10 February 2017
EMA/799446/2016
ENCePP Secretariat

ENCePP Work Plan 2017-2019

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

Adopted by the ENCePP Steering Group on 10/02/2017

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1. Introduction

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP®) is a network coordinated by the European Medicines Agency (EMA). The members of this network (the ENCePP partners) are public institutions and contract and research organisations (CRO) involved in research in pharmacoepidemiology and pharmacovigilance. Research interests are not restricted to the safety of medicines but may include the benefits and risks of medicines, disease epidemiology and drug utilisation. Participation to ENCePP is voluntary.

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.

ENCePP provides a unique opportunity for collaboration to improve pharmacoepidemiological research and post-authorisation safety surveillance of medicinal products in Europe through access to a robust network of resources working in a transparent and independent manner and support to conduct joint studies. Individual centres and networks that are registered in ENCePP may be contacted directly or by submitting a request to the ENCePP Secretariat to place an announcement in the ENCePP partners forum.

Since its establishment ENCePP has produced a number of key outputs:

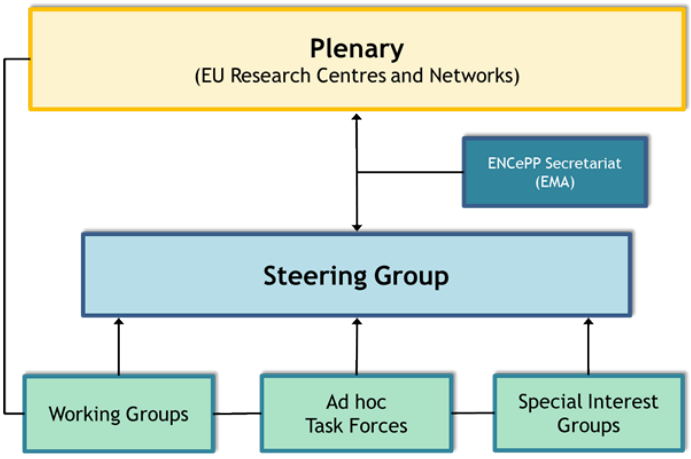
- ENCePP Database of Research Resources: a publicly accessible index of available European research resources
- ENCePP Code of Conduct: a set of rules and principles for pharmacoepidemiology and pharmacovigilance studies to promote transparency and scientific independence throughout the research process
- ENCePP Checklist for Study Protocols: a tool to promote the quality of studies
- ENCePP Guide on Methodological Standards in Pharmacoepidemiology: a resource for methodological guidance in pharmacoepidemiology

2. ENCePP Working Model

The working model of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance consists of the following elements:

- ENCePP Plenary: The totality of representatives from registered research centres and networks/collaborations; they meet once yearly at the European Medicines Agency (EMA)
- ENCePP Steering Group: The Steering Group oversees the network
- ENCePP Secretariat: Supports the operational and administrative work of the Steering Group; the Secretariat has been established by the European Medicines Agency

- Working groups: To operationalise the relevant expertise within ENCePP, there is a rolling programme of working groups and ad hoc task forces to which ENCePP partners contribute on a voluntary basis
- Special interest groups: ENCePP fosters the development of internal networks based around a shared interest in particular topics



3. Background and current status

The overall objective of the 2015-2016 work plan was the continued consolidation of the network as an important resource in the field of post-authorisation research on medicinal products, and the extension of the scope of ENCePP to support regulatory decision-making across the product life cycle.

Whilst progress has been made over the past two years, the objective of ENCePP delivering to the lifecycle of medicines has not yet been optimised and will remain an important focus over the next three years.

With this work plan the network is moving from currently two to a three year planning cycle which coincides with the mandate of the ENCePP Steering Group.

3.1. Overview of deliverables and milestones achieved from ENCePP Work Plan 2015-2016

Deliverable	Comment / Milestones achieved
Agency position on researcher's (not limited to ENCePP) sharing data prior to publication. Agency position on ENCePP researchers declaring any interests if (a) data and information submitted to EMA in the context of ongoing procedures, and (b) providing input directly to EMA on methodologies on substance-specific (single drug or class) post-authorisation studies to support regulatory decision-making.	• ENCePP draft concept paper endorsed by SG • ENCePP paper to feed into EMA general policy relating to interaction with researchers providing information in support of EMA's regulatory decision-making.

