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ENCePP Secretariat

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

ENCePP Work Plan 2013 - 2014

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

Adopted by the ENCePP Steering Group on 18/12/2012

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance is a scientific network coordinated by the European Medicines Agency (EMA) and developed in collaboration with European experts in the fields of pharmacoepidemiology and pharmacovigilance. Its goal is to further strengthen the post-authorisation monitoring of medicinal products in Europe by facilitating the conduct of multi-centre, independent, quality research focusing on safety and on benefit:risk. This is achieved by optimising the use of available expertise and research experience across Europe.

The ENCePP Work Plan organises the activities of the network including those of the Secretariat, the Steering Group and Working Groups, in line with the overall goal of ENCePP and taking account of EMA Work Programmes, the European Risk Management Strategy and the EMA Roadmap to 2015.

The present ENCePP Work Plan defines the objectives and milestones for the years 2013 - 14 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.

1. Background and current status

In 2011 and 2012 a number of milestones were achieved towards the further development and consolidation of ENCePP.

Overview of deliverables and milestones achieved from ENCePP Work Plan 2011-2012:

Deliverable	Comment / Milestones achieved
Review of the 'ENCePP Code of Conduct' as agreed by the Steering Group in May 2010	• 2nd revision of the Code of Conduct completed (November 2011), including o implementation guidance for sharing ENCePP

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Deliverable	Comment / Milestones achieved
	study data (Annex 4 of the Code), o inclusion of specific provisions for publicly funded studies, and o development of a researcher Declaration of Interest form for ENCePP studies (Annex 5 of the Code) • Inclusion of Code of Conduct as a reference document in the GVP Module VIII on post-authorisation safety studies (July 2012).
Review of the 'Checklist of Methodological Standards for ENCePP Study Protocols'.	• 1st revision of Checklist completed including renaming to: 'ENCePP Checklist for Study Protocols' to reflect broader application (August 2011). • Inclusion of Checklist as a reference document in the GVP Module VIII on post-authorisation safety studies (July 2012). • Recommendation in GVP Module VIII that a completed ENCePP Checklist for Study Protocols should be included as an annex to the protocol for post-authorisation studies (July 2012). • 2nd revision of Checklist to align with the provisions in the '*Guidance for the format and content of the protocol of non-interventional post-authorisation safety studies*' (December 2012)
Publication and dissemination of a Guide on Methodological Standards in Pharmacoepidemiology.	• The ENCePP Guide on Methodological Standards in Pharmacoepidemiology published following a public consultation (May 2011). • 1st Revision completed (June 2012), including further expert peer review and taking account of the new pharmacovigilance legislation and good pharmacovigilance practices (GVP). • Inclusion of Guide as a reference document in the GVP Module VIII on post-authorisation safety studies.
Exploration of the merits of developing an accreditation system and its features.	• On-going discussions in WG1 on a proposal to include national accreditation information in the ENCePP resource database.
Further development of the ENCePP Resources Database and of the E-Register of Studies, including: - overview of post-authorisation safety studies, - interaction with HTA bodies, and - exploring collaboration with EnprEMA, the paediatric medicines network.	• The ENCePP E-Register will serve as the EU-PAS Register specified in the GVP. A corresponding gap analysis has been conducted. • On-going liaison with WHO regarding inclusion of the E-Register/EU PAS Register in the ICTRP. • Discussions ongoing between ENCePP and EUnetHTA relating to linking their respective databases. • EUnetHTA attendance at ENCePP Plenary meetings. • An ENCePP Working Group on HTA has been established to inform, where applicable, future activities of ENCePP in terms of health technology assessment, particularly study methodologies (November 2012). • Steering Group agreement on reciprocity and

