EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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ENCePP Secretariat

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

Report on ENCePP Activities in 2012

Executive Summary

Milestones

In 2012 a number of milestones were achieved towards the further development and consolidation of ENCePP.

Following expert peer review and taking account of the new pharmacovigilance legislation and good pharmacovigilance practices (GVP), the **1st revision of the ENCePP Guide on Methodological Standards in Pharmacoepidemiology** was completed in June 2012. The importance of the Guide is not only reflected in the fact that it is the most consulted and downloaded document on the ENCePP website (on average ~3000 hits/month), but that it has also been included as a reference document in the GVP Module VIII on post-authorisation safety studies (in effect July 2012).

In addition, GVP Module VIII also recommends that the **ENCePP Checklist for Study Protocols** be included as an annex to the protocol for post-authorisation studies. It therefore became necessary to align the Checklist with the provisions in the *Guidance for the format and content of the protocol of non-interventional post-authorisation safety studies*, and the resulting Revision 2 of the Checklist was adopted by the Steering Group in December 2012.

In July 2012 the ENCePP Steering Group (SG) adopted **revision 3 of the Plenary mandate** which now includes a statement that each ENCePP centre is expected to actively work on registering studies in the ENCePP E-Register. The new version of the mandate also includes a reference to the use of the ENCePP logo and a corresponding statement which ENCePP partners are encouraged to publish on their websites. All these measures relate to the promotion of ENCePP and its principles.

ENCePP continues to **input to developments in policy, legal and societal change that impact on non-interventional research**. In this context, during 2012 the network submitted a formal response to the EC public consultation on scientific information in the digital age, and responded to an EFPIA consultation on the scientific research agenda of the next generation bio-pharmaceutical research public-private partnership.

The **ENCePP Working Group on Health Technology Assessment (HTA)** was established in October 2012. The aim of the group is to lead and inform, where applicable, future activities of ENCePP in terms of HTA. Its mandate includes the development of guidance on study methodology to support health technology assessment taking account of existing guidance, including the ENCePP Guide on Methodological Standards in Pharmacoepidemiology.

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Following a presentation on the topic during one of its meetings the SG agreed that there was scope for developing further methodological guidance on assembling safety and benefit:risk data sufficiently quickly and comprehensively to inform regulatory decision making. For this purpose the **Drafting Group 'ENCePP Guide on Data Integration and Pooling of Studies'** was established in November 2012. The aim of the group is initially to perform an assessment of the current situation in terms of existing guidance and landmark papers, followed by the development of the guideline itself that will seek to address gaps in guidance where identified.

Aiming at further developing the **ENCePP Resources Database**, the online questionnaire for including a data source has been extensively streamlined and the website updated to facilitate registration of data sources. The number of data sources registered in the ENCePP Resources Database has risen to 28.

The ENCePP E-Register currently serves as the **EU-PAS Register** as specified in the GVP Module VIII. For the publically available register to continue to meet the requirements of academics, industry and regulators in terms of the ENCePP Study Seal and the added requirements of the GVP, a gap analysis of the current E-Register was conducted and the necessary updates to the current E-Register have been mapped. In parallel, discussions are ongoing with the WHO regarding inclusion of the E-Register/EU PAS Register in the International Clinical Trials Registry Platform (ICTRP).

Finally, following a round of consultation with the ENCePP Working Groups, the **ENCePP Work Plan 2013-2014** was adopted by the Steering Group in December 2012. The new work plan defines the objectives and milestones for the years 2013 and 2014 in the context of the operation and future development of the network, as well as the means of delivering results in a structured and timely manner. The agreed focus during 2013 and 2014 will be on optimisation of the network including continued capacity building and resource efficiency, and generating best evidence to support regulatory decision-making.

