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SCIENCE MEDICINES HEALTH

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ENCePP Secretariat

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

ENCePP activity report 2016

Executive Summary

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) aims to strengthen the monitoring of the benefit-risk balance of medicinal products in Europe by:

- Facilitating the conduct of high quality, multi-centre, independent post-authorisation studies (PAS) with a focus on observational research;
- Bringing together expertise and resources in pharmacoepidemiology and pharmacovigilance across Europe and providing a platform for collaborations;
- Developing and maintaining methodological standards and governance principles for research in pharmacovigilance and pharmacoepidemiology.

The network published the 5th revision of the ENCePP Guide on Methodological Standards in Pharmacoepidemiology, as well as an improved version of the ENCePP Checklist for Study Protocols. 2016 also saw the creation of a new Special Interest group (SIG) on impact to support the implementation of the PRAC Strategy on Measuring the Impact of Pharmacovigilance Activities adopted in January 2016. The EU PAS Register underwent a technical upgrade featuring a number of performance and study management enhancements. During 2016 the registration of studies in the EU PAS Register continued to rise to a total of 968 studies (a 40% increase over twelve months), with the use of the ENCePP website and information resources increasing alike.

The network's success is based on the expertise and commitment of those participating and the Steering Group takes the opportunity of the activity report to thank all the ENCePP partners for their contributions.

Key achievements

- In consultation with the PRAC Interest Group (IG) on Impact, the ***ENCePP Special Interest Group on Measuring the Impact of Pharmacovigilance Activities*** ('SIG Impact') was established in June 2016. The mandate of the ENCePP SIG is to provide recommendations (e.g. in form of guidance documents or publications in peer-reviewed journals) to the PRAC IG on the key

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methodologies for measuring health outcomes of pharmacovigilance activities which contribute to the overall evaluation of the impact of pharmacovigilance systems in line with the PRAC Strategy on Measuring the Impact of Pharmacovigilance Activities.

- The fifth annual review of the **ENCePP Guide of Methodological Standards in Pharmacoepidemiology** was completed in July 2016 by the ENCePP Working Group on research standards and guidances (Chair: Alejandro Arana), with updates, amendments or clarifications of most chapters. This latest version also includes a new chapter on using data from social media and electronic devices as a data source. The Guide continues to be the most popular document on the ENCePP website with around 16,000 downloads, plus around 40,000 views of individual chapters in the online version in 2016.
- The ENCePP Working Group on research standards and guidances was also the lead on revision 3 of the **ENCePP Checklist for Study Protocols** which was published in July 2016. The Checklist was revised to include reference to sections, rather than page numbers of protocols. It also underwent editorial review and a reference to HTA endpoints has been added.
- A new version of the **EU PAS Register** was released on 14 July 2016. This upgrade included a number of performance enhancements and important improvements in terms of searching and data management, most importantly the possibility to search the database by the unique study identifier which is also displayed with the study record on screen and included on printouts. A new mandatory data field titled 'RMP study category' was also introduced. In parallel, the ENCePP website and relevant documents were revised to remove all references to the old ENCePP E-Register.
- The new **ENCePP Steering Group** took up its three year mandate following the election of ENCePP partners at the plenary meeting in November 2016. The group will oversee the implementation of the ENCePP work plan 2017-2019.

Meetings and Networking

The ENCePP Secretariat organised the annual meeting of the plenary in November 2016; a report of the meeting and presentations given have been published on the ENCePP website.

The Steering Group met twice in 2016; minutes of those meetings are published on the ENCePP website.

Since its inception earlier in the year, the coordinators of the special interest group 'Impact of pharmacovigilance activities' (SIG Impact) met regularly to agree its mandate and detailed work plan. Meetings of the Working Group on research standards and guidances, and the coordinators of the special interest groups (SIG) 'Pregnancy' and 'Impact' took place in the margins of the plenary. Updates on the individual groups' activities were provided at the plenary meeting.

The exchange of information with other international initiatives with similar goals continues to be an important part of ENCePP networking activity, and representatives from Health Canada, US FDA and PMDA Japan are invited regularly to attend the ENCePP plenary meetings as observers.

Network growth & strengthening

ENCePP guidance has been cited in scientific articles, as well as industry and CRO publications. The network is referenced in a forthcoming publication titled *Post-Authorization Safety Studies of Medicinal Products: The PASS Book* (Ayad K. Ali, Editor).

