



4 March 2010  
EMA/113497/2010

## Minutes of Inaugural Meeting of the ENCePP Steering Group

19 February 2010 –chaired by Peter Arlett

### List of Participants

Present:	Peter Arlett (PA), Stella Blackburn (SB), Corinne de Vries (CdV), Hans-Georg Eichler (HGE), Henry Fitt (HF), Joan-Ramon Laporte (JRL), Hubert Leufkens (HL – <i>partly, via TC</i> ), Jytte Lyngvig (JL), Nicholas Moore (NM), Yola Moride (YM), Ingemar Persson (IP), June Munro Raine (JMR), Valerie Simmons (VS), Miriam Sturkenboom (MS), Giuseppe Traversa (GT)  <i>ENCePP Secretariat:</i> Stefanie Prilla (SP), Dagmar Vogl (DV), Eeva Rossi (ER)
Apologies:	David Haerry

### Agenda

1	<b>Adoption of draft agenda</b>
2	<b>Tour de Table</b>
3	<b>Declaration of Conflict of Interest</b>
4	<b>Organisational &amp; administrative issues</b> 4.1 Mandate of Steering Group – roles & responsibilities, meetings, etc. 4.2 Election of SG Vice Chair 4.3 Meeting Plan 2010
5	<b>Brief update on current status of ENCePP</b> 5.1 Activities/issues of Working Groups 5.2 Database of Research Resources 5.3 Registry of PEpi & PV studies
6	<b>ENCePP Code of Conduct and Checklist of Methodological Research Standards</b> 6.1 Results of Public Consultation: Discussion on implementation of comments
7	<b>Future direction of ENCePP - Agreement on long-term priorities</b>
8	<b>Work Plan 2010:</b> 8.1 Discussion of draft Work Plan 2010 8.2 Review of WG priorities for future activities



Agenda	
	8.2.1 Need for a new Working Group or amendments of mandate(s)? 8.3. ENCePP/EFPIA Info Day – discussion on agenda
9	<b>General discussion/ Issues raised by ENCePP partners</b> 9.1 Data privacy and protection 9.2 Repository of Col
10	<b>Summary of discussions &amp; next steps</b>
11	<b>A.O.B</b>

## 1. Adoption of draft agenda

The draft agenda was adopted without changes.

## 2. Tour de Table

PA welcomed all participants to this inaugural meeting of the ENCePP Steering Group (SG) where the main task would be to take stock of the current situation and decide on the future direction of ENCePP.

The welcome was followed by a tour de table during which all participants briefly introduced themselves.

## 3. Declaration of Conflict of Interest

HF gave a short overview on “Conflicts of Interest and Confidentiality”, a standard practice for all experts involved in European Medicines Agency (the Agency / EMA) activities, and also a requirement for all ENCePP SG members, as noted in the [SG mandate](#).

The presentation was followed by a discussion on what should be considered confidential or not. PA confirmed that – as set down in the SG mandate – by default everything is considered confidential, unless mentioned otherwise. Some members of the SG voiced the concern that the default confidentiality might affect the reporting back to the organisation which they represent and emphasised that maximum transparency towards the network and the general public should be strived for. The latter was supported by all SG members and PA confirmed that it is the role of the SG to report back to their communities and all ENCePP centres. It was highlighted that the minutes of the SG meeting and supporting documents will be made available to all participants in ENCePP on the ENCePP webpage. It was agreed that at the end of each meeting, the chair should summarise which information/documents are to be considered confidential.

## 4. Organisational and administrative issues

### 4.1. Mandate of Steering Group

SP gave a short [presentation](#) to summarise the roles and responsibilities of the SG members and the SG's rules of procedure.

Further to previous discussions on transparency and confidentiality, it was decided to run with the present default confidentiality clause for the time being. Should major problems arise, the issue could be revisited at a later stage.

JMR reiterated that a good flow of information is an important issue to those SG members who represent a constituency, and for which a consistent way should be found. PA confirmed that this is an important discussion which will be addressed at a future meeting in 2010.