Deliverable	Comment / Milestones achieved
Review of available ENCePP resources in database (filter by speciality).	• Draft report from ENCePP Secretariat including sub-list of ENCePP data sources discussed with WG2, and taken into consideration in context of ongoing EMA mapping exercise of existing EU data sources.
Approach to validating impact of results from methodology research projects using PROTECT as an example.	• Presentation of 'lessons learned from PROTECT on common protocols for multi-database studies' at ENCePP plenary 2015, and follow-up discussions at SG level.
Input to EMA strategy on registries (on standard protocols, data fields, governance).	• Presentations to Plenary November 2015; draft strategy published on EMA website.
Input to EMA guidance on special populations, including paediatrics and pregnancy.	• Adoption of revised mandate of *joint ENCePP-ENprEMA working group*, including contribution to the revision of the new module of GVP on paediatric pharmacovigilance. • Review of data sources for drug safety in pregnancy research and publication of revised version on ENCePP website (June 2016).
Methodological input to PRAC strategy on measuring impact of PhV activities	• SG Agreement to set up new ENCePP Special Interest Group (SIG) on *Measuring the Impact of Pharmacovigilance Activities* (December 2015). • Call for expressions of interest sent to ENCePP partners (January 2016). • SIG mandate and work plan adopted by SG; mandate published on ENCePP website (July 2016).
Revision of Q&A clarifying the issues identified in the 2014 ENCePP survey.	• Revision of Q&A adopted by SG. • Update of ENCePP website in line with revisions (January 2016).
Business case for upgrade of functionality of E-Register/EU PAS Register.	• Agreement on prioritisation of requirements for EU PAS Register upgrade. • First phase of EU PAS Register upgrade released in July 2016.
Establish a business case for upgrade of functionality of ENCePP Resources Database.	• Prioritised business requirements defined and endorsed by SG.
Stand-alone guidance on data integration from completed observational studies of safety of medicines.	• SG agreement to include guidance as an Annex to Methods Guide, rather than keeping it a stand-alone document. Public consultation not considered necessary, given the status as

Deliverable	Comment / Milestones achieved
	Annex to Methods Guide and the ongoing review of the Guide. • Annex I to Methods Guide adopted by SG and published on ENCePP website (December 2015).
Revision of ENCePP Guide on Methodological Standards in Pharmacoepidemiology including possible new chapters on special populations/topics.	• Rev.4 of Methods Guide published on 6 July 2015. • Rev.5 of Methods Guide published on 12 July 2016, including a new chapter on using data from social media and electronic devices as a data source. • Publication of third revision of the ENCePP Checklist for Study Protocols (July 2016).
Define a Communication Plan in line with the agreed 2014 communication priorities.	• Key messages for communication on ENCePP adopted by SG on 16/12/2015. • Publication of key messages and standard slide set on ENCePP website; circulation of key messages and slides to all ENCePP partners (January 2016).

The following deliverables from the work plan 2015-2016 have been carried over to the new work plan:

- Recommendation on methods of measuring effectiveness of PhV activities
- Third party funding mechanism for PAS, including potential governance models
- Recommendations for strategy on pregnancy research, including funding
- Improved functionality of ENCePP Resources Database and EU PAS Register
- Gap analysis of existing guidance documents in relation to efficacy and effectiveness, in particular taking account of new guidance on PAES

3.2. Other achievements 2015-2016

- Organisation of annual plenary meetings:
    - 24 November 2015
    - 22 November 2016
- Dissolution of dedicated working group on HTA, and integration of three of its members into working group *Research Standards and Guidances;* revision of the group's mandate to include reference to HTA.
- Re-branding of ENCePP E-Register of Studies to EU PAS Register.
- Election of a new ENCePP Steering Group for the 2017-2019 term.

