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SCIENCE MEDICINES HEALTH

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ENCePP Secretariat

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

# ENCePP activity report 2013

## Executive summary & Impact evaluation

### Milestones

Whilst continuing to consolidate the Network as an important resource in pharmacovigilance and pharmacoepidemiology, the focus during 2013 -2014, as stated in the ENCePP work plan, is on optimisation of the Network, including continued capacity building, resource efficiency and supporting regulatory decision-making.

2013 saw the achievement of a number of milestones towards meeting these goals. A summary is provided in this document in the context of the ongoing impact evaluation of ENCePP in strengthening the benefit-risk evaluation of medicines across the European Union.

- The second annual review of the **ENCePP Guide of Methodological Standards in Pharmacoepidemiology** was completed in June 2013 and its latest version includes two new chapters on comparative effectiveness research and vaccine safety and effectiveness. This revision of the Guide has been published on the ENCePP website in a more user-friendly format as HMTL webpages which provide easy access to individual chapters. The Guide remains the most downloaded document on the ENCePP website with around 25,000 downloads in 2013.
- To explore further engagement in **dialogue with industry**, and in light of the relatively slow uptake of the ENCePP Study Seal by industry, a meeting between the ENCePP Steering Group and industry associations took place in May 2013. In line with this, the key discussions at the meeting related to exploring the means of stimulating/facilitating the uptake of the Network's outputs for industry to conduct methodologically robust post-authorisation studies in a transparent and scientifically independent manner. In preparation for the meeting a survey of industry associations was conducted to obtain feedback on the industry's awareness of ENCePP and the use of its outputs. The meeting resulted in some key findings to be further explored by the Steering Group.
- Following a successful session dedicated to 'special populations - pregnancy' at the plenary meeting in October 2012 - where delegates had expressed their interest in working together and sharing information (e.g. study plans, data, signal evaluation) on the **benefit:risk of medicines used in pregnancy** - a special interest group (SIG) on this subject within ENCePP has been established. The inaugural meeting of the SIG took place in the margins of the June 2013 plenary meeting and the group will work largely through virtual means.

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- One of the essential deliverables of the ENCePP Working Group on 'Data sources and multi-source studies' is the development of approaches to facilitate the conduct of multi-national studies in the context of the protection of individuals with regard to the processing of personal data. To progress the deliverable it was agreed to establish the current status regarding national requirements for data privacy among individual EU Member States. This has led to a **survey of EU Member States** which resulted in 13 individual responses. The consolidated report of the responses was published on the ENCePP website in July 2013.
- A virtual joint **Enpr-EMA / ENCePP working group on paediatric pharmacovigilance** was established in October 2013 and is due to take up its mandate in early 2014. Enpr-EMA - the European Network of Paediatric Research at the European Medicines Agency - is a network of research networks, investigators and centres with recognised expertise in performing clinical studies in children. The group will support the planned revision of the paediatric pharmacovigilance guideline.
- To inform ENCePP partners of the latest signals discussed by PRAC - thereby informing further data analysis and study - a link has been placed on the ENCePP website to the **listing of PRAC recommendations on safety signals** which is published monthly on the EMA website.
- One of the priorities of the Network is to use available expertise to build capacity, in particular to conduct collaborative multi-centre studies across the European Union, to increase the generalisability of the results. In this context, during 2013 the Network continued to **inform on drug-safety issues and support regulatory decision-making** in a number of ways, e.g.
    - through ENCePP partners' coordination of the majority of the European Commission Seventh Framework Programme (FP7) funded research consortia on drug safety;
    - with individual partners providing expertise in ad-hoc expert meetings on specific safety issues;
    - by providing relevant published and unpublished data in response to requests for information, and
    - by final study results feeding into formal regulatory procedures.
- A **new ENCePP Steering Group** (SG) was established following the election of the ENCePP representatives to the group at the plenary meeting in November 2013. The term of service of the new SG will be three years which is in line with the most recent revision of the SG mandate adopted earlier this year.

