EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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ENCePP Secretariat

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

ENCePP activity report 2015

Executive Summary

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) aims to strengthen the monitoring of medicinal products by facilitating the conduct of multi-center, independent studies focusing on safety and on benefit-risk throughout the product life-cycle. 2015 has seen further consolidation of the network's core activities with a focus on a more systematic interaction and active contribution to the data, information and knowledge that feed into regulatory decision-making at EMA's scientific committees e.g. in context of referral procedures. Through its working groups the network provided input into EMA's strategy on registries, the lessons learnt from methodological research projects PROTECT and ADVANCE, and published a stand-alone guidance on data integration from completed observational studies of the safety of medicines, in addition to the 4th revision of the ENCePP Guide on Methodological Standards in Pharmacoepidemiology. To further promote ENCePP's guiding principles of scientific independence and transparency to all stakeholders a targeted communication plan and revised ENCePP Q&A was published. Also in 2015 the registration of studies in the EU PAS Register continued to rise significantly to a total of 690 studies (a 56% 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

- The biennial **ENCePP work plan 2015-2016** was adopted by the Steering Group and published on the ENCePP website in March 2015. The main goal and objective of this working period is continued consolidation of the network as an important resource in the field of post-authorisation research on medicinal products. The focus during 2015 and 2016 will be on extending the scope of the network to support regulatory decision-making across the product life cycle. This will take ENCePP to the next level as a key provider for data and information for regulatory and health-care decision-making and patient access to medicines.

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- In agreement with the working group Chairs and the Steering Group, the mandates of all ENCePP working groups and special interest groups were aligned with the ENCePP work plan 2015-2016. The updated mandates have been published on the ENCePP website.
- Following further discussions between EUnetHTA (the European Network for Health Technology Assessment) and the European Medicines Agency it was proposed – and agreed by the Steering Group - to focus activities on methods for research with combined outcomes rather than continue with a stand-alone working group on **health technology assessment (HTA)**. As a consequence, three members of the working group on HTA joined the Working Group on Research Standards and Guidances whose mandate was revised accordingly to include determining the need for, and implementing as appropriate, additional guidance in the ENCePP Guide on Methodological Standards on conducting post-authorisation studies with clinical and health outcomes that meet the needs of regulators and HTA bodies. Close cooperation with EUnetHTA will continue in the form of consultation, e.g. on gaps in the ENCePP Methods Guide and on guidelines currently developed by EUnetHTA.
- The fourth annual review of the **ENCePP Guide of Methodological Standards in Pharmacoepidemiology** was completed in July 2015 by the ENCePP Working Group on research standards and guidances (Chair: Alejandro Arana), with a revision or update of most chapters. The Guide continues to be the most popular document on the ENCePP website and has seen a further increase in its popularity over the previous year with around 20,000 downloads, plus around 30,000 views of individual chapters in the online version in 2015.
- **Annex 1 to the ENCePP Guide of Methodological Standards in Pharmacoepidemiology** was adopted by the Steering Group and published on the ENCePP website in December 2015. This methodological guidance addresses the conduct of systematic reviews and meta-analyses of drug safety endpoints generated in completed (published or unpublished) comparative pharmacoepidemiological studies.
- In December 2015 the Steering Group adopted a set of **key messages** which may be used by ENCePP partners for communication on the network. As a further communication tool a **standard slide set** has been developed for use by ENCePP partners.

Meetings and Networking

The ENCePP Secretariat organised the annual meeting of the plenary in November 2015; a report of the meeting and presentations given have been published on the ENCePP website.

Meetings of the Working Group on research standards and guidances, and the special interest group (SIG) 'Pregnancy' took place in the margins of the plenary. Most ENCePP working groups met regularly – either face to face or via TC – making good progress on their work plan deliverables. Updates on the individual groups' activities were provided at the plenary meeting.

The Steering Group met three times in 2015; minutes of those meetings are published on the ENCePP website.

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.

A delegation from PMDA Japan visited the European Medicines Agency in January 2015 with the specific aim to learn more about the ENCePP initiative.

Presentations on ENCePP were given in a number of international fora, including the NEWDIGS Data Program Workshop in Boston, the Industry Stakeholder Forum at the European Medicines Agency, DIA Washington, and the Heads of Medicines Agency meeting in Slovenia in May 2015. ENCePP featured prominently in the EMA/DIA Information Day on Post-Authorisation Studies which took place in June 2015.