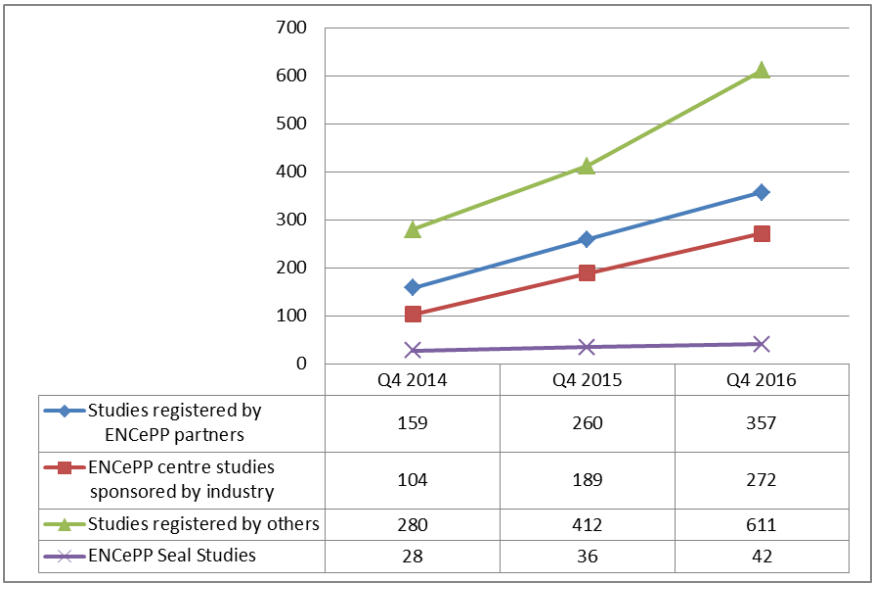
3.3. Number of research resources in ENCePP database (2015-2016)

Numbers as of 31/12/2016:

1. Centres: 164
2. Networks: 25
3. Data source: 53

3.4. Number of studies in EU PAS Register (2015-2016)

Figure 1: Number of studies registered (totals as of 31/12/2016)



	Q4 2014	Q4 2015	Q4 2016
Studies registered by ENCePP partners	159	260	357
ENCePP centre studies sponsored by industry	104	189	272
Studies registered by others	280	412	611
ENCePP Seal Studies	28	36	42

Figure 2: ENCePP Seal Studies *(as of 31/12/2016)*

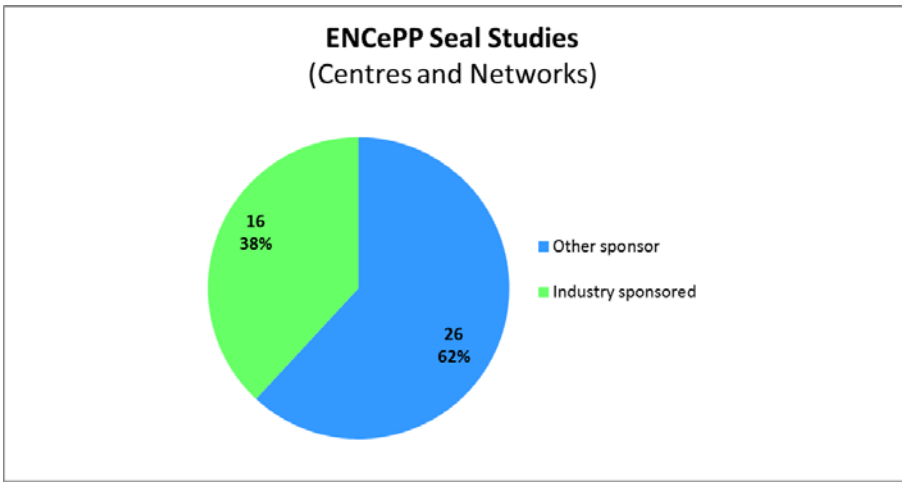
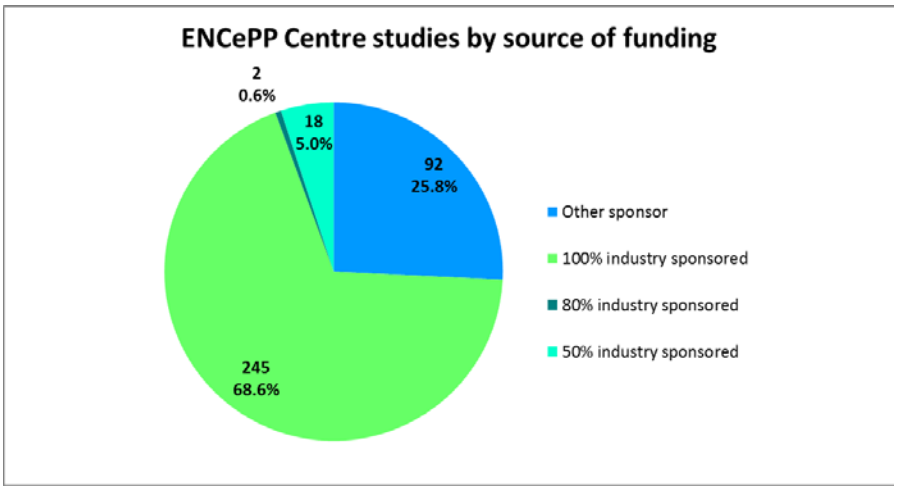


