EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

18 June 2013
EMA/369510/2013
ENCePP Secretariat

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

Report - 11th ENCePP Plenary Meeting

18 June 2013 – chaired by Peter Arlett

Meeting Agenda:

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8668
E-mail encepp_secretariat@ema.europa.eu **Website** www.encepp.eu

1. General Matters

The Chair welcomed all delegates, particularly those attending their first Plenary. He welcomed observers from India, Croatia, Montenegro and Serbia, and from the French Haute Autorité de Santé, representing EUnetHTA (European Network for Health Technology Assessment).

He announced that a first meeting of the Special Interest Group (SIG) on 'Drug Safety in Pregnancy' would be taking place in the form of a breakout session during the morning coffee break. The EMA lead of this SIG is Corinne de Vries, and the aim of the meeting would be to review the group's mandate and to appoint a Chair.

The plenary agenda was adopted without changes.

2. Report from the Steering Group & Working Groups

2.1. Announcement of Steering Group Election 2013

Earlier this year Corinne de Vries resigned from the SG to take up a post with the European Medicines Agency. According to the SG mandate, a call for nominations for election for the vacated position should be held. Peter Arlett explained that the next Steering Group (SG) elections are due to be held at the plenary meeting in November 2013, when the two-year mandate of the current SG expires. It is therefore being proposed that no separate election would be held to fill the vacated position until the elections later this year. There were no objections from the Plenary to this proposal.

2.2. Report from the ENCePP Steering Group

On behalf of the absent Deputy Chair, Morten Andersen reported on the activities of the Steering Group since the last plenary meeting. His presentation included statistics from the ENCePP Research Resources Database, highlighting the continued growth of the network, and from the E-Register of Studies/EU PAS Register, which recently reached a significant milestone by marking its 100th study registration. He also provided a progress update on the SG deliverables from the current ENCePP work plan.

Finally, he reminded the delegates that the next ENCePP Plenary meeting will be taking place at the EMA on Tuesday, 12 November 2013.

2.3. Updates from ENCePP Working/Drafting Group Chairs

Meetings of all ENCePP working/drafting groups were held during the day preceding the Plenary, and the Chairs were asked to provide a report on the discussions that had taken place.

Working Group 1

The Chair, Alejandro Arana started by informing that the membership of the working group had increased and welcomed three new members.

Good progress has been made on the review of the ENCePP Guide on Methodological Standards in Pharmacoepidemiology with a focus on further development of the methods section (missing data and effect modification), and the integration of new chapters on vaccines and comparative effectiveness research. The revision has included consultation of ENCePP partners, chapter review

by authors and expert review of selected chapters. The WG is also looking into ways of enhancing the dissemination of the Guide, which includes publishing a web version on the ENCePP website, a demo of which was presented to the Plenary. It is expected that a final draft of Revision 2 of the Guide will be available by the end of June 2013.

Discussion on the accreditation of centres is ongoing and Xavier Kurz added that important lessons were learned from a meeting with the paediatric network Enpr-EMA which operates a system of self-accreditation for its members. He clarified that the intention of accrediting centres did not imply value judgement of ENCePP centres. The focus, however, could be on completeness of information and completeness of characterisation of centres in terms of resources in the ENCePP database, rather than categorisation based on the capacity of centres.

Working Group 2

The current Chair, Laura Yates started by thanking Helen Dolk for her major contribution over the past years as Chair of the Working Group. She provided an overview of WG2's key deliverables from the current work plan, their current status and planned future activities.

She reported that, taking into account the feedback from the ENCePP meeting with industry on 22nd May 2013, it had been agreed that at this stage the WG should focus on the review of the Code of Conduct with a view to making the Code's principles more generally applicable. This review will include a stock-take of the experience with the ENCePP Seal to date and more clarity on the ENCePP Seal concept including procedural aspects and the purpose of the ENCePP E-Register/EU PAS Register.

With the aim of further encouraging public registration of studies in the E-Register, it was agreed that review of information on the ENCePP website relating to these topics should be addressed as a matter of priority.

Thomas Goedecke presented an overview of studies registered by ENCePP centres to date which had been circulated to all ENCePP partners prior to the plenary meeting for information. He reminded the delegates that in line with the mandate of the ENCePP Plenary participating centres are expected to actively work within each calendar year on at least one study which is registered with the ENCePP E-Register.