Meetings and Networking

The ENCePP Secretariat organised two ENCePP Plenary meetings in May and October, respectively, in the margins of which meetings of all three Working Groups took place. The Steering Group met four times in 2012. Minutes of the Plenary and Steering Group meetings are published on the ENCePP website. The inaugural meeting of the new HTA Working Group took place in the margins of the October plenary. The inaugural meeting of the Drafting Group on Data Integration took place by teleconference in December 2012.

With a view to continuing to exchange information and consider complementarity with similar international initiatives, representatives of the US FDA and Health Canada were invited to attend the ENCePP Plenary meetings. Furthermore, ENCePP was again represented at FDA Sentinel meetings during 2012.

To further enhance the ENCePP website and make it more user-friendly, a Google search function was integrated in the site.

In an effort to further promote the network, the European Medicines Agency funded a successful ENCePP booth at ICPE 2012 (International Conference on Pharmacoepidemiology and Therapeutic Risk Management) which took place during August in Barcelona.

The following article was published in the peer reviewed journal *Pharmacoepidemiology and Drug Safety* by ENCePP:

- Increasing scientific standards, independence and transparency in post-authorisation studies: the role of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (Blake KV et al. PDS 2012;21(7):690-696 - published July 2012)

In addition, the following articles published in 2012 referenced ENCePP:

- Should Preregistration of Epidemiologic Study Protocols Become Compulsory? (Lash, TL and Vandenbroucke JP. Epidemiology 2012;23:184-188 - published March 2012)
- Prospective Observational Studies to Assess Comparative Effectiveness: The ISPOR Good Research Practices Task Force Report (Berger, ML et al. Value in Health 2012;15:217-230 - published March 2012)
- Open Clinical Trial Data for All? A View from Regulators (Eichler, H-G et al. PLoS Med 2012;9(4):e1001202 - published April 2012)
- Why all Pharmacoepidemiology and Pharmacovigilance studies should be entered into ENCePP's electronic register of studies (Murray, ET and Maier WC. PRM 2012;12:8 - published August 2012)
- Making available observational study protocols and results: the role of ENCePP (on behalf of ENCePP - Letter to the Editor, Circulation: Cardiovascular Quality and Outcomes - published 4 September 2012)
- A Pathway to Improved Prospective Observational Post-Authorization Safety Studies (Kiri VA. Drug Saf 2012; 35 (9): 711-724 - published September 2012)

ENCePP Impact Evaluation

To emphasise the importance of the on-going analysis aimed at measuring the impact of ENCePP on current research practices and on regulatory activities, the ENCePP Steering Group revised its mandate to include a commitment to contribute to this task.

Quantitative Outcome Measures

As of December 2012, the number of centres and existing networks in the ENCePP Database stood at 115 (*99*) and 17 (*13*), respectively from 18 different European countries. The number of data sources stood at 28 (*20*). The figures in brackets and italics are the corresponding numbers as of end 2011. The characteristics of the 115 ENCePP centres registered in the database are described in figures 1 - 5. All of these figures demonstrate a continued important role of ENCePP in research capacity building across Europe.