Figure 3: Studies registered by ENCePP partners by source of funding *(as of 31/12/2016)*



4. Main goal and objectives of the 2017-2019 work plan

The main goal during 2017 to 2019 will be to optimise the network's input to regulatory decision-making throughout the product life-cycle.

Particular focus will be on the development of methods in impact research and to identify enablers and barriers to measuring the impact of pharmacovigilance.

4.1. Key objectives

- ENCePP delivering to the lifecycle of medicines
- Develop methods for modelling health outcomes of pharmacovigilance activities for impact measurement
- Support capacity for evaluating medicine safety in pregnancy
- Explore additional models for good governance of PhEpi research
- Address methodological aspects of the generation of evidence-based information supporting the needs of regulatory and HTA decision-making
- Optimise functionality and utility of the ENCePP resources database and EU PAS Register
- Implement ENCePP Communications Plan

4.2. International activities

FDA, Health Canada and PMDA will be invited as observers to the annual plenary meetings. Discussions and exchanges with international partners will be organised as appropriate.

5. Resources and possible constraints

The delivery of this ENCePP work plan is dependent on the EMA ENCePP budget for each of the years 2017 to 2019. This budget will cover, *inter-alia*, ENCePP Plenary, Steering Group, Working Group (WG) and Special Interest Group (SIG) meetings.

The achievement of the key deliverables described above requires continued voluntary collaboration within ENCePP, including the exchange of information and knowledge. The Agency shall continue to coordinate the network through the provision of a Secretariat and maintaining ENCePP databases.

The ENCePP Secretariat will ensure timely flow of information and organise the activities of the network, including meetings.

The current ENCePP WGs and SIGs will work according to their agree mandates and prioritised activities. The ENCePP Secretariat, Senior Agency staff and SG sponsors will support the WGs and SIGs and will, together with the respective Chairs, ensure adequate progress. The WGs and SIGs will meet regularly by teleconference or the Agency's interactive meeting tool AdobeConnect®, in line with work plan deliverables. Subject to the availability of necessary funds, at least one annual face to face meeting per group will be organised. Which members are invited to face-to-face meetings will depend on responsibilities and deliverables assigned within the working group.

A list of current working groups, special interest groups and their mandates may be consulted on the ENCePP website.

The ENCePP Steering Group will meet face to face (at least twice per year) or virtually on an ad hoc basis as needed to oversee the delivery of the outcomes of the various groups.

6. Action plan

See attached table of deliverables.

7. Deliverables – ENCePP Work Plan 2017-2019

Objective	Deliverable	Lead	SG sponsor	Milestones	Deadline
ENCePP delivering to the lifecycle of medicines	ENCePP input to regulatory decision-making throughout the product life-cycle.	SG	Tom MacDonald	• ENCePP review of draft EMA Strategy on Real World Evidence • Peer review by WG3 of EU/EEA data sources for longitudinal patient-based studies • Consultation with ISPE on need to revise *ISPE Guidelines for good database selection and use in pharmacoepidemiology research* • Revised ENCePP mandate for adoption	Q2 2017 Q2 2017 Q3 2017 Q4 2017
Develop methods for modelling health outcomes of pharmacovigilance activities for impact measurement	Review of studies on risk minimisation effectiveness to determine health impact of pharmacovigilance activities. This review should also include selected examples from scientific literature.	SIG Impact	Marieke de Bruin Teresa Herdeiro	• Draft report for SG consultation • Final report for SG endorsement	Q2 2017 Q3 2017
	Recommendations on methods of measuring effectiveness of pharmacovigilance activities.	SIG Impact	Marieke de Bruin Teresa Herdeiro	• Draft report to SG • Consultation of ENCePP network	Q3 2017 Q1 2018

