University of Bath have recently been awarded the first contract in the framework of a call for expressions of interest for drug safety studies funded by the Agency. The objective of the contract is the evaluation of the safety of A/H1N1 vaccines in pregnant women and their offspring. Corinne de Vries presented on her experience of the shortlisting and tendering process and gave an outline of the project itself.

In reply to a query from the Plenary, Noël Wathion confirmed that the Agency is committed to continuing this kind of funding for studies. Although there was only a limited fund available for this

activity in its first year, it is foreseen to increase this fund in 2011 and possibly even further in 2012. However, he stressed that future funding is dependent on the Agency's overall budget which is under immense pressure due to a cut in the European Commission's subsidy and the uncertainty of future income from industry fees.

Peter Arlett elaborated further in relation to the decision-making process regarding the subject of the individual tenders. The ENCePP Steering Group is not consulted in the decision-making. The decision on topics comes from the Agency and its regulatory committees, aiming at finding relatively quick solutions to ongoing scientific discussions. This is a learning process for the Agency, but the long-term objective is to get the CHMP looking into safety issues more pro-actively. The Agency will not and cannot replace the FP7 funding programme, which looks at big, longer term safety issues requiring major funding.

3.3. Lessons learned from first ENCePP studies

Camilla Smeraldi presented a summary of lessons learned from the three ENCePP studies awarded to date. Her presentation also included a reminder of the requirements to obtain an ENCePP seal and the obligations that come with it.

Peter Arlett summarised this session by saying that this was a learning exercise and it will become clearer in time how the Code of Conduct works in reality. The review of the Code foreseen in 2011 will be important. The revised version will be even better and address detailed practical issues that have come up during the award of the first seals.

4. Highlights of the new Pharmacovigilance Legislation relevant to ENCePP

At the start of this session Peter Arlett explained that some ENCePP partners had requested a presentation on the new pharmacovigilance legislation during a previous Plenary. Due to the fact that the Agency has no formal role in the law making process, addressing this request was delayed for institutional reasons. However, with recent developments – i.e. the final favourable vote in the European Parliament in September 2010 - it was felt that the time was right to discuss the key changes relating to ENCePP.

His talk included the why, how, what and when of the new pharmacovigilance legislation, highlighting items of particular relevance to ENCePP. Attention was drawn to the new PRAC (Pharmacovigilance Risk Assessment Committee) which will replace the current Pharmacovigilance Working Party. Six of the members of this new Committee will be appointed by the European Commission based on a call for expressions of interest which is likely to be published at the end of 2011. He encouraged ENCePP colleagues to consider this call; the ENCePP Secretariat will inform the network when the call is published.

Peter pointed out that the Clinical Trials Directive is not in the scope of changes to the legislation. The European Council has been calling for a revision of the definition of 'non-interventional'

It was also raised that clarification is needed around the requirements to report to regulators individual case safety reports from non-interventional studies in which it is intended to perform analysis of aggregated data only.

The following discussion focussed on details which require elaboration in the implementing measures, and particularly stressed the need for a definition for PASS studies and efficacy studies. Peter, on behalf of the EMA, committed to discuss any questions or concerns the ENCePP community may have

on the new legislation, and the Agency will seek dialogue with its stakeholders over the next two years or so looking for input. The new legal provisions will apply from autumn 2012.

5. Database of studies

5.1. Presentation of Studies' database & feedback from pilot phase

The e-Register of studies was officially launched on the day of the ENCePP Plenary. Rocio Fernandez introduced the delegates to this new tool with the help of a live demonstration of the study database. She also provided a summary of feedback received from the pilot phase which ran from September and involved some internal EMA staff and the ENCePP Steering Group. All comments have been logged and will be taken into consideration for future releases of the database.

Peter Arlett thanked everybody who was involved in the development of the e-Register.

6. ENCePP Guide on Methodological Standards in Pharmacoepidemiology

6.1. Presentation on new Guide

Susana Perez, chair of WG1 sub-group "guidances and recommendations", together with Kevin Blake from the ENCePP Secretariat, co-presented on the *Guide on Methodological Standards in Pharmacoepidemiology* which was published on the ENCePP website for public consultation on 5 November 2010.

Susana presented a brief history of the document and thanked everybody involved in drafting the individual sections as well as its peer reviewers.

Kevin briefly introduced the different sections of the Guide and reported that the document had received very positive feedback during a recent presentation to the Pharmacovigilance Working Party. He urged all delegates to report to the ENCePP Secretariat any additional documents that they would like to see included in future updates of the Guide.