Network growth & strengthening

A number of articles in peer reviewed journals as well as industry and CRO publications that were published in 2015 made reference to ENCePP, particularly to its guidance. ENCePP guidance is cited in a number of international regulatory, clinical and pharmacoepidemiological guidances, including ISPE's Guidelines for good pharmacoepidemiology practice (GPP) published in November 2015.

As of end December 2015, the number of centres and networks in the ENCePP Database stood at 155 (*147*) and 24 (*22*), respectively from 19 different European countries. The number of registered data sources stood at 53 (*51*). The figures in brackets and italics are the corresponding numbers as of end 2014. The characteristics of the 155 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 (2015)
y axis = number of centres (multiple answers possible)

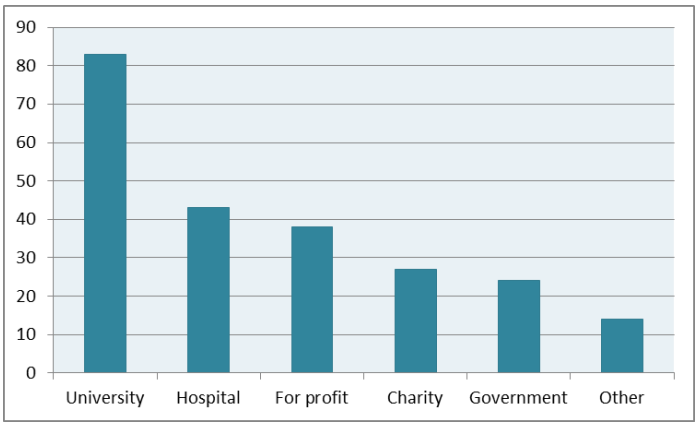


Figure 2: Expertise available in centres (2015)
x axis: number of centres (multiple answers possible)

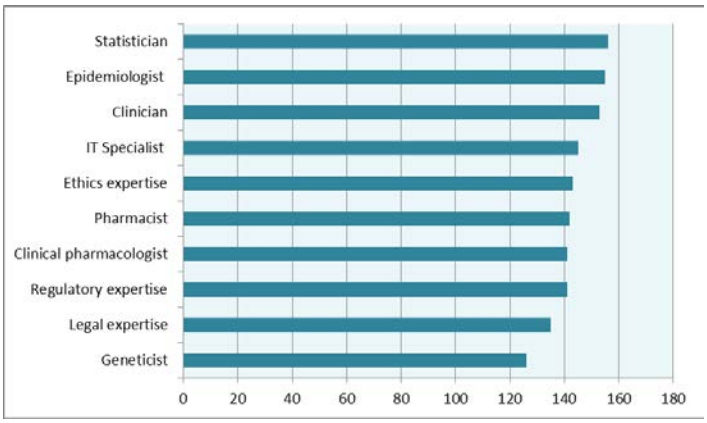


Figure 3: Experience with study designs (2015)
y axis: number of centres (multiple answers possible)

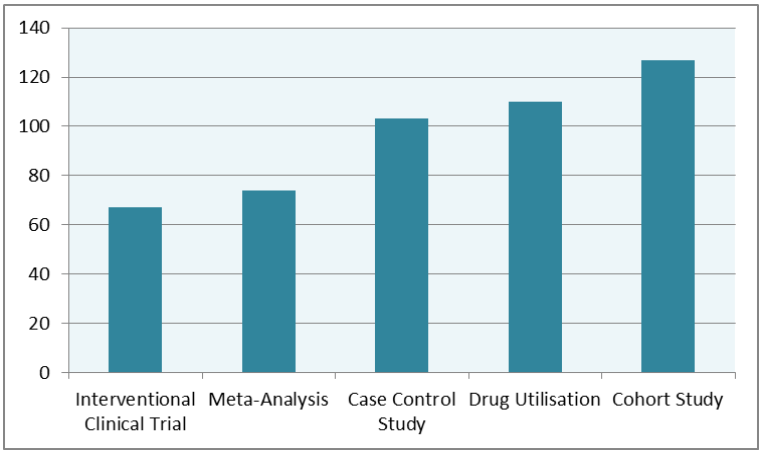


Figure 4: Experience in therapeutic areas (2015)
x axis: number of centres (multiple answers possible)