Objective	Deliverable	Lead	SG sponsor	Milestones	Deadline
Support capacity for evaluating medicine safety in pregnancy	Recommendations for strategy on pregnancy research, including funding.	SIG Pregnancy	Corinne de Vries	• Draft appendix to the Methods Guide with methodological aspects (high-level) specific to this area of research • Review and update of *Overview of data sources for drug safety in pregnancy research* • Input into EMA pregnancy strategy and GVP special populations (III): medicines in pregnancy and breastfeeding • Develop proposed mechanisms for research infrastructure & funding	Q2 2017 Q3 12017 Q4 2017 Q2 2018
Explore additional models for good governance of PhEpi research	Third party funding mechanism for PAS.	EMA/SG	Tom MacDonald Xavier Kurz	• Draft paper on potential governance models • Consult ENCePP and stakeholders on potential governance models • Deliver possible models for joint studies, including options of trustee administered industry funding	Q2 2017 Q3 2017 Q1 2018
	Strengthen the Code with additional tools to support good governance of pharmacoepidemiological research.	WG2	Rosa Gini	• Review and amend the Code as needed taking into account other initiatives (e.g. ADVANCE)	Q2 2018

Objective	Deliverable	Lead	SG sponsor	Milestones	Deadline
Address methodological aspects of the generation of evidence-based information supporting the needs of regulatory and HTA decision-making	Gap analysis of existing guidance documents in relation to efficacy and effectiveness, in particular taking account of new guidance on PAES.	WG1	Olaf Klungel	• Gap analysis completed & report to SG	Q3 2017
	Recommendations on methods for benefit/risk integration in *ENCePP Guide on Methodological Standards in Pharmacoepidemiology*	WG1	Hans Hillege	• Recommendation to SG	Q2 2018
	Revision of *ENCePP Guide on Methodological Standards in Pharmacoepidemiology* including possible new chapters on special population/topics.	WG1	Olaf Klungel Vera Ehrenstein Rosa Gini	• Publication of annual revision	Q3 2017
	Revision of the *ENCePP Checklist for Study Protocols.*	WG1	Olaf Klungel	• Publication of revised checklist	Q3 2018
	If needed, revision of *Guidelines for good database selection and use in pharmacoepidemiology research*, in collaboration with ISPE.	WG1	Olaf Klungel	• Report to SG on need to revise the Guidelines • Publication of revised Guidelines (as needed)	Q1 2017 Q1 2018

Objective	Deliverable	Lead	SG sponsor	Milestones	Deadline
	Development of checklist to support data custodians in self-assessing their database in comparison with *ISPE Guidelines for good database selection and use in pharmacoepidemiology research*	WG1	Olaf Klungel	• Draft to SG • Publication of checklist	Q4 2017
	Input into relevant aspects of the EMA Patient Registries initiative.	WG1	Xavier Kurz	• Review of action points arising from Registries workshop • Review of methodological guideline for registries • Input into inventory of registries and quality criteria (if applicable)	Q1 2017 Q4 2017 Q4 2017
	Input to EMA guidance on special populations.	Joint WG EnprEMA-ENCePP	Xavier Kurz	• Revision of the new module of the *Good pharmacovigilance practices (GVP) on paediatric pharmacovigilance*	Q2 2017
Optimise functionality and utility of the ENCePP resources database and EU	Improved functionality of the ENCePP resources database and EU PAS Register.	WG2	Gianluca Trifiro	• 2nd wave upgrade of EU PAS Register according to prioritised business requirements • Release of technical upgrade of ENCePP resources database based on defined business requirements endorsed by SG	Subject to technical feasibility and EMA IT budget

Objective	Deliverable	Lead	SG sponsor	Milestones	Deadline
PAS Register	Increase study registration and status of the EU PAS Register.	WG2	Gianluca Trifiro	• Publication on EU PAS Register • Communication with ISPE to increase awareness of EU PAS Register	Q4 2017
	Increase routine surveillance of registrations and compliance follow-up.	EMA	Rosa Gini	• Agree process with SG	Q4 2017
Implement ENCePP Communications Plan	Evaluation of achievements of 10 years of ENCePP (2007 to 2017).	EMA/SG	Tom MacDonald (S. Perez-Gutthann)	• 10 year anniversary publication: impact of ENCePP to date • Anniversary Plenary 2017 • Publication of revised '*key messages for communication on ENCePP*'	Q2 2017 Q4 2017 Q1 2018
	Strengthen tools of communication with ENCePP partners	EMA/SG	Tom MacDonald	• Draft proposal to SG	Q4 2017