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European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

Report - 13th ENCePP Plenary Meeting

25 November 2014 – chaired by Peter Arlett

Meeting Agenda:

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1. General Matters

1.1. Welcome and Adoption of Agenda

The Chair welcomed all delegates, highlighting new ENCePP partners and those representatives attending their first plenary meeting.

He also welcomed observers from Health Canada and the US FDA.

1.2. Introductory remarks

In his introductory remarks the Chair provided updates on a number of topics of potential importance to the network:

- Publication of survey on multi-source studies:

  A report on the outcome of a survey of researchers coordinating multi-database drug-safety projects that have been publicly funded by the European Commission has been published on the ENCePP website (http://www.encepp.eu/publications/documents/Survey_Multi-source_studies.pdf). The survey was conducted by the ENCePP working group 'data sources and multi-source studies' (Chair: Miriam Sturkenboom) with the aim of elucidating current practice in Europe in combining data from multiple sources. These results will inform as a baseline for future activities on data combination.

- Publication on estimation of renal function in the elderly and the revision of the pharmacokinetic guideline :

  As a follow-up to previous ENCePP discussions on estimating renal impairment the delegates were informed that the paper 'Renal function estimations and dose recommendations for dabigatran, gabapentin and valaciclovir: a data simulation study focused on the elderly' has been published in BMJ Open (http://bmjopen.bmj.com/content/3/4/e002686.full). The study was conducted by ENCePP researchers and the findings have been forwarded to the Pharmacokinetic Working Group for consideration in the ongoing revision of the guideline on estimating renal function. Copies of the paper were made available at the meeting.

- Impact of pharmacovigilance:

  The Chair drew attention to the importance placed by the Agency on measuring the impact of pharmacovigilance on public health, including the impact of legislation and highlighted that the network has the potential to play a key role in evidence generation to support the Agency in achieving this.

- EMA pharmacovigilance IT projects:

  The broad range of ongoing IT projects and processes at the EMA linked to pharmacovigilance was presented as was the role of pharmacovigilance fees in supporting these initiatives. Specifically over the next two years, the following services are expected to come on-line: a literature monitoring service for the industry; a new database of products and substances on the EU market; a new database of periodic safety reports, and an enhanced EudraVigilance database of suspected adverse reactions.

- Dialogue with industry:

It was again confirmed that in line with discussions at the previous ENCePP plenary meeting that dialogue with industry on issues of significance to the network would be managed by the EMA.

- Adverse reaction reporting requirements from post-authorisation studies (PAS):

  A summary of requirements on non-interventional PAS arising from revision 1 of the Good Pharmacovigilance Practices (GVP) Module VI was presented. It was agreed that slides highlighting the changes would be circulated to all plenary participants as an immediate follow-up to the meeting. The continued input of the network in highlighting the need for areas of the GVP that were unclear was acknowledged.

2. Report from the Steering Group

Susana Perez Gutthann, in her role as deputy chair of the ENCePP Steering Group, presented slides outlining achievements since the last plenary meeting and some key objectives and deliverables from the draft work plan for 2015-2016. Her presentation included feedback from the meeting the previous day of the ENCePP special interest group (SIG) on 'pregnancy'.

She particularly acknowledged the work done by the individual working groups and their contributions to the overall aim of ENCePP to further promote best methodological and governance practices in pharmacoepidemiology and pharmacovigilance, giving examples of each of the groups' key achievements over the past twelve months. In this context, she invited individuals who are interested in joining any of the existing working groups to express their interest and approach either the relevant WG Chair directly or the ENCePP Secretariat. The Deputy Chair concluded with an invitation to ENCePP partners to actively support the promotion of the network and its activities and outputs.

A number of suggestions were made by the Plenary in relation to the ENCePP work plan 2015-2016. These related to data collection methods (biomarkers), links to other European initiatives (e.g. Biobanks), potential overlap in training initiatives (Eu2P), and the involvement of social media in the promotion of ENCePP. The suggestions will be considered for further discussion at Steering Group level.

3. ENCePP and methods

3.1. Use of routinely collected electronic healthcare data – lessons learned

The presentations by Massoud Toussi (IMS Health, France) and Alison Bourke (CSD Medical Research, UK) provided methodological and personal insights into generating evidence from real world data.

3.2. ENCePP Guide for conducting systematic reviews and meta-analysis of pharmacoepidemiology studies investigating the safety of medicinal products

Nawab Qizilbash, Chair of the ENCePP Working Group on Data Integration, provided the plenary with a progress report on the development of a guidance for conducting systematic reviews and meta-analysis of pharmacoepidemiology studies. The draft guide is currently under revision following consultation of the ENCePP Working Group on Research Standards and Guidances. He

informed the plenary that a public consultation on the new guide is expected to be launched during the first half of 2015.

3.3. PROTECT project outcome

Xavier Kurz's presentation provided an insight into the ongoing impact assessment of regulatory sciences and how to turn research outputs into tangible outcomes, with an example of the PROTECT project. He stressed that defining criteria for prioritisation of regulatory science activities is work in progress, and invited ENCePP partners to comment on this initiative and provide feedback on experiences through their involvement in other projects.

Other initiatives in this area mentioned were the Innovative Medicines Initiative's (IMI) efforts to look into the sustainability of outcomes of IMI projects, and the UK universities' Research Excellence Framework (REF) 2014 which has developed a methodology for assessing the impact of research.