## Meetings and Networking

The ENCePP Secretariat organised two ENCePP Plenary meetings in June and November respectively, in the margins of which meetings of all five Working Groups took place. The Plenary meetings are key in obtaining feedback from the network on initiatives proposed by the Steering Group.

The Steering Group met four times in 2013, including a combined meeting with industry associations. Minutes of the Plenary and Steering Group meetings are published on the ENCePP website.

In the interest of transparency it has been agreed that in future progress reports from Working Group Chairs to the Steering Group would be published regularly on the ENCePP website.

The inaugural meeting of the new SIG 'Pregnancy' took place in the margins of the June Plenary, with a follow-up meeting in November (again, in the margins of the Plenary).

There has been ongoing exchange of information with other international initiatives with similar goals, e.g. representation of Health Canada and an observer from the Indian Council of Medical Research (ICMR) at ENCePP Plenary meetings, and ENCePP representation at US FDA Sentinel meetings. The ICMR is in the process of establishing a network of pharmacoepidemiological research in India and has expressed interest in collaborating with the ENCePP network.

The ISPOR conference (Dublin, October 2013) featured a workshop communicating on ENCePP and the HTA working group. The poster and presentations from the workshop have been published on the ENCePP website.

Information material on ENCePP was displayed in the EMA booth at US DIA in June 2013. Additionally, ENCePP presentations featured at Euro DIA (Amsterdam, March 2013), ICPE (Montreal, August 2013) and EACPT (Geneva, August 2013). An update on the Network was provided to the Pharmacovigilance Risk Assessment Committee (PRAC) in May 2013.

In November 2013 discussions took place with the European CRO Federation (EUCROF) to explore possible areas of collaboration. It was agreed that in the first instance the focus would be on the dissemination and promotion of ENCePP standards among EUCROF members.

## Qualitative measures of ENCePP Impact Evaluation

A number of articles in peer reviewed journals that were published in 2013 referenced ENCePP. The references ranged from citing that the study of interest had been awarded the ENCePP Study Seal and what this implied,[1] through to application of the ENCePP Code of Conduct in practice,[2] and ENCePP being a regulatory initiative towards more rigorous post-marketing surveillance.[3] Significantly, a study identified potential databases for the long-term safety evaluation of a particular medicine through a search of the ENCePP website.[4] Additionally, ENCePP guidance was cited in a number of regulatory,[5] [6] clinical[7] and pharmacoepidemiological[8] guidances. ENCePP in current practice is also cited in a number of industry and CRO publications.[9] [10]

[1] What are the immunological consequences of long-term use of biological therapies for juvenile idiopathic arthritis? (Swart JF, de Roock S, Wulffraat NM. Arthritis Research & Therapy 2013, 15:213 doi:10.1186/ar4213 - 24 May 2013)

[2] Tilson H, et al. Methodological challenges in monitoring new treatments for rare diseases: lessons from the cryopyrin-associated periodic syndrome registry. Orphanet Journal of Rare Diseases 2013, 8:139

[3] Breckenridge A, Eichler H-G. Towards a prevention model of health care. Nature Reviews – Drug Discovery 2013; 12:563-564 – published August 2013.

[4] Murray ML, Suppachai I, et al. An inventory of European data sources for the long-term safety evaluation of methylphenidate. Eur Child Adolesc Psychiatry. 2013; 22: 605–618. Published online 2013 March 19. doi: 10.1007/s00787-013-0386-x

[5] Introduction to Developing a Protocol for Observational Comparative Effectiveness Research: A User's Guide (Scott R. Smith, Ph.D. Agency for Healthcare Research and Quality (AHRQ) , Rockville, MD)

[6] Reference to ENCePP checklist and Guide under Background/Prior guidelines and guidance documents (p6), Guidance for Industry and FDA Staff "Best Practices for Conducting and Reporting Pharmacoepidemiologic Safety Studies Using Electronic Healthcare Data", May 2013