#### **4.2. Election of SG Vice Chair**

This item was postponed until after lunch to give eligible SG members an opportunity to reflect on whether they wish to put themselves forward as candidates. JRL mentioned whether the SG should see the declarations of interest before considering who to vote for as Vice-Chair. HF stated that they were as yet not available.

**Post-meeting note:** The declarations of interest of all nominated experts have been received and will be made available to all ENCePP SG members.

Ingemar Persson was unanimously elected as Vice-Chair.

#### **4.3. Meeting Plan 2010**

ER presented a [meeting plan](#), based on the results from the availability polls circulated earlier this year. The meeting plan includes a second face-to-face meeting in May 2010, and two virtual (Vitero) meetings later in the year.

JRL pointed out that there is a potential clash with a meeting scheduled to take place on 21 & 22 May in Slovakia which would potentially involve many participants in ENCePP. It was agreed that HF would contact the organiser (Prof. Milan Kriška) to find out more information.

**Post-meeting note:** Prof. Milan Kriška confirmed that the meeting on 21 & 22 May will go ahead. Therefore, the SG meeting on the 21<sup>st</sup> was re-scheduled and taking into account the availability of SG members will now take place on 7 May.

JL suggested that the time of 15.00-17.00 for a Vitero meeting is not very convenient for participants based in Central Europe. The ENCePP Secretariat will look into bringing the meeting time forward by an hour; however, Vitero meetings have to take place in the afternoon to enable participation of a member located in Canada.

**Post-meeting note:** The Vitero meeting taking place on 16 September has been rescheduled to 14.00-16.00 to make it more convenient for participants based in Central Europe.

### **5. Update on current status of ENCePP**

SP updated the group on ongoing activities and issues concerning the individual [ENCePP Working Groups](#).

In this context, **Working Group 1: ENCePP Research Standards and Guidances** was highlighted as the most active at present. Its major task is the development of the inventory of PE guidelines and the development of a guide on methodological research standards. The guide should be based on existing guidances and only provide new guidance for areas where no or insufficient guidance is available. The WG had agreed to avoid unnecessary repetition or duplication of efforts. Eventually, the guide should be published online and it should be possible to make reference to the guide. Currently, the main sections of the guide have been identified and a call for authors has been sent out.

The SG took major interest in the work of WG 1 and decided to follow it closely. The majority of SG members expressed the concern that the proposal could potentially be a repeat of guidance already in existence, rather than filling existing gaps. It was highlighted that the guidance should have a place in

the concept of ENCePP studies, and that there is a need to further discuss at SG level the best way to do so, including issues relating to ownership and applicability.

SB confirmed that the guide should be an overarching document that points to the different guidance documents already in existence. Updates of the actual guidance documents would be the responsibility of the actual owner; a respective disclaimer should be included in the ENCePP guide. SP confirmed that it is intended to undergo public consultation and therefore all organisations possibly affected would have a chance to comment.

As for **Working Group 2: Independence and Transparency**, SP indicated that the Code of Conduct will be discussed under agenda point 6. HF gave a brief update on the current status of the registry of studies whose data fields have been developed through discussions of subgroup 2 ("Registry of Studies") of WG2. He informed the Steering Group that the project had stalled slightly because of questions relating to the registry's interaction with the EUDRACT clinical trials database. Extensive internal discussions have taken place and IT developers have started looking into how to best establish the database. The WHO trial registration data set and other relevant databases are also being looked at in this context. It is hoped that the registry will become available mid year 2010. A template for a study synopsis has been made available by JRL which is taken into consideration as an appendix to the database.

JRL highlighted that the "clinicaltrials.gov" database includes more than 14,000 observational studies. A possible overlap should be further discussed.

JRL informed the group that there have been efforts by other organisations including journal editors regarding the promotion and practicalities of registration of observational studies. In summary, the journal editors are in favour of registration of observational studies in a similar way to clinical trials.