Comments from the Plenary included a caution to keep in mind that the overview only names the leading study entity, whereas many of the studies are, in fact, conducted by multiple centres. Comments were also made that some centres might be relatively new and had not published yet and that access to databases was not always available to academic centres which hindered publication.

Peter Arlett confirmed that this would be considered in future. He also stressed that - in the spirit of capacity building - the current position of the Steering Group is to encourage centres to register studies.

Working Group 3

Miriam Sturkenboom reported that the WG discussions had focussed on two major issues which are the survey amongst publicly funded multi-source studies, and secondly the topic of data protection.

The purpose of the multi-study survey was to glean information on methods of collaboration, pooling of data etc. The survey had been conducted amongst the ten FP7-funded projects, the seven EMA-funded studies and the IMI-PROTECT project. The feedback received has been summarised in a paper and the WG discussions were aimed at deciding on how to take this further

and develop the knowledge gained from the survey. The group decided that a comparison with practices in the US and the EU would be helpful. To take this forward the respondents will be contacted again shortly and asked for additional clarifications.

As regards the data protection issue it has been decided that the information compiled from Member State responses to a non-urgent information request issued last year would be published on the ENCePP website. In parallel, WG3 will be looking at two specific examples (i.e. the SALT and VAESCO studies) with a view to identifying examples of issues encountered in practice and how this might be further considered in light of the finalisation of the current revision of the General Data Protection Regulation.

Miriam noted that there has been a significant increase to 46 in the number of data sources that are registered in the ENCePP resource database and that recruitment of new sources will continue.

Working Group on HTA

Marlene Sinclair and Nicholas Moore provided the report from this relatively new working group. They stressed that the group is still in the process of establishing its working patterns, but has agreed its terms of reference and established a reciprocal relationship with EUnetHTA, the European Network of Health Technology Assessment.

The Vice Chair of the group is François Meyer from EUnetHTA who was unable to attend the meeting, but who was represented by Irena Guzina. During the meeting four main areas of cooperation between EUnetHTA and ENCePP were identified:

- Development of guideline/concept paper on the appropriate trial design to meet the needs of regulators and HTA
- Development of guideline/concept paper on how to best formulate the research question
- Pilot of a common core protocol
- Governance of activities

It was stressed that the efforts of Working Group 1 should not be duplicated, and that WG1 is being consulted for input into the development of methodological guidelines on studies relevant to regulators and HTA.

Finally, it was agreed that an abstract describing the working group's activities would be drafted for submission to the ISPOR meeting taking place in Dublin in November 2013.

Peter Arlett thanked Irena Guzina for attending the meetings and representing EUnetHTA. He said that there is a great amount of interest in generating evidence to support HTA which can feed into medicines regulation; this work is fully supported by EMA.

Drafting Group 'Data Integration'

Nawab Qizilbash explained that the purpose of the group is to draft a stand-alone guide to help conduct methodological reviews and multi-database studies, as it was felt that not enough guidance on this topic was available at present.

This had been the first face to face meeting of the group, and good progress has been made. Following the development and adoption of a checklist, a number of relevant papers had been identified which reinforced the need for specific data integration guidance.

For now it has been decided that the group would focus on developing guidance for systematic review, and to address the topic of multi-collaborative database studies at a later stage taking into account the ongoing work of WG3 on the subject.

As regards working methods, it is envisioned that sections will be drafted by individuals. Regular meetings will be taking place via TC; the next face-to-face meeting of the drafting group is planned in the margins of the November Plenary. A draft of the guidance will be sent to an external advisory group, and the final guidance would be for adoption by the Steering Group.

3. Session on Special Populations - Paediatrics

3.1. European Network of Paediatric Research at the European Medicines Agency (Enpr-EMA)

Irmgard Eichler, coordinator of Enpr-EMA, presented slides providing detail on this 'network of networks'. Her intervention also explored communalities between Enpr-EMA and ENCePP, and suggestions for potential cooperation.

The Chair thanked her for a very clear presentation and for highlighting opportunities for collaboration. He stated that the work of EMA in paediatrics has led to a wealth of information that is potentially of high interest to ENCePP, and he sees a great opportunity for dialogue and cooperation.

3.2. Global Research in Paediatrics (GRiP)

On behalf of GRiP, Miriam Sturkenboom and Jan Bonhoeffer presented slides on this FP7-funded network of excellence, highlighting potential links with both ENCePP and Enpr-EMA.