As of end December 2016, the number of centres and networks in the ENCePP Database stood at 164 (*155*) and 25 (*24*), respectively from 19 different European countries. The number of registered data sources remained unchanged at 53. The figures in brackets and italics are the corresponding numbers as of end 2015. The characteristics of the 164 ENCePP centres registered in the database are described in figures 1 - 5. These figures demonstrate the engagement in ENCePP and its important role in research capacity building across Europe.

Figure 1: Classification of centres (2016)
y axis = number of centres (multiple answers possible)

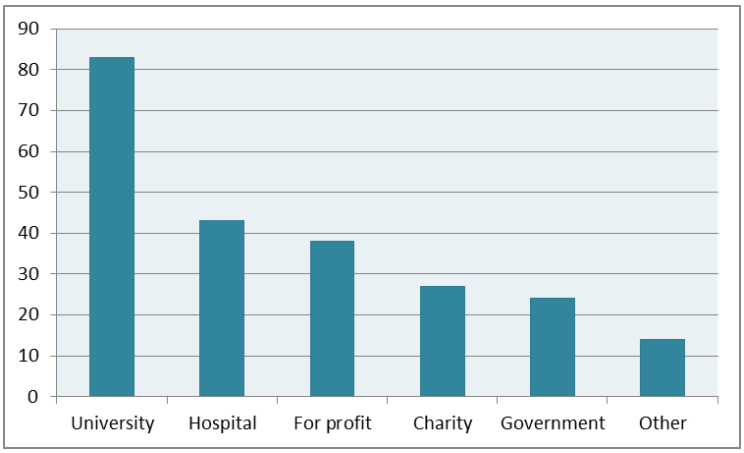


Figure 2: Expertise available in centres (2016)
x axis: number of centres (multiple answers possible)

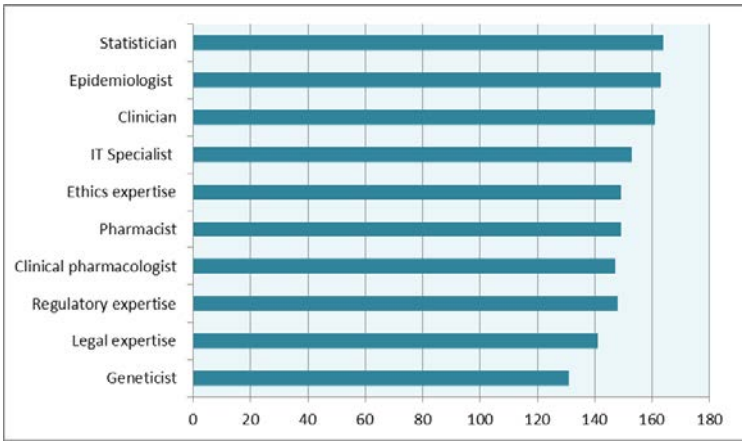


Figure 3: Experience with study designs (2016)
y axis: number of centres (multiple answers possible)

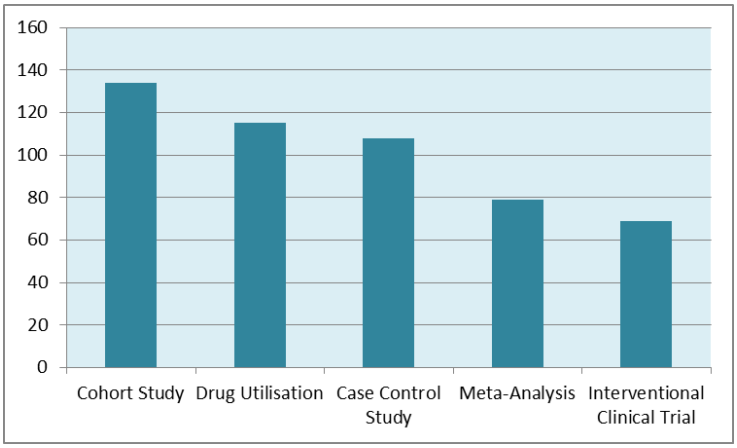


Figure 4: Experience in therapeutic areas (2016)
x axis: number of centres (multiple answers possible)

