19 August 2011
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ENCePP Secretariat

ENCePP Workshop with Medical Journal Editors

29 June 2011

List of Attendees

Medical Journal Editors:

- Virginia Barbour (Public Library of Science Medicine)
- Joan Bathon (Arthritis & Rheumatism)
- Jörg Hasford (Pharmacoepidemiology and Drug Safety)
- Toby Lasserson (Cochrane Editorial Unit)
- Kirsten Patrick (BMJ)
- Caren Solomon (NEJM)

ENCePP Delegation:

- Joan-Ramon Laporte (Fundació Institut Català de Farmacologia, Barcelona)
- Jytte Lyngvig (Heads of Medicines Agencies – HMA)
- June Munro Raine (CHMP PhVWP)
- Miriam Sturkenboom (Erasmus Medical Centre)
- Giuseppe Traversa (Istituto Superiore di Sanità)
- Susana Perez-Gutthann (RTI Health Solutions)
- Peter Arlett (European Medicines Agency)
- Henry Fitt (European Medicines Agency)
- Camilla Smeraldi (European Medicines Agency)
- Kevin Blake (European Medicines Agency)
- Thomas Goedecke (European Medicines Agency)
- Monika Benstetter (European Medicines Agency)

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Executive Summary

- The Checklist for ENCePP Study Protocols and the Guide of Methodological Research Standards were presented as examples of the activities undertaken by ENCePP to promote high quality research. Journal editors welcomed the fact that the guidance documents had been developed through collaboration of the ENCePP partners and subject to public consultation. In addition, the transparency requirements for 'ENCePP Studies' were very well received.
- The editors were reminded that for those studies following the ENCePP Code of Conduct, investigators are committed to publishing an abstract of the main findings in the ENCePP E-register of studies within 3 months of the completion of the final study report and the entire study report without delay. These provisions for transparency were not seen as having a negative impact on subsequent publication in medical journals. On the contrary, the editors were of the opinion that disclosure of the final study report through the ENCePP E-Register of studies prior to publication is extremely useful. It was considered as introducing a further level of accountability, as such disclosure provides the possibility for journal reviewers to look at the data and for readers to scrutinise the full study report.
- There was general agreement that sharing data of public health importance by researchers with regulatory authorities prior to their publication is understandable and not an obstacle to their subsequent publication in a journal. The editors also encouraged researchers to detail at the time of the submission of a manuscript if regulators had been informed of the findings of a study and/or whether disclosure of results in the ENCePP E-Register had been made. It was also agreed that, in cases where there is a need for urgent communication of a potential risk to public health, dialogue between press offices of journals and regulatory authorities should take place in advance of publication.

Next steps

- A follow-up meeting is planned to take place within the next 12 months.

Minutes

1. Welcome and introductory remarks

P Arlett opened the meeting and welcomed all the participants to the workshop, both those attending in person and those joining remotely through web conference. He highlighted that this was the first time ENCePP was meeting with representatives medical journal editors and thanked the participants for accepting the invitation to the workshop.

He explained that the objectives of the workshop were to raise awareness of ENCePP and its related initiatives and the exchange of views on more specific topics. Participants were invited to join in at any time with questions or clarifications.

In a brief overview of ENCePP, P Arlett presented the rationale behind the creation of ENCePP and how the network has now evolved into a unique resource dedicated to pharmacovigilance, pharmacoepidemiology and post authorisation research, covering 17 different European countries and counting more than 100 centres and networks, ranging from hospital, research institutions and contract research organisations. It was stressed how participation in ENCePP is completely voluntarily and the only pre-requisites for organisations to take part are to have experience in conducting

pharmacovigilance and pharmacoepidemiological research for a third party and to have a base in Europe.

Lastly, an important distinction was made between the concept of an ENCePP study (and the related obligations that are attached to it) and the use of the ENCePP E-register of studies, an electronic resource that has been developed for the registration of post authorisation studies, open to everybody and entirely voluntary.

2. ENCePP and the ENCePP Study concept: scientific independence in commissioned research, transparency and application of methodological standards

Discussion topics on the agenda were:

- What are your views on the ENCePP Code of Conduct?
- How do you consider the concept of an ENCePP Study supports science and evidence-based decision-making?
- What other principles would you consider as pivotal in strengthening post-authorisation medicines research?

This session was introduced by S Perez-Gutthann, representing the Working Group dedicated to the development of standards and methodological guidance. In her presentation she provided a brief summary of the three key pillars of ENCePP (independence, standards, and transparency) and how they have been translated into practical tools and documents to assist investigators throughout the whole research process.