Figure 1: Classification of centres

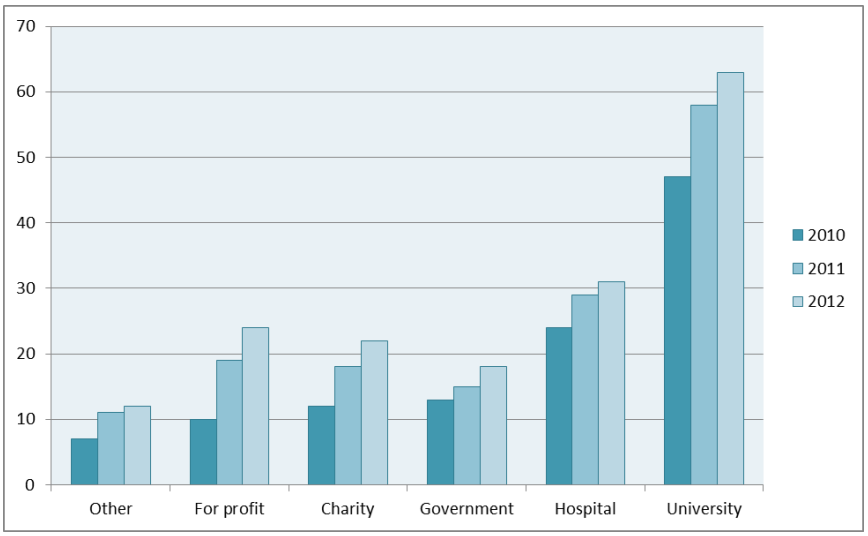


Figure 2: Expertise available in centres

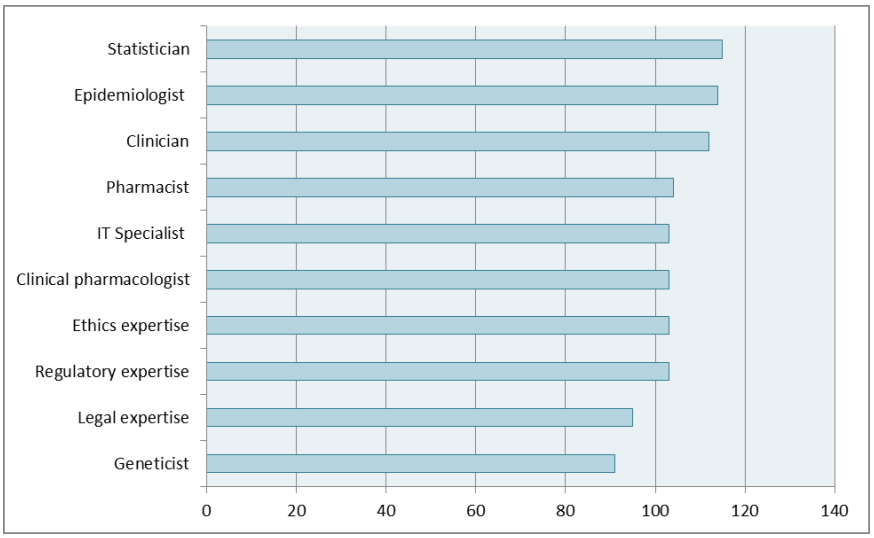


Figure 3: Experience with study designs

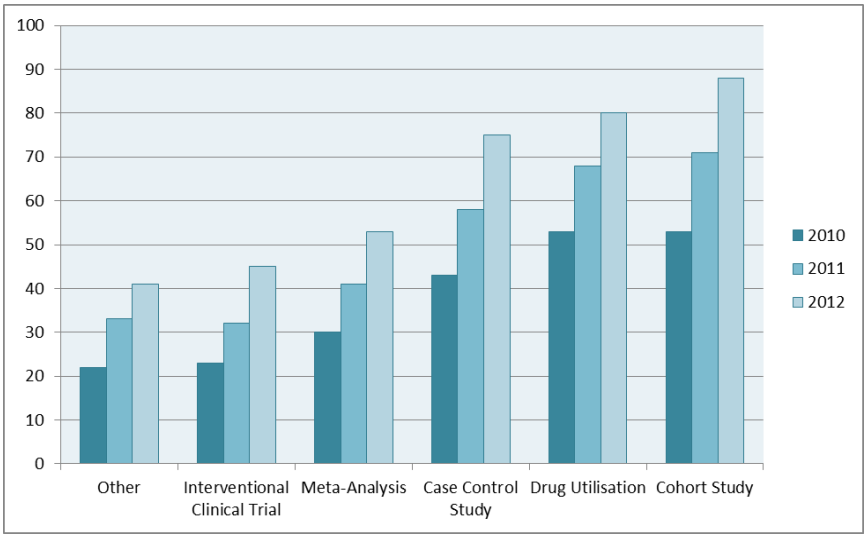


Figure 4: Experience in research collaboration

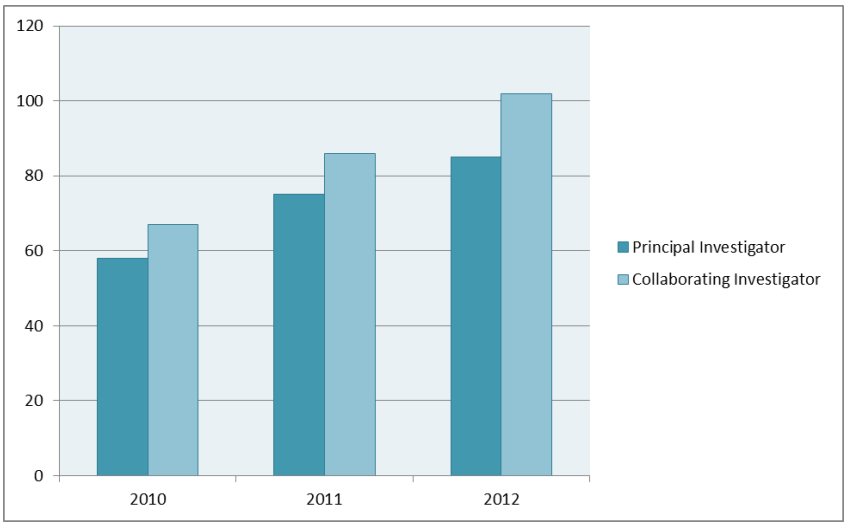