[7] Reference to ENCePP E-Register Studies Guide in EUCERD (EU Committee of Experts on rare Diseases) core recommendations on rare disease patient registration and data collection to the European Commission, Member States and all Stakeholders, June 2013

[8] International Society for Pharmacoepidemiology (ISPE) Statement on American Society of Clinical Oncology's New Policy for Relationships with Companies https://www.pharmacoepi.org/pub/B7FA6BE8-BFDF-EB39-2CC7-C54EAC1DD9B2

[9] Post-approval safety studies: an industry perspective of current EU climate (PRM Newsletter – Issue 13, January 2013)

[10] International Clinical trials: Priority PASS http://www.samedanltd.com/magazine/13/issue/191/article/3456

## Quantitative measures of ENCePP Impact Evaluation

The ENCePP Secretariat continues to monitor the impact of the Network on current research practices and on regulatory activities.

### *Quantitative Outcome Measures*

As of end December 2013, the number of centres and existing networks in the ENCePP Database stood at 129 (*115*) and 22 (*17*), respectively from 19 (*18*) different European countries. The number of data sources stood at 49 (*28*). The figures in brackets and italics are the corresponding numbers as of end 2012. The characteristics of the 129 ENCePP centres registered in the database are described in figures 1 - 5. These figures demonstrate the appeal of ENCePP and its important role in research capacity building across Europe.