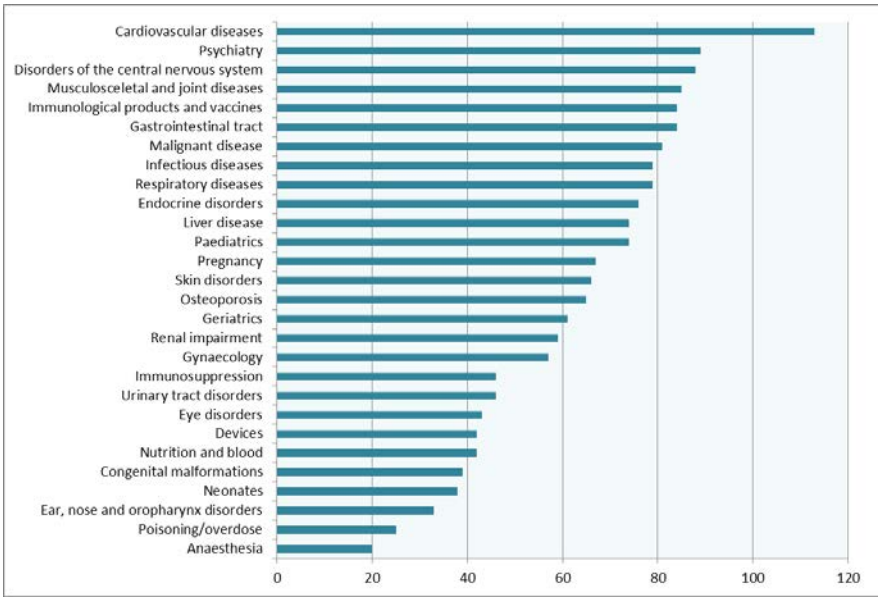


Figure 5: Research experience (2015)
y axis: number of centres (multiple answers possible)

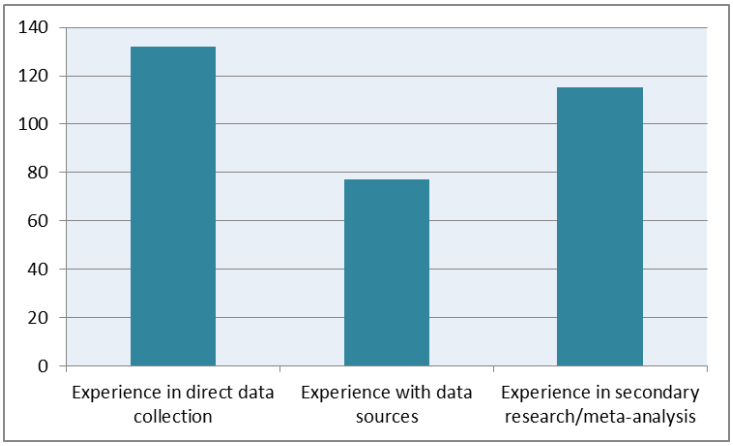
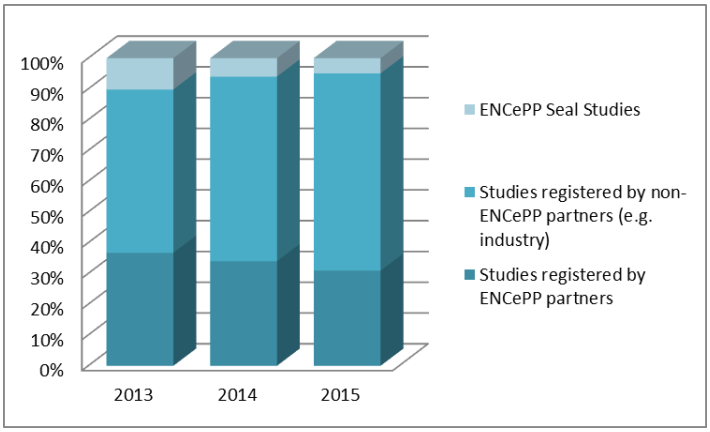
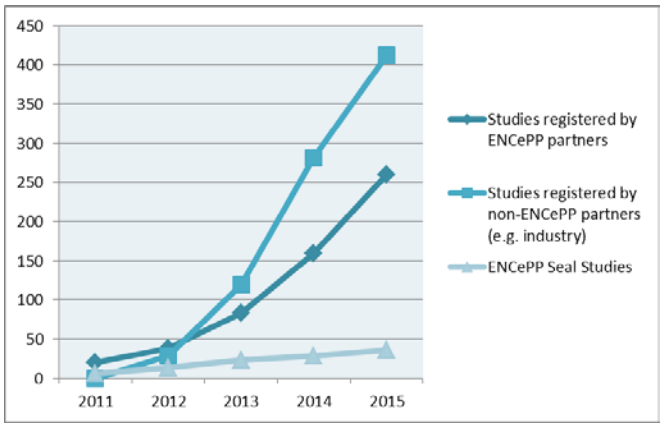