Deliverable	Comment / Milestones achieved
	cooperation with EnprEMA (February 2011). EnprEMA invited to all ENCePP meetings.
To liaise with medical journals editors on the aims of ENCePP as regards independency and transparency in research and to increase the visibility of the network to the broader scientific community.	• Discussion paper presented to Steering Group meeting (Feb 2011). • 1st ENCePP Workshop for Medical Journal Editors organised (June 2011). • On-going efforts to align the ENCePP/EU PAS register of studies with WHO ICTRP and thereby ICJME requirements.
To develop approaches to facilitate the conduct of multi-national studies in light of existing differences in data privacy laws across the EU, in collaboration with Working Group 3.	• Submission of ENCePP response to public consultation on the European Commission's (EC) strategy to strengthen EU data protection rules (January 2011) • Follow-up meeting with DG Justice of the European Commission (April 2011). • Parallel surveys of Member States via the PhVWP and ENCePP partners on national requirements for data protection conducted (May 2012).
Establish a strategy to be used in an on-going impact analysis aimed at measuring the impact of ENCePP on current research practices and on regulatory activities.	• Adoption by SG of concept paper for the impact evaluation of ENCePP (May 2011). • Revision of Steering Group mandate to include reference to impact assessment (Q2 2012). • Quantitative outcomes measures published in the ENCePP 2011 annual report. • Further impact assessment in ENCePP 2012 annual report.
To further define the role of ENCePP as regards its interaction with regulatory decision-making and in light of the changes introduced by the new Pharmacovigilance legislation.	• 9 FP7-funded consortia in ENCePP • 6 EMA-funded studies conducted by ENCePP partners • Number of research resources and studies registered in ENCePP database (see table on page 5)
To ensure that the ENCePP Studies database feeds in, as appropriate, to any international discussions on standardisation of data fields.	• Business requirements identified in terms of WHO/ICTRP standardisation and the implementation of GVP. • ENCePP requirements provided to HL7. • Presented to SG (September 2012)
To elaborate an ENCePP consensus statement on the definition/interpretation of the definition of non-interventional study.	• ENCePP response to the public consultation on the EC concept paper on the revision of the 'Clinical Trials Directive' 2001/20/EC submitted (May 2011) and published on EC website (June 2011). • ENCePP position paper on the interpretation of the definition of non-interventional trials under the current legislative framework ("Clinical Trials Directive" 2001/20/EC) published on ENCePP website (November 2011).
Ensure visibility of the network through promotional events, including participation in international conferences, symposia.	• 2nd "DIA/EMA ENCePP Information Day" held (November 2011). • Presentations at: o ISPE mid-year meeting, Florence (April 2011) o NICE Technical Forum, Manchester (June

Deliverable	Comment / Milestones achieved
	2011) o Post-Approval Summit, Zurich (September 2011) o EUReMS meeting, Barcelona (May2012) o DIA HTA Forum, Amsterdam (September2012) o DIA Clinical Forum, The Hague (October2012) • ENCePP symposia at: o PharmSciFair, Prague (June 2011). o DIA Euro Meeting, Geneva (March 2011). o ICPE, Chicago (August 2011). • ENCePP information booth at: o ICPE, Barcelona (August 2012)
2 Plenary meetings each year	• Plenary meetings held: o 30 June 2011 o 23 November 2011 o 3 May 2012 o 11 October 2012
Continue contact with international initiatives with complementary objectives to exchange information and consider complementarity with their respective initiatives.	• Ongoing participation of FDA and Health Canada in ENCePP Plenary meetings including trilateral meetings in margins of plenary. • ENCePP represented at FDA Sentinel meetings in 2011 & 2012.

Other Achievements 2011-2012:

- Election of a new ENCePP Steering Group for the 2012-2013 term.
- The ENCePP E-Register of studies becoming the EU-PAS Register, which will meet the requirements of academics, industry and regulators in terms of the ENCePP Study Seal and the registration and transparency requirements from the new PV legislation/GVP. The necessary updates to the current E-Register have been mapped.
- Formal response to EC public consultation on scientific information in the digital age.
- Response to EFPIA consultation of ENCePP on the scientific research agenda of the next generation bio-pharmaceutical research public private partnership.
- Use of ENCePP logo and corresponding statement which ENCePP partners are encouraged to publish on their websites.
- The Plenary meeting mandate amended to include a statement that each ENCePP centre is expected to actively work on registering studies in the ENCePP/EU PAS register.
- Review and update of the on-line questionnaire to facilitate registration of data sources in the Resources Database. This has contributed to a significant increase in the number of data sources registered.
- Enhancement of ENCePP website:
  - ➢ Q&A Section

- Policy on links to other websites
- 'Notice Board' section
- Process to facilitate interaction between ENCePP and third parties (including industry) through the ENCePP partners' forum
- Integration of Google search function

- Publication of articles in peer reviewed journals:
  - *European Medicines Agency review of post-authorisation studies with implications for the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance*, PeDS, October 2011
  - *The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance: application to diabetes and vascular disease*, BJDVD, December 2011
  - *Increasing scientific standards, independence and transparency in post-authorisation studies: the role of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance*, PeDS, April 2012

- Number of **research resources** in ENCePP database:

	Q1 2011	***Q4 2012***[1]
Centres	79	115
Networks	12	17
Data Sources	11	27
Total Resources	*102*	*159*

- Number of **studies** in E-Register of Studies:

ENCePP Seal Studies	3	13 (13)
Other Studies	6	54 (25)
Total Studies	*9*	*67 (38)*

(Figures in brackets represent the number of studies registered by ENCePP centres)

2. Main goal and objectives of the 2013 – 2014 Work Plan

Whilst continuing to consolidate the network as an important resource in the field of pharmacovigilance and pharmacoepidemiology, the focus during 2013 and 2014 will be on optimisation of the network including continued capacity building and resource efficiency, feeding studies into regulatory decision-making.