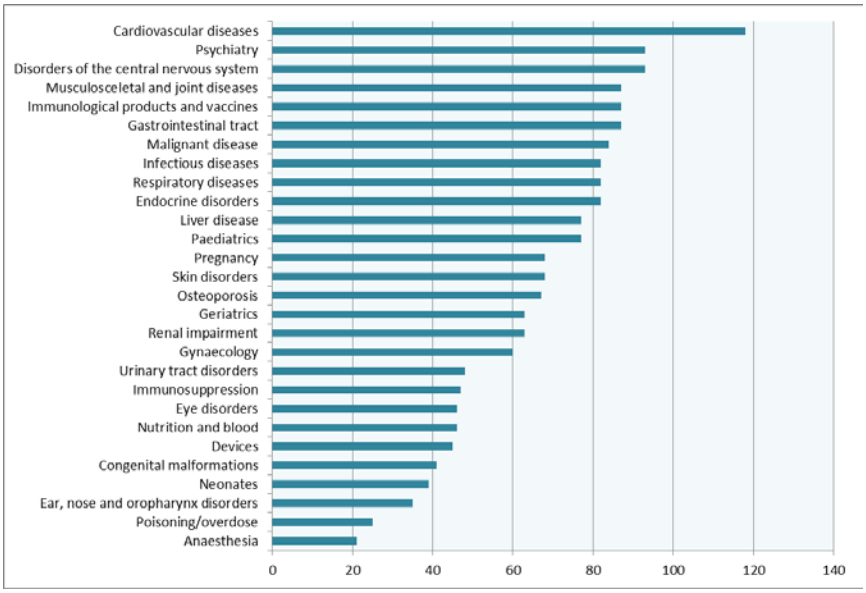


Figure 5: Research experience (2016)

y axis: number of centres (multiple answers possible)

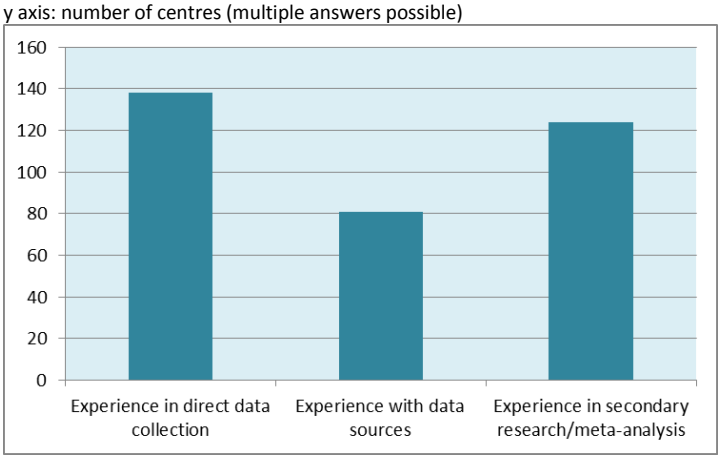
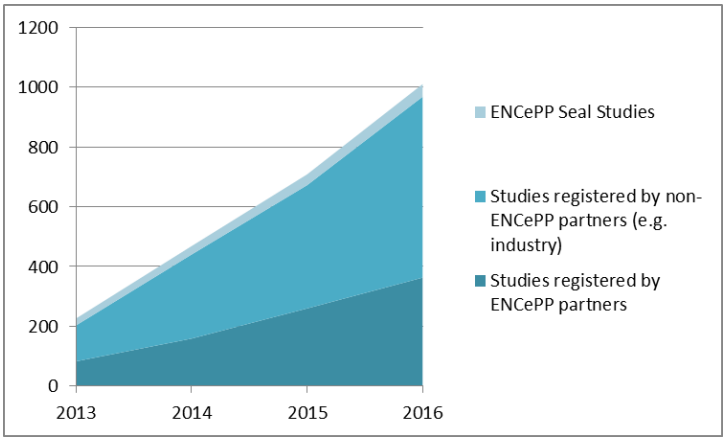
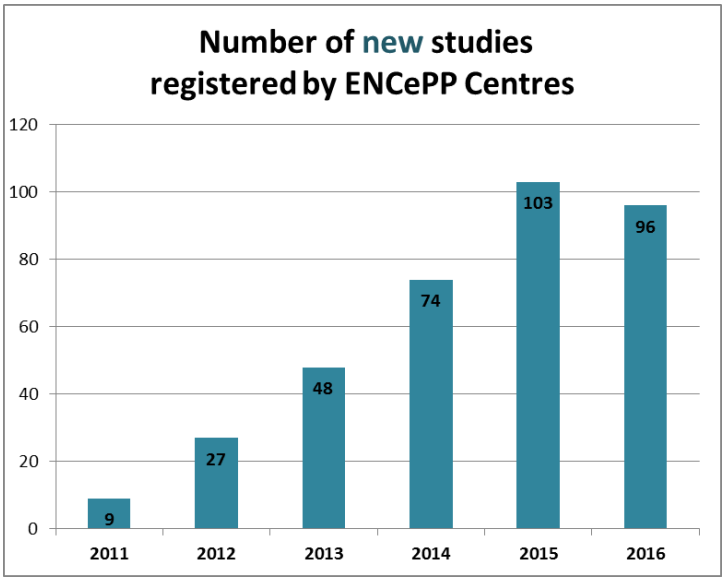


Figure 6 - 7: EU PAS Register

The number of studies registered in the EU PAS Register (currently hosted on the ENCePP website) has risen from 690 to 968 (40% increase) between January and December 2016. A total of 42 of studies registered have the ENCePP Study Seal.