Figure 5: Research experience

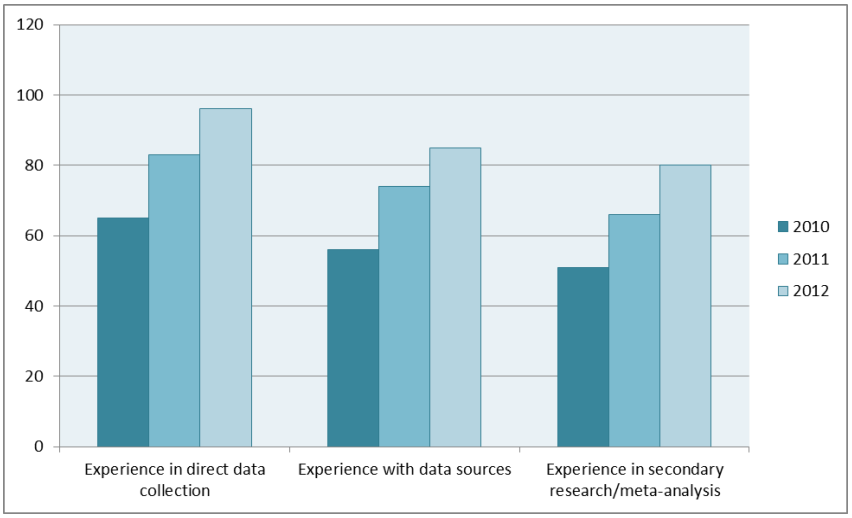
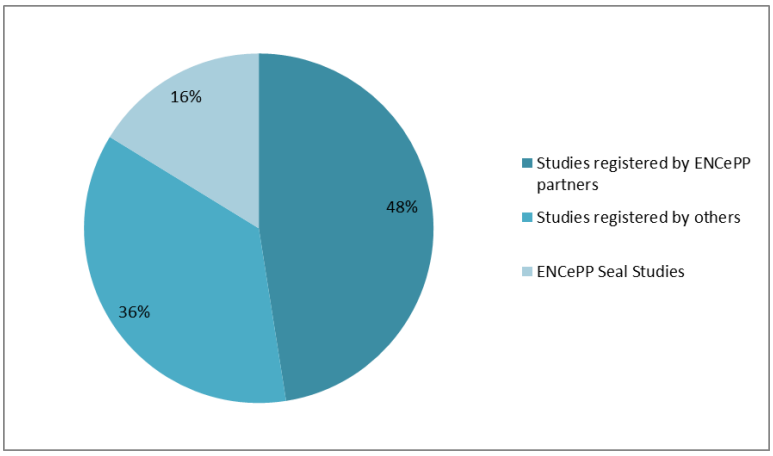


Figure 6: E-Register of Studies

The number of registrations in the ENCePP E-Register of Studies has risen significantly from 20 to 72 between January and December 2012, whereby 13 of these studies have been awarded the ENCePP Study Seal.