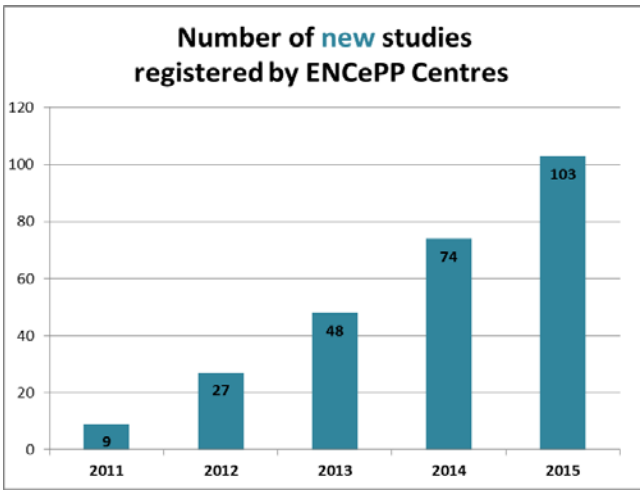
Figure 6 -8: ENCePP (EU PAS) Register

The number of studies registered in the ENCePP (EU PAS) Register has risen from 440 to 690 (56% increase) between January and December 2015. A total of 36 of studies registered have the ENCePP Study Seal.

The continued increase in study registrations can be explained in part by the E-Register of Studies currently serving as the 'EU PAS Register' as referred to in the guideline on Good Pharmacovigilance Practices (GVP) module VIII, chapter VIII.B. However, the voluntary registration of studies by ENCePP partners and pharmaceutical industry continues to rise substantially. The number of new studies registered by ENCePP partners continues to rise steadily.







ENCePP Website statistics

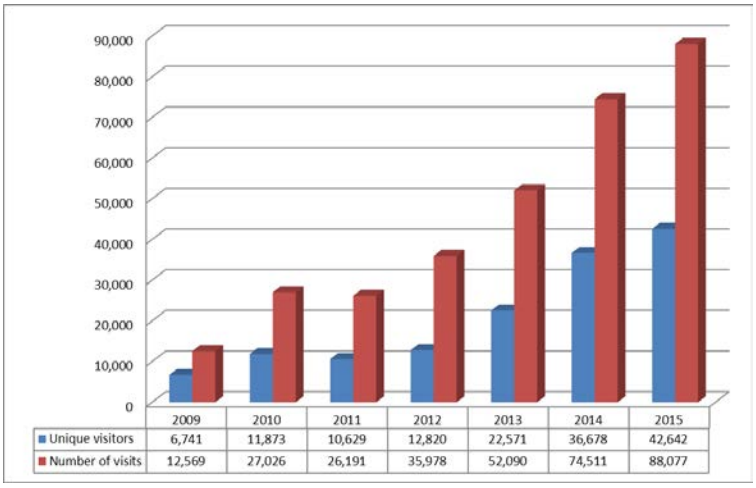
The ENCePP website – hosted by the European Medicines Agency (EMA) – is the Network's interactive platform to maintain access and promote ENCePP. It is used for ENCePP-related announcements and for making ENCePP outputs (e.g. meeting minutes, mandates, code of conduct, standards and guidance documents, etc.) publically available. Key features of the website are the *ENCePP Database of Research Resources* and the *ENCePP E-Register of Studies (de facto 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. Figure 7 includes EMA internal access. All other figures represent external (i.e. non-EMA) access only.

During 2015 a substantive number of queries (~200) relating to the ENCePP (EU PAS) Register or to ENCePP in general were dealt with by the ENCePP Secretariat. Based on the most frequently asked questions relating to the EU PAS Register over the past couple of years, a FAQ document has been compiled and published on the ENCePP website. Between August and December 2015 the FAQ document has received approx. 1,300 hits.

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.