The continued increase in study registrations can be explained in part by the EU PAS Register being referred to in the guideline on Good Pharmacovigilance Practices (GVP) module VIII, chapter VIII.B. In addition, the voluntary registration of studies by pharmaceutical industry continues to rise. On the other hand, the number of new studies registered in 2016 by ENCePP centres has fallen slightly compared to the previous year.





ENCePP Website statistics

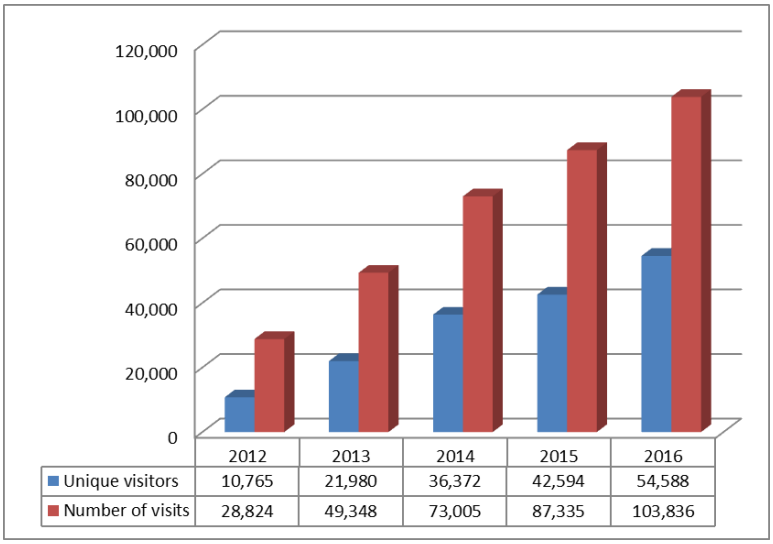
The ENCePP website – hosted by the European Medicines Agency (EMA) – is the Network's interactive platform to maintain access and promote ENCePP. It is used for ENCePP-related announcements and for making ENCePP outputs (e.g. meeting minutes, mandates, code of conduct, standards and guidance documents, etc.) publically available. Key features of the website are the *ENCePP Database of Research Resources* and the *EU PAS Register*. Both databases are publicly accessible and searchable by any stakeholder.

The number of visits to the ENCePP website has continued to rise. The following figures provide some statistics on the use of the website. All figures represent external (i.e. non-EMA) access only.

In 2016 the ENCePP Secretariat had to deal with a record number of queries (~300). The majority of these queries related to the EU PAS Register, but also to ENCePP in general. Although the publication of a FAQ document (which has received approx. 3,300 hits in 2016) has been helpful, the number of EU PAS Register queries has increased compared to the previous year. This can be explained by the increased use of the EU PAS Register, but is also related to the technical upgrade released in July 2016, and the introduction of compliance and disclosure checks.

The Secretariat also continues to provide technical and administrative support for the EU PAS Register, as well as notifying Member States when a PAS (post-authorisation study) that has been requested by a regulator and funded by industry is registered. It also performs compliance and disclosure checks related to ENCePP Seal Studies and imposed non-interventional post-authorisation safety studies (PASS) in the context of GVP VIII regulatory requirements.

Figure 7: Visitor statistics (2009-2016)



	2012	2013	2014	2015	2016
Unique visitors	10,765	21,980	36,372	42,594	54,588
Number of visits	28,824	49,348	73,005	87,335	103,836

Figure 7 shows a steady upward trend in visitors since 2012.