**Figure 1: Classification of centres**

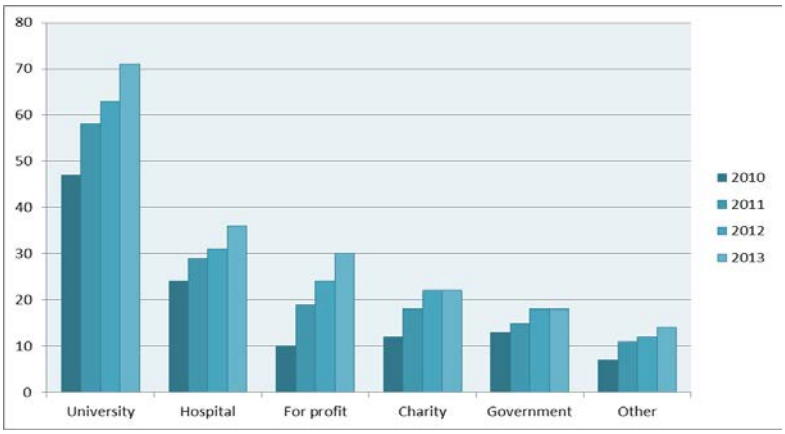



**Figure 2: Expertise available in centres**

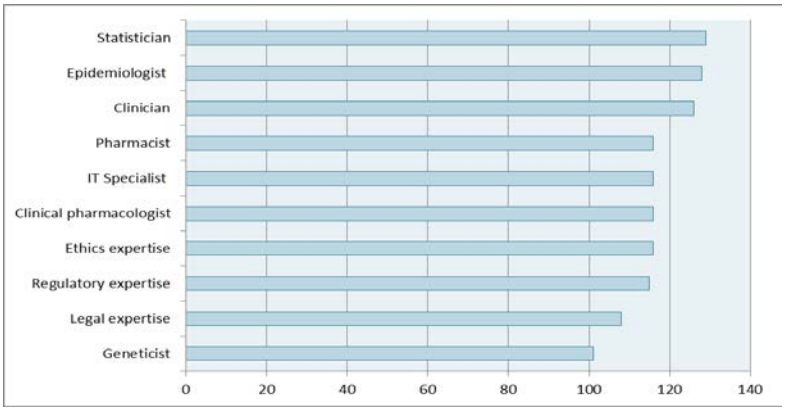



**Figure 3: Experience with study designs**

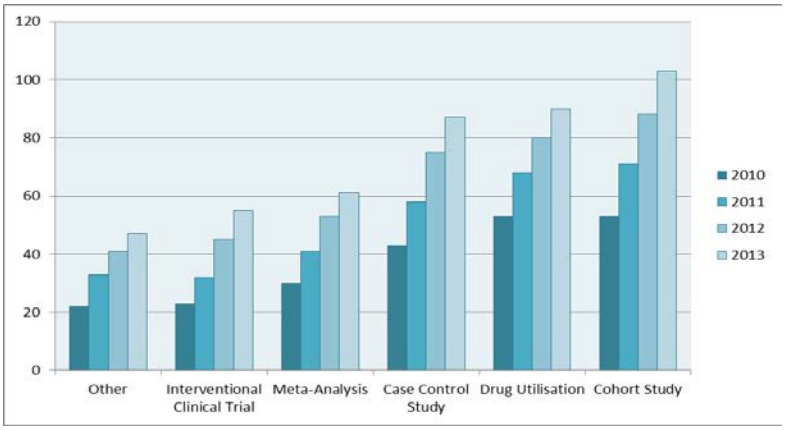


**Figure 4: Experience in therapeutic areas**

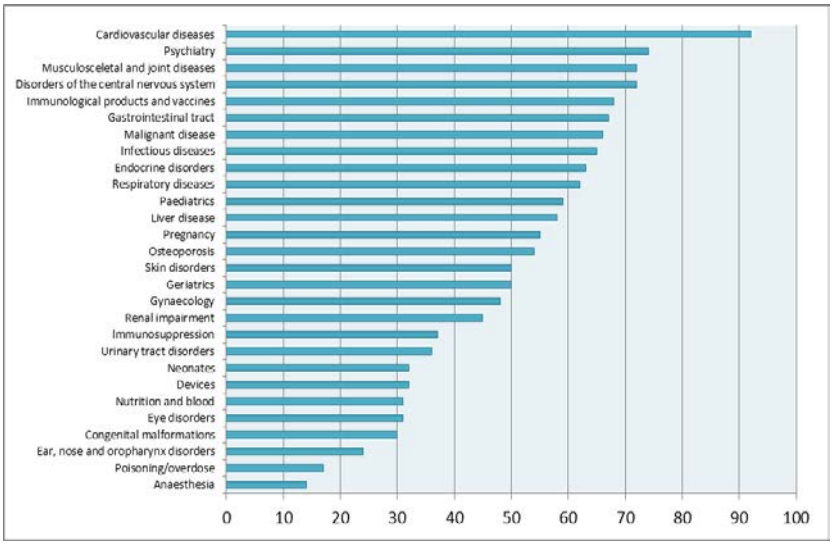



**Figure 5: Research experience**

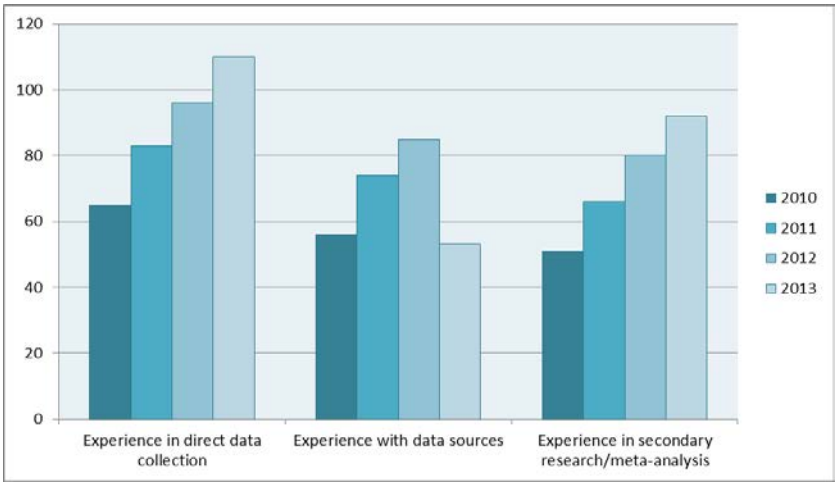
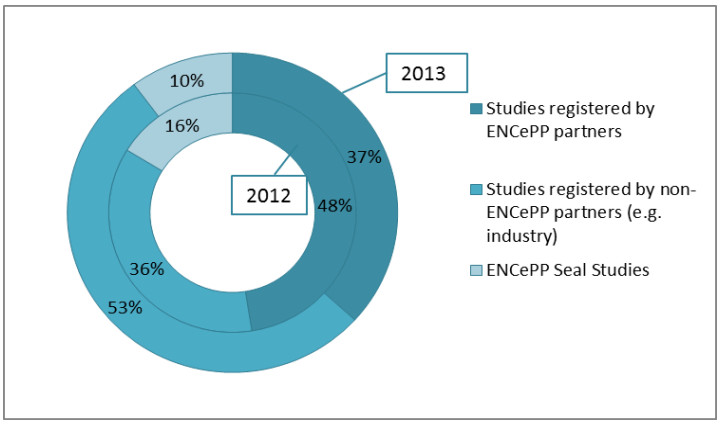
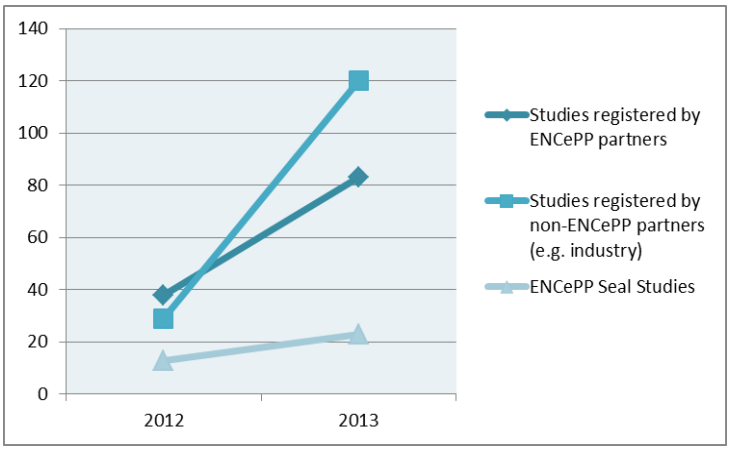



**Figure 6 & 7: E-Register of Studies / EU PAS Register**

The number of studies registered in the ENCePP E-Register of Studies has risen significantly from 72 to 203 between January and December 2013. A total of 23 of studies have the ENCePP Study Seal.

The sharp increase in study registrations (~180%) 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.4. However, there has also been a very substantial increase in the number of studies registered voluntarily by ENCePP partners.






## ENCePP Website statistics

The ENCePP website – hosted by the European Medicines Agency (EMA) – is the Network's interactive platform to maintain 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 *E-Register of Studies (de facto the 'EU PAS Register')*. Both databases are publicly accessible and searchable using pre-defined terms.

The number of visits to the ENCePP website continues to rise steadily. 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 2013 the ENCePP Secretariat dealt with a substantive number of queries (>150) relating to ENCePP in general or the EU PAS Register. 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 (2009-2013)**