4. ENCePP and research in practice

4.1. CODEMISUSED project

Marie Claire Van Hout, project coordinator and principal investigator, presented on CODEMISUSED, an FP7 funded collaboration that aims to estimate and gain further understanding into the extent of codeine use, misuse and dependence in Ireland, the UK and South Africa, in order to design protective mechanisms for pharmacies to be able to track, monitor, support and refer for treatment.

ENCePP partners interested in working with Dr Van Hout or who would like to share any information on similar work done were invited to contact her directly. For that purpose, it was agreed that her contact details would be circulated to all participants following the meeting.

4.2. Lessons learned on post-authorisation safety studies (PASS)

Pierre Engel presented the outcome of a study conducted in collaboration with Marieke de Bruin on the experience of PRAC review of PASS and lessons learned on the design of PASS under the new pharmacovigilance legislation.

The study highlighted compliance with registration requirements of PRAC imposed PASS. There was an extensive discussion around the legislative and GVP requirements for registration of study protocols and final reports. The pharmacovigilance legislation requires the final report of imposed PASS to provide the date of registration in the publicly available register maintained by the EMA. It was therefore agreed that the requirements for the registration of studies should be made clearer when the results of the PRAC study are presented.

5. ENCePP supporting product life-cycle

5.1. ENCePP and research that supports HTA

Nicholas Moore presented a summary of the outcome of the survey of ENCePP partners conducted by the HTA working group earlier this year to map existing ENCePP experience in undertaking research with outcomes that might support decision making by HTA bodies in the European Union.

The outcome of the survey confirms that some ENCePP partners have experience in conducting studies with endpoints directly relevant to HTA. ENCePP may, therefore, be a useful platform to develop European capacity to deliver such studies.

The results of the survey have also been presented to ISPE (October 2014) and ISPOR (November 2014) and will be presented at the EMA-EUnetHTA meeting in December 2014, thereby also increasing the awareness of ENCePP among HTA bodies. In the short term it is planned to enhance the working group's membership with increased involvement of individuals from HTA bodies. This will help in defining specific deliverables for the working group which will in the meantime serve as a forum for consultation on relevant guidance.

5.2. Report on Agency pilot on adaptive pathways

Francesca Cerreta informed the delegates about the ongoing EMA project on Adaptive Pathways, providing feedback on the initial experience, lessons learned and a look at next steps.

She stated that this could be an area where ENCePP could potentially make a significant contribution due to the network's experience in conducting benefit:risk studies on medicines. It was suggested that the Steering Group discuss a potential link between ENCePP and adaptive licensing during one of its upcoming meetings.

5.3. Registries

Jim Slattery presented an update on the development of an EMA strategy and pilot phase for patient registries.

He elaborated that from the EMA's perspective, the current approaches to registries are sometimes seen as suboptimal in scientific and resource terms, plus it is difficult to assess the validity of results from individual registries. There is also an apparent lack of coordination between national and EU initiatives. The Agency has therefore established a cross-Agency task force to develop a strategy paper on registries and start discussions with its Scientific Committees. It is also proposed to launch a pilot phase.

The project is still in its early phase, and further details will be explored in the coming months, including avenues of interaction with the ENCePP network, which the Resources Database has documented has extensive experience with registries.

The Plenary was supportive of the need for work in this area and provided feedback on the need for clarity around why such a strategy is needed now and also proposed that registries may be viewed as prospective cohort studies thereby emphasising the need for clarity around terminologies.

6. Governance models for collaborative studies

6.1. Results of ENCePP partner survey on registering studies and the ENCePP Study Seal

Laura Yates, Chair of Working Group 'Independence and Transparency' presented on the results of the survey of ENCePP centres on registering studies in the ENCePP (EU PAS) Register and of the

ENCePP Study Seal. She explained that the purpose of the survey was to better understand how the register and the concept of the ENCePP Study Seal could be better promoted in the future to increase uptake.

As a result of the survey some key issues have been identified which will be addressed through specific deliverables for the working group in the 2015 – 2016 work plan. One of which is a draft concept paper on approaches to industry funding of research of medicines used in pregnancy which is due to be submitted for consideration by the Steering Group shortly.

In response to a query relating to the upgrade of the ENCePP (EU PAS) Register, Peter Arlett confirmed that any future release would include certain changes that should make the database more functional and user friendly. A lot of very useful feedback has already been received, and will continue to be collected, from various stakeholders which will support the business case for upgrade of the database.

There was a discussion on the ENCePP Study Seal during which it was emphasised that the Seal is not a quality mark, but rather a tool to make public the researcher's commitment to transparency and independence.

6.2. ADVANCE – feedback from survey on models for public-public and public-private interactions

Xavier Kurz presented the main results of a survey conducted among ENCePP centres in May 2014 to identify existing models of private public partnerships for a framework for the benefit:risk monitoring of vaccines in the ADVANCE project. He explained that in parallel to the survey a literature search had been conducted.

The survey and literature search identified a number of strengths, weaknesses and areas of improvement across the various models of private public partnerships. The final report is due to be submitted to IMI for agreement soon and will consequently be published on the ADVANCE website. In the meantime, further information on the project outputs can be obtained from the website http://www.advance-vaccines.eu/

In the long term the goal is to have in place clear governance principles and a code of conduct for vaccine studies to support transparency in this area. A consultation that will include ENCePP is planned for Q1 2015.