The key principles of the ENCePP Code of Conduct were presented, highlighting the importance of this document in defining clear roles, rights and responsibilities of researchers and study funder, thus ensuring independence of the study conducted.

As regards the role of ENCePP in driving up standards and building capacity in post authorisation research, the development of methodological standards including the Checklist for ENCePP Study Protocols and the Guide of Methodological Research Standards were presented as examples of the activities undertaken by ENCePP to promote high quality research. The fact that the guidance documents were developed through collaboration of the ENCePP partners and subject to public consultation was considered a strength by the journal editors.

The transparency requirements for ENCePP Studies were also presented and were very well received by the journal editors. It was clarified that the current ENCePP Code of Conduct requirements do not prohibit conduct of post hoc analysis on the study data, but they do oblige to make publicly available the different versions of the study protocol to disclose what were the pre-specified analysis versus the changes that have occurred in light of preliminary analysis of the data (post-hoc analyses).

3. Findings of public health importance: sharing results prior to their publication

Discussion topics on the agenda were:

- Do you consider peer-review as mandatory prior to publication of all study results?
- How can we balance the sometimes more urgent need for data to support regulatory decision making and publication in peer-reviewed journals?

- Do you envisage a process that enables publication of results in the ENCePP Register of Studies (E-Register) without this being necessarily considered as prior publication, similar to how the ICJME considers results of data posted in the tabular format required by ClinicalTrials.gov?

During this session, led by M Sturkenboom, participants were encouraged to discuss the interaction between researchers, regulatory authorities and journals in the event of findings of public health relevance being shared prior to publications. Journal editors were reminded that for those studies following the ENCePP Code of Conduct, investigators are committed to publishing an abstract of the main findings on the ENCePP E-register of studies within 3 months of the completion of the final study report and the entire study report without delay. Overall these provisions for transparency were very well received by the journal editors present at the workshop, and in no way were they seen as having a negative impact on the publication of the study in the journals. Journal editors were of the opinion that disclosure of the final study report through the ENCePP E-Register of studies prior to the publication is extremely useful and additionally it introduces a level of accountability, since such disclosure provides the possibility for journal reviewers to look at the data and readers to scrutinise the full study report.

Similarly, there was general agreement that sharing data of public health importance with regulatory authorities prior to their publication is in no way an obstacle to their publication. In these circumstances it was however, recommended that in case of urgent communication there was dialogue between journals and regulatory authorities in advance of publication. The editors also encouraged researchers to detail at the time of the submission of a manuscript if regulators had been informed of the findings of a study and/or whether disclosure of results in the ENCePP E-Register had been made.

4. The ENCePP Register of studies as a register for all post-authorisation studies

Discussion topics on the agenda were:

- How can journals encourage the registration of studies in the ENCePP E-Register?
- Could citing a registration number in the ENCePP E-Register be considered essential for publication of a manuscript?
- Do you see a role for the ENCePP E-Register of studies in facilitating systematic review and meta-analysis?
- Are there potential downsides to the registration of studies in the ENCePP E-Register?
- Do you see the ENCePP Databases being used to locate appropriate reviewers or to find authors for commissioned articles?

The last session of the workshop, presented by K Blake, was aimed at introducing the ENCePP E-register of studies and its role as a publicly accessible tool for the registration of pharmacoepidemiology, pharmacovigilance and post-authorisation studies. Once again it was emphasized that registration of the studies in the E-Register prior to their start is mandatory only for ENCePP Studies, while it is completely voluntarily for all other studies. It was explained that the register has been designed specifically for, but not limited to, observational studies, with a main focus on post-authorisation safety studies of medicines. The role of this register was discussed as compared to the already established registers such as clinicaltrials.gov that are already hosting information on observational research while concentrating on interventional trials. It was explained that as the ENCePP register was at a relatively early stage, having only been launched last November, the view of

journal editors on this resource and its utility as a disclosure, transparency and information tool, will be highly influential. The future role of the ENCePP E-Register will also be impacted by the provisions of the new pharmacovigilance legislation and possible collaboration with health technologies assessment bodies, and both these influences are likely to increase its use.

5. Final round of Q&A

P Arlett concluded the workshop thanking the participants for the fruitful discussion and anticipating that the dialogue with the journals should continue in the future, with a follow-up meeting in 6 – 12 months.