Additionally, during this work plan period, work will continue to reinforce the network on health outcomes research (including studies on post-authorisation benefit-risk and on effectiveness of risk minimisation, and studies to support health technology assessment). This will further embed ENCePP as a key service provider for data and information for regulatory and health-care decision-making.

[1] As of 19 December 2012

Key deliverables:

- Management of the transition to the new pharmacovigilance legislation and Guideline on good pharmacovigilance practices (GVP), including:
  - optimising ENCePP support to EMA Committees in terms of providing evidence to support regulatory decision-making,
  - Review of CoRe ENCePP documents.
- Promotion of the ENCePP Study Seal concept to increase uptake, including by the ENCePP community and the pharmaceutical industry.
- Encouraging public registration of non-interventional studies.
- Development of a stand-alone *ENCePP Guide on Data Integration and Pooling of Studies.*
- Map current practice for multi-source (two or more) pharmacoepidemiology studies, including methodological approaches.
- Develop an impact analysis of national data privacy legislation on the conduct of multi-national (two or more Member States) pharmacoepidemiology studies.
- Continued input to developments in policy, legal and societal change that impact on research, including network responses to public or other consultations.
- Keeping up to date with the revision of EU data protection rules with expert input to legal rules or guidance considered relevant to the ENCePP mandate.
- Develop guidance on study methodology to support health technology assessment.
- Development of ad-hoc special interest groups, including on methodologies and on special populations (e.g. paediatric, the elderly, pregnant women) based on suggestions from the ENCePP community.
- Further investigate potential for cooperation with other sources of healthcare data.
- On-going impact analysis of ENCePP on current research practices and on regulatory activities.
- Promotion of ENCePP and its principles, including participation in international conferences, symposia.

3. Resources and possible constraints

The delivery of this ENCePP work plan is dependent on the EMA ENCePP budget for each of the years 2013 and 2014. The budget for 2013 has been confirmed as in line with that of 2012. This budget will cover, *inter-alia*, ENCePP Plenary, Steering Group and Working Group 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 continue to ensure timely flow of information and organise the activities of the network, including meetings.

The current ENCePP Working Groups will work according to their agreed mandates and prioritised activities. Senior Agency staff and SG members will serve as EMA Lead and SG Sponsors respectively to the Working Groups and will, together with the respective Working Group Chairs,

ensure adequate progress. In addition to the Working Groups a Drafting Group (*Guidance on Data Integration and Pooling of Studies*) and a new ad-hoc Working Group (*Health Technology Assessment*) have been established in Q4 2012. Both groups will meet regularly by teleconference and when possible, face to face meetings will be organised around the ENCePP plenaries.

The ENCePP SG will meet face to face or virtually on a regular basis (at least quarterly) to oversee the delivery of the outcomes of the various groups.

4. Action plan

See attached table of key deliverables.

KEY DELIVERABLE	WORKING GROUP	EMA LEAD	MILESTONES	INITIAL DEADLINE(S)
Managing the transition to the new pharmacovigilance legislation and Guideline on good pharmacovigilance practices (GVP), including review of CoRe ENCePP documents and supporting regulatory decision making with best evidence.	WG1	X. Kurz	Publish 2nd revision of Checklist for Study Protocols.	Q1 2013
	WG2	T. Goedecke	Establishing a link on ENCePP website to safety signals.	Q1 2013
	WG1	X. Kurz	2nd revision of Guide on Methodological Standards including a section on vaccines and expansion on efficacy methods.	Q2 2013
	WG2	T. Goedecke	3rd revision of the Code of Conduct.	Q3 2014
	Steering Group	K. Blake	Annual review of ENCePP support to EMA Committees in terms of providing evidence to support regulatory decision-making.	Q4 2013
Promotion of the ENCePP Study Seal concept to increase uptake, including by the ENCePP community and the pharmaceutical industry.	WG2	T. Goedecke	Maintain a list(s) of ENCePP centres indicating the number of ENCePP registered studies and of seal applications per centre and the numbers of each sponsored by an MAH.	Ongoing
	WG2	T. Goedecke	Survey of ENCePP centres regarding uptake of the seal. Results to be taken into account for the next revision of the Code of Conduct.	Q2 2013
	Steering Group	H. Fitt	Meeting with representatives of industry associations.	Q2 2013
	WG1	X. Kurz	Report on exploration of the merits of developing an accreditation system and its methodologies	Q4 2013
	n/a	T. Goedecke	Organisation of ENCePP Information Day taking account of suggestions from industry associations.	Q4 2013
	WG1	X. Kurz	Identify training needs for the implementation of the ENCePP standards.	Q1 2014
	WG2	T. Goedecke	Finalising action plan to better monitor/verify compliance of ENCePP studies with the Code.	Q4 2014
Encouraging public registration of non-interventional studies.	Steering Group	K. Blake	Discuss and agree the level of involvement of non-EU research centres and networks in ENCePP.	Q2 2013
	WG2	T. Goedecke	Liaison with medical journal editors including submission of material for publication and possibly a follow-up workshop with journal editors.	Q3 2013