7. Implementing rules for Code of Conduct: Access to data

7.1. Presentation of Implementing rules adopted by SG

At the start of her presentation, Stefanie Prilla explained that the revision of the Code of Conduct was triggered by comments made during the last Plenary meeting in relation to access to data. The ENCePP Steering Group made a decision not to delay the launch of the ENCePP study concept, but decided that in parallel a guidance document in relation to this topic should be drafted. The resulting *Implementing Guidance for Access to Study Data* and a revised Code of Conduct were adopted by the Steering Group on 12 September 2010.

Stefanie's presentation included a list of issues that remain open for discussion and clarification. These have been included in the issues log for future review of the Code.

The following discussion highlighted the need for further elaboration of this topic. Issues highlighted by the participants included access to data which in the first place had only been obtained under a licence agreement or governance rules that prohibit passing on the data to third parties and the questions about a time limit for maintaining the data set. Whilst all these issue require further discussion, the principle of maximum transparency should be maintained.

In conclusion, Peter Arlett summarised that for the moment this is more a theoretical than a real issue since no requests for data access have been received yet. However, it should be addressed proactively and will be tackled in 2011 by a dedicated ENCePP 'task force'. He assured the delegates that all comments provided during the Plenary will be taken on board for discussion by the task force. A call for expression of interest to participate in the task force will be issued shortly.

8. ENCePP Work Plan 2011-12

8.1. Presentation of Work Plan & Next steps for ENCePP Working Groups

Camilla Smeraldi presented the draft work plan for 2011-12 which is due for adoption by the Steering Group at its next meeting on 2nd December 2010. The presentation included deliverables and suggested timelines by working groups. She reminded all delegates that the call for volunteers is still open for anybody interested in joining any of the working groups. The ENCePP Secretariat will circulate another reminder soon.

Delegates were invited to come forward with any other suggestions for additions to the work plan and working groups. These suggestions will be taken into consideration for an updated version of the work plan which will be circulated to all ENCePP partners for comments prior to its adoption by the Steering Group on 2nd December.

In the context of the work plan, Peter Arlett confirmed that a meeting will be organised asap, drawing on the Plenary and EMA colleagues from Inspections/Good Clinical Practice and co-chairs of the Clinical Trials Facilitation Group. This is to progress quickly to an ENCePP position on interventional vs non-interventional trials that would feed into the EC review.

Camilla Smeraldi reiterated that the issue of access to the analytical data set needs to be addressed as a matter of urgency, as highlighted by the comments raised in response to the presentation of the Implementing rules for the Code of Conduct. It appears evident that differences in local legislation or interpretation of data privacy laws need to be identified to elaborate possible common solutions that can ensure transparency. It was proposed to set up a specific task force specifically dedicated to this topic. The output of the task force will be then fed into both existing Working Groups 2 and 3. This work will be coordinated at EMA-level by Stefanie Prilla (see also point above).

9. Upcoming Events

9.1. ENCePP Info Day

Peter Arlett very briefly presented the programme of ENCePP Info Day which will take place in London on 26 November 2010. All partners are welcome to attend, however, since the event is organised by DIA, a registration fee is involved.

Miriam Sturkenboom voiced her concern over the fact that most of the presenters are affiliated with regulatory agencies and that none of the ENCePP working group representatives appear to have been invited to present. Peter Arlett explained that the list of speakers was based on availability, but that the comment has been noted and will be taken into consideration for the future.

10. Summary of discussions & next steps

Peter Arlett summarised the 6th Plenary by reminding the ENCePP partners the new legislation presents new opportunities for the research community, he also highlighted the launch of the e-Register of studies, as important milestone in the ENCePP project.

He reminded the delegates that the Guide on Methodological Standards has been published for public consultation and invited them to submit their comments by 3rd January 2011.

The dedicated Task Force will be working hard on a proposed solution for access to data/the analytical data set.

He thanked everybody for attending the meeting by concluding that "ENCePP is the brave new world."

Action points arising:

- ENCePP Secretariat to organise a meeting to progress quickly with an ENCePP position on interventional vs non-interventional trials that will feed into the EC paper.
- ENCePP Secretariat to circulate updated draft work plan to all ENCePP for comments prior to adoption by SG on 2nd December.
- ENCePP Secretariat to issue a call for expression of interest for working groups, including task force 'access to data/analytical data set'.
- ENCePP Partners are invited to report to the ENCePP Secretariat any additional documents that they would like to see included in future updates of the Guide on Methodological Standards, as well as comments on the draft by 3 January 2011.

11. A.O.B

None.

Encl:

Presentations (see hyperlinks in text)