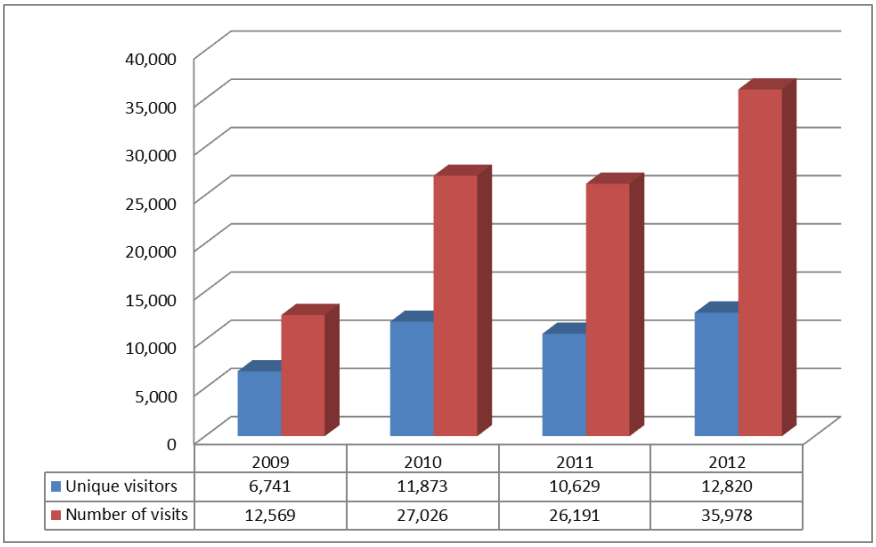


ENCePP Website statistics

The ENCePP website – hosted by the European Medicines Agency – is the network's interactive platform to maintain and promote ENCePP. It is used for official 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 *E-Register of Studies/EU PAS Register*. Both databases are readily accessible and searchable using pre-defined terms.

The following figures provide some statistics on the use of the website. Figure 7 includes EMA internal access. For figures 8 – 9 EMA access is excluded and for figure 10, EMA access is shown separate to external access.

Figure 7: Visitor statistics (2009-2012)



	2009	2010	2011	2012
Unique visitors	6,741	11,873	10,629	12,820
Number of visits	12,569	27,026	26,191	35,978

Figure 7 shows a reversal of the downward trend in visitors that was seen in 2011.

Figure 8: Pages viewed by country (2012)

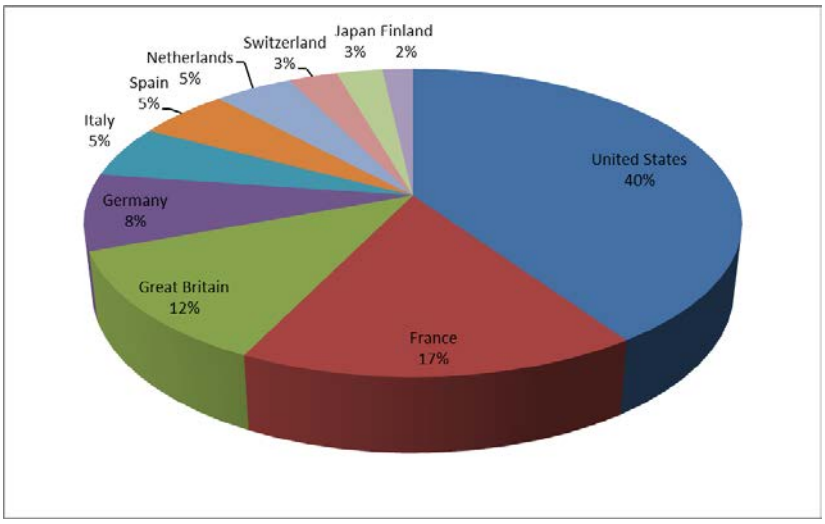


Figure 8 clearly shows global interest in ENCePP in particular from the United States and Japan.