Figure 7: Visitor statistics (2009-2015)



	2009	2010	2011	2012	2013	2014	2015
Unique visitors	6,741	11,873	10,629	12,820	22,571	36,678	42,642
Number of visits	12,569	27,026	26,191	35,978	52,090	74,511	88,077

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

Figure 8: Pages viewed by country (2015)

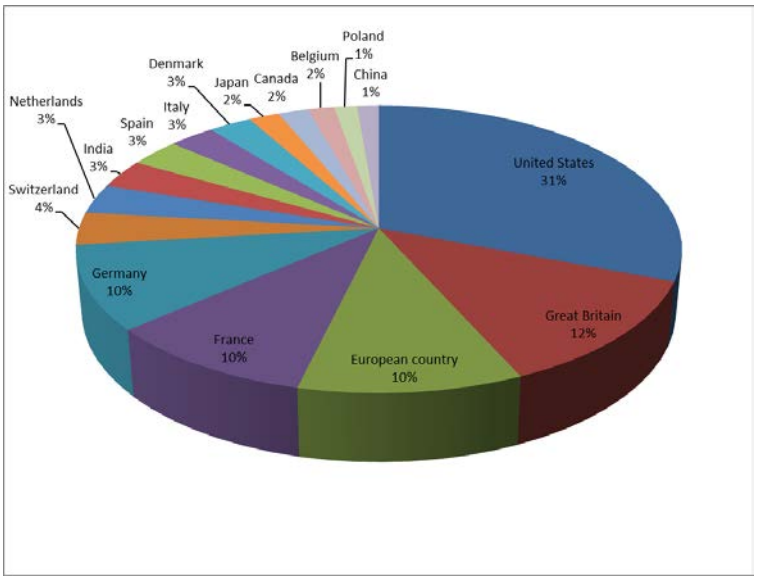


Figure 8 shows global interest in ENCePP in particular from the United States.

Figure 9: Most downloaded documents (2015)

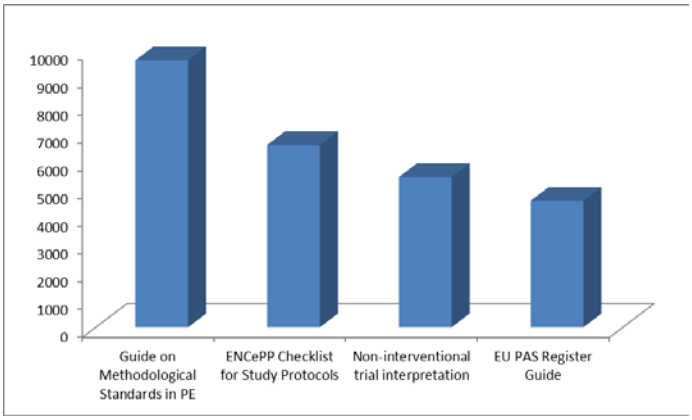
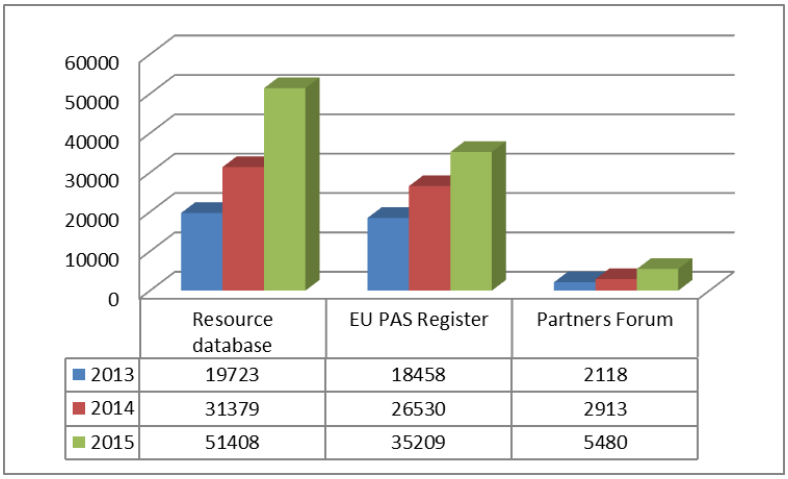


Figure 9 demonstrates the continued interest in the Guide on Methodological Standards in Pharmacoepidemiology, although the number of downloads has steadily decreased over the past two years, as stakeholders make more use of the online version of the Guide with approx. 25,000 views of individual chapters.

Figure 10: Hits on databases & partners' forum (2013-2015)



	Resource database	EU PAS Register	Partners Forum
2013	19723	18458	2118
2014	31379	26530	2913
2015	51408	35209	5480