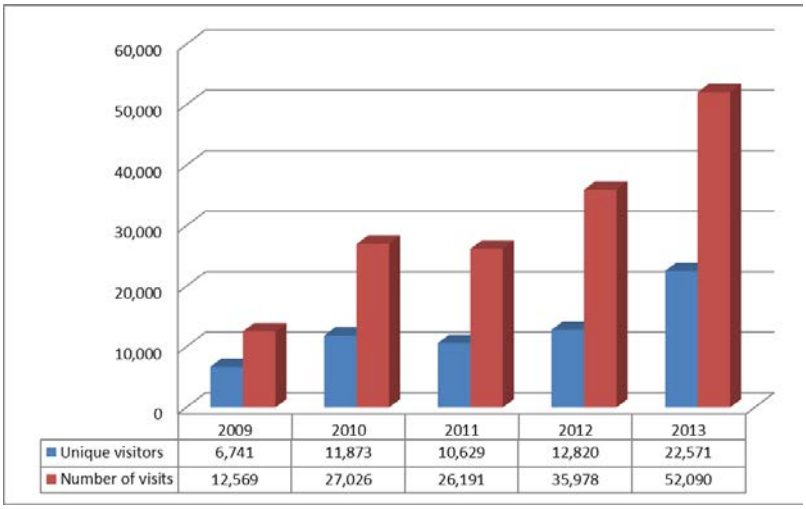



Figure 7 shows a continued upward trend in visitors since 2012.

**Figure 8: Pages viewed by country (2013)**

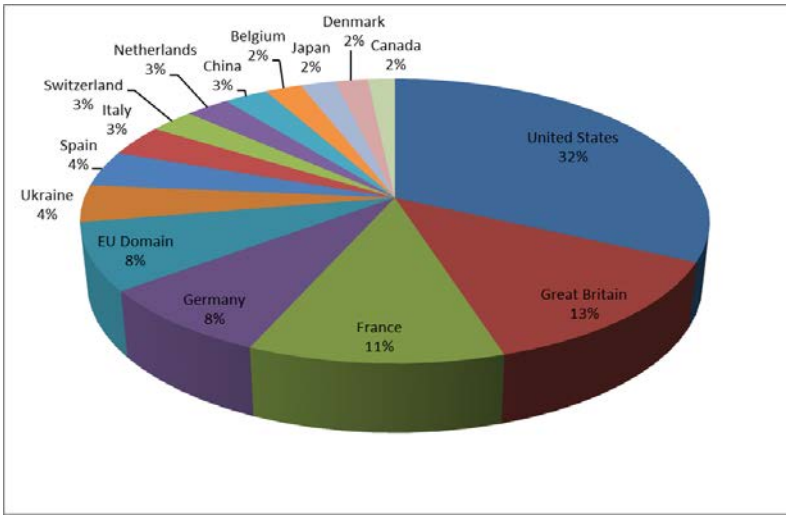



Figure 8 clearly shows global interest in ENCePP in particular from the United States.

**Figure 9: Most downloaded documents (2013)**

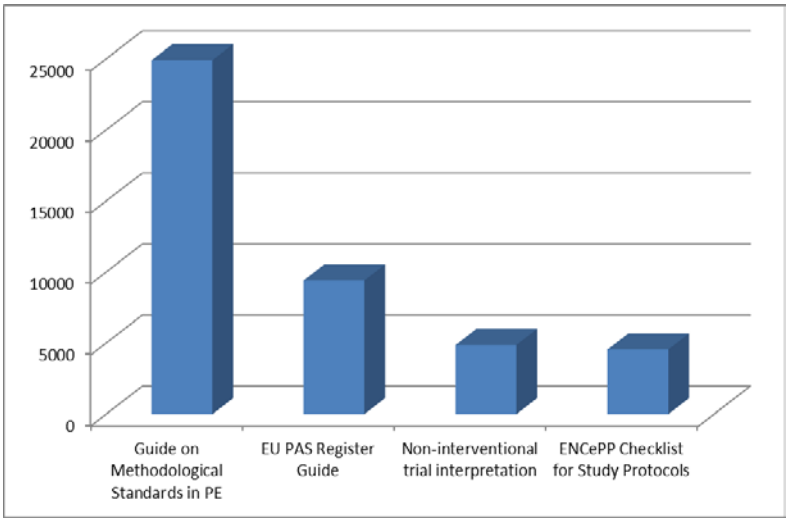



Figure 9 demonstrates the extensive interest in the Guide on Methodological Standards in Pharmacoepidemiology.

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