Figure 9: Most downloaded documents (2012)

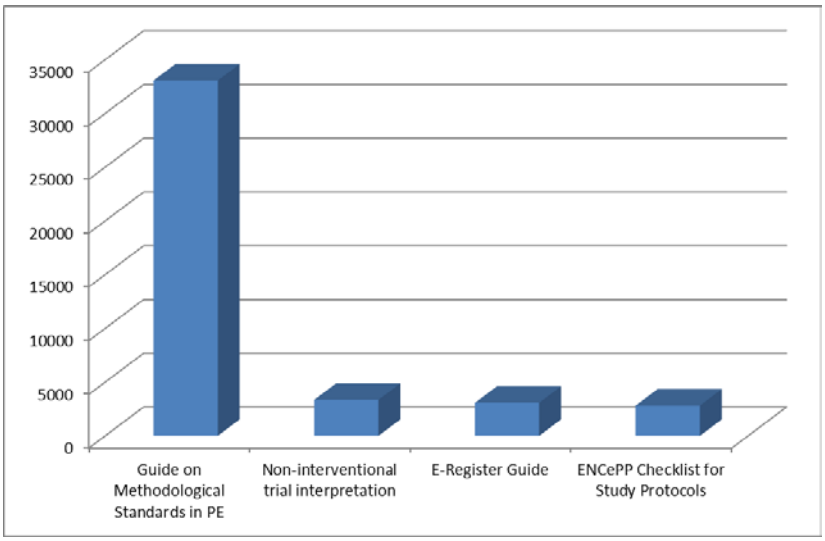
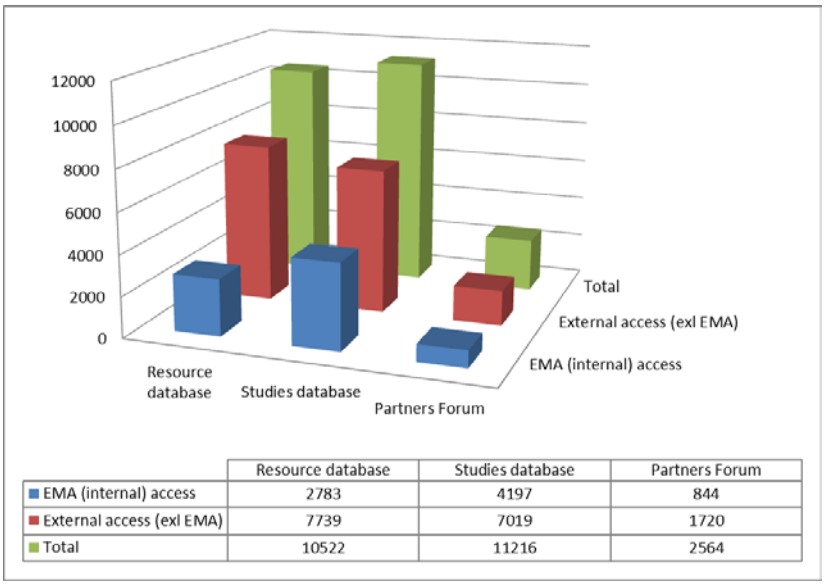


Figure 9 demonstrates the extensive interest in the Guide on Methodological Standards in Pharmacoepidemiology.

Figure 10: Hits on databases & partners' forum (2012)



	Resource database	Studies database	Partners Forum
EMA (internal) access	2783	4197	844
External access (exl EMA)	7739	7019	1720
Total	10522	11216	2564