KEY DELIVERABLE	WORKING GROUP	EMA LEAD	MILESTONES	INITIAL DEADLINE(S)
Development of a stand-alone *ENCePP Guide on Data Integration and Pooling of Studies*.	Drafting Group	K. Blake J. Slattery X. Kurz	Consolidate the membership and scope of the Drafting Group established Q4 2012.	Q1 2013
			Deliver scope document including proposal for expertise to be involved.	Q1 2013
			The Drafting Group to compile and review existing guidances.	Q4 2013
			Finalise and publish a guidance document following expert peer review.	Q4 2014
Map current practice for multi-source (two or more) pharmacoepidemiology studies, including methodological approaches.	WG3	K. Blake	Describe current practice based on 2012 survey of EMA/EC funded research.	Q2 2013
			Develop and maintain a list of current practice via published research conducted by ENCePP partners.	Q4 2013
Develop an impact analysis of national data privacy legislation on the conduct of multi-national (two or more Member States) pharmacoepidemiology studies.	WG3	K. Blake V. Newbould A. Spina	Consolidate information received in response to May 2012 PhVWP and ENCePP surveys on data privacy.	Q1 2013
			Draft reflection paper relating national data privacy requirements to pharmacoepidemiology research in practice.	Q3 2013
			Publication and dissemination of reflection paper on impact of data privacy on conduct of pharmacoepidemiology research in the EU.	Q2 2014
Continued input to developments in policy, legal and societal change that impact on research, including network responses to public or other consultations.	Steering Group	K. Blake	Monitor developments and liaise with external organisations including ISPE/ISoP/FDA/Pharmaceutical Industry/EC/IMI to respond to issues as they arise.	Ongoing
Keeping up to date with the revision of EU data protection rules with expert input to legal rules or guidance considered relevant	WG3	K. Blake A. Spina	Follow the progress of the revision of the EU data protection rules.	Ongoing
			Once revised rules adopted, analyse implications for ENCePP.	Q2 2014 (tbc)
			If appropriate, contribute to any implementing technical guidelines.	Q4 2014 (tbc)

KEY DELIVERABLE	WORKING GROUP	EMA LEAD	MILESTONES	INITIAL DEADLINE(S)
to the ENCePP mandate.				
Develop guidance to further inform on health technology assessment methodologies.	WG HTA	L. Prieto	Consolidate the scope of the ENCePP HTA Working Group established Q4 2012.	Q1 2013
			Draft a concept paper on methodological guidance to support HTA taking account of existing ENCePP guidance on pharmacoepidemiology.	Q3 2013
			Finalisation of HTA methodological guidance on studies to support HTA and medicines regulation.	Q4 2014
Development of virtual ad-hoc special interest groups (e.g. paediatric, the elderly, pregnant women, drug utilisation) based on suggestions from the ENCePP community.	ad hoc SIG	T. Goedecke	Establishment of a special interest group on drug safety in pregnancy as a pilot.	Q2 2013
			Develop other groups in light of experience with pregnancy group and proposals from ENCePP.	Ongoing
Further investigate potential for cooperation with other sources of healthcare data.	Steering Group	K. Blake	To liaise with other organisations under the instruction of the SG and taking account of legal/societal factors.	Ongoing
On-going impact analysis of ENCePP on current research practices and on regulatory activities.	Steering Group	K. Blake	Quantitative measures relating to resources in ENCePP and capacity building.	Q4 2013 (Annual report)
			Qualitative outcome measures using multiple sources (e.g. results included in EMA committees assessment report, citations in literature, feedback from the ENCePP community and the pharmaceutical industry).	Q4 2013 (Annual report)
Promotion of ENCePP and its principles, including participation in international conferences, symposia.	n/a	H. Fitt	Journal articles published on ENCePP. Minimum of 4 conferences/symposia.	Ongoing