One of the objectives of the project is to develop an integrated electronic infrastructure for paediatric pharmacoepidemiological research, linking existing healthcare databases from around the world. The current under-representation of European sites was highlighted and an invitation issued to ENCePP partners to participate in this global network. Contact details were provided and interested parties were encouraged to get in touch.

3.3. PHARMacovigilance for Adverse effects in Childhood arthritis focussing on Immune modulatory Drugs (PHARMACHILD)

Nicolino Ruperto presented slides informing on the PRINTO network and its work on juvenile idiopathic arthritis, as well as the FP7-funded PHARMACHILD project. He also illustrated some very relevant examples of problems encountered in international collaboration relating to ethics and funding.

In conclusion of this session on paediatrics the Chair thanked all speakers and announced that – provided there is sufficient interest - the establishment of a special interest group in paediatrics will be considered. This will be discussed further at the level of the ENCePP Steering Group.

4. Break-out session: Special Interest Group 'Drug Safety in Pregnancy'

Corinne de Vries gave a brief summary of the meeting of the SIG 'Pregnancy' which had taken place during the morning coffee break. She reported that 25 people participated and that the group had appointed Elizabeth Ursell as Chair, and Janine Collins as Vice-chair.

The group reviewed the mandate which had recently been adopted by the Steering Group, and it was agreed that a first TC of the group is to be organised shortly.

5. Session on Methodology

5.1. Case-population strategy in pharmacovigilance

Joan-Ramon Laporte presented slides on case-population strategy in pharmacovigilance, highlighting the strengths and limitations of this method.

Following the presentation Susana Perez-Gutthann outlined her thoughts on the subject, providing a basis for the ensuing discussion.

6. ENCePP Best Evidence

6.1. Experience so far

Kevin Blake presented slides outlining various examples of best evidence support provided by ENCePP to regulatory decision-making to date.

In this context he reminded partners that ENCePP centres are invited to submit their applications to the EMA's current call for expressions of interest for shortlisting to conduct EMA funded drug safety studies. Applications are possible until 2 January 2015.

He concluded by saying that although some challenges remain – particularly in relation to funding – after years of putting in place the necessary building blocks, ENCePP is delivering tangible benefits and concrete contributions are being made by ENCePP centres to regulatory decision making.

The ensuing discussion focussed mainly on the issue of funding of research into new/emerging safety issues and the sustainability of existing research infrastructure beyond the timeframe of a specific project.

The Chair concluded that ENCePP will continue to reflect on the sustainability of drug safety research and noted the concrete contribution ENCePP is making to best evidence for regulatory decision-making.

7. Interface ENCePP and industry

7.1. Results of ENCePP survey of industry

Kevin Blake presented slides summarising the results from a survey which was launched and disseminated with the help of industry associations among their members. This survey was conducted to prepare for a meeting of industry representatives with the ENCePP Steering Group.

The Chair added that, although ENCePP had been very successful in establishing an academic network, there is a clear need for ENCePP to facilitate dialogue to further engage with industry.

7.2. Report from ENCePP meeting with industry associations

Morten Andersen provided a summary report to the Plenary on the meeting between the ENCePP Steering Group and industry representatives which took place on 22 May 2013.

He started by saying that the key discussions related to exploring the means of enhancing the utility of the network's outputs for industry to conduct robust post-authorisation studies in a transparent and scientifically independent manner.

The feedback from industry confirmed that the ENCePP methodological guidances are well received and widely used. However, aspects of the Code were raised as requiring clarification, particularly relating to access to documents and the involvement of study funders in the research itself. Another issue of concern raised was how the work undertaken by industry pharmacoepidemiologists might be acknowledged, including in publications and in the ENCePP E-Register/EU PAS Register.

It was raised that there might be a particular utility of ENCePP to SMEs in that they may have less substantive pharmacoepidemiology resources in comparison to large companies, and in potentially bridging requirements of stakeholders to health technology and regulatory agencies.

During the ensuing discussions it was agreed that relevant sections of the ENCePP website require review to further clarify that the ENCePP Seal stands for transparency, independence and application of standards, but is not an indicator of the overall quality of a study or its results. Another important task will be to review the Code to ensure the principles within are not overtaken by processes, for example, around applying for the ENCePP Seal. It was raised that any revisions of the Code would be taken forward through public consultation before adoption.

The Chair concluded by saying that there is a clear need to continue the dialogue with industry; the Steering Group will decide on the best way forward, and the establishment of a joint ENCePP-industry working group might be one of the possible options to achieve this.