Figure 8: Pages viewed by country (2016)

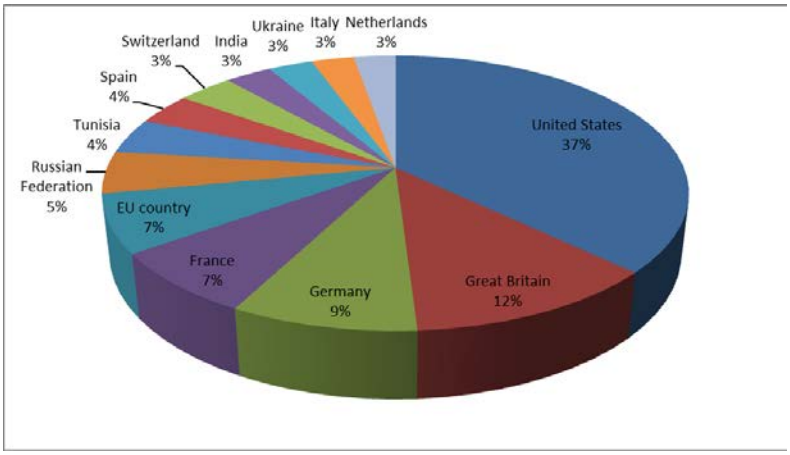


Figure 8 shows global interest in ENCePP in particular from the United States.

Figure 9: Most downloaded documents (2016)

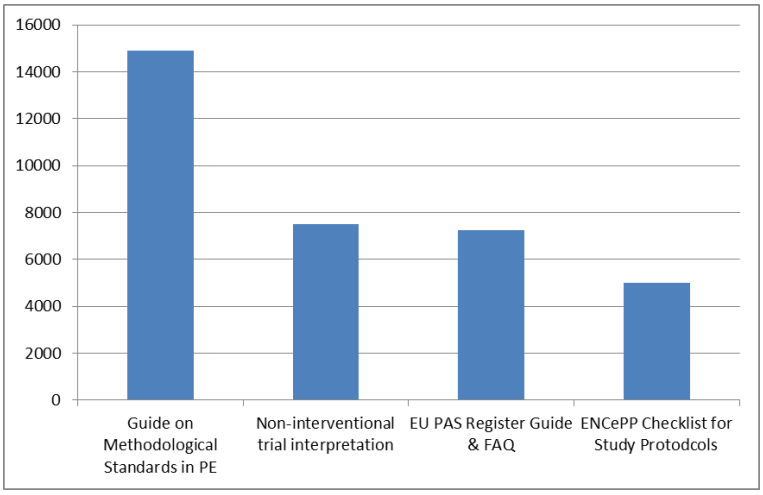


Figure 9 demonstrates the continued interest in the Guide on Methodological Standards in Pharmacoepidemiology, although the number of downloads has steadily decreased over the past two years, as stakeholders make more use of the online version of the Guide.

Figure 10: Top ten ENCePP URLs (2016)

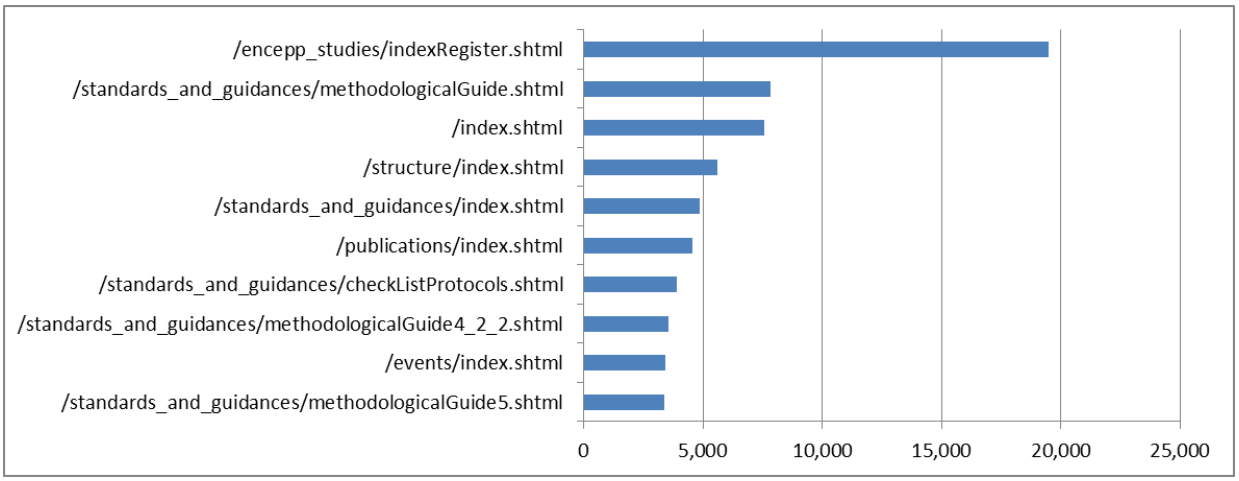


Figure 10 demonstrates interest in the EU PAS Register, but also reflects the popularity of ENCePP standards and guidances; the Methods Guide and its individual chapters received approx. 40,000 views in total.