**Post-meeting note:** JRL provided links to relevant documents:

- ECETOC Workshop report (24-25 Sept, London): available at [http://members.ecetoc.org/Documents/Document/20100108131222-WR\\_18.pdf](http://members.ecetoc.org/Documents/Document/20100108131222-WR_18.pdf)
- BMJ Editorial *Registration of observational studies* (E. Loder, T. Groves, and D. MacAuley, 2010; 340:375-6): available at <http://www.bmj.com>.

During the following discussion it was agreed that it would be very helpful to start a dialogue between ENCePP and journal editors to maximise the registry's usefulness and to explore their view on issues such as publication of the full protocol, data protection and ethical issues. To this end it was agreed to take further the contacts already established by NM with ICMJE.

**Post-meeting note:** NM provided a copy of his correspondence with the ICMJE Secretariat on Conflicts of Interests to the ENCePP Secretariat.

The main output of **Working Group 3: Inventory of EU data sources and methodological approaches for multi-source studies** during 2009 was the development of a data entry form for available data sources in Europe. SP confirmed that the registry of data sources will be available with the 2<sup>nd</sup> release of the research resources database at the end of Q1 of this year. MS highlighted the importance of a working link between centres/networks and data sources.

SB gave a short update on the work of **Working Group 4: Inventory of PhV and PhEpi research centres in ENCePP** whose main output in 2009 was the development of the data entry form for research centres and networks to join ENCePP. Version 1.0 of the database of centres and networks was released in January 2010 and, although the deadline for registration is April 2010, centres are urged to register as soon as possible. SP concluded this part of the presentation by explaining the features of the current version of the resources database and the plans for the 2<sup>nd</sup> release.

During the discussions, HL and JRL raised the issue of interaction between regulators, academics and ENCePP in relation to studies requested by regulators or with a potential regulatory impact. The

processes and ways to facilitate exchange between the aforementioned parties should be discussed by the SG (to be included as an agenda item for the next SG meeting).

## **6. ENCePP Code of Conduct and Checklist of Methodological Research Standards (MRS)**

SP presented on the results of the public consultation on the ENCePP Code of Conduct and Checklist of MRS. A large number of comments have been received and in order to deal with the material in the most efficient way, an internal review group has been established to look at the comments. As the workload is high it is envisaged that the review won't be finalised for a few months yet.

During this initial review a small number of strategic issues have emerged for which a steer from the SG is being sought.

An extensive discussion ensued on the concept of ENCePP partnership and the level of endorsement of the Code of Conduct. PA reiterated that ENCePP is an all-inclusive network; this is already laid down in adopted documents like the SG mandate, the Plenary mandate and the core values of the ENCePP study document. He said that ENCePP is a network to build capacity particularly in Europe for the conduct of high quality and transparent studies where the Plenary is open to any interested party that fulfils the criteria of participation in ENCePP, with decision being made at the level of the SG.

He reminded everybody that ENCePP studies are an absolutely essential part of the concept of the network. As a matter of priority, all necessary measures would have to be put in place to start producing ENCePP studies. Other important topics such as the possible accreditation of centres were decided to be postponed for discussion at a future SG meeting.

In response to PA's question on the view of the pharmaceutical industry, VS confirmed that there is a high interest and general agreement with the principles of ENCePP, the Code and the concept of ENCePP studies. However, there is also the need for more clarity on certain aspects, e.g. as regards the interface between the clinical trials directive and the provisions of the Code and concrete implications when deciding to follow the Code. It was clarified that there should be no ambiguity and that it should be possible to apply both existing law and the Code at the same time. In addition, the terminology used in the Code should be simplified in that it should only provide for studies outside the scope/concept of ENCePP and ENCePP studies, but no longer "studies performed in accordance with the Code".

The SG discussed the possible impact of contradictory results from ENCePP studies versus studies performed outside of ENCePP. Currently, it is not mandatory for centres in the ENCePP Inventory to perform only ENCePP studies. It will be important to look into performance markers to measure the value of the ENCePP study concept.

The following decisions were taken in relation to issues arising from the public consultation:

### **Code of Conduct**

#### **Issue 1:** Scope of ENCePP Studies

The current amended wording was approved. Though, in principle the scope should be inclusive, it was highlighted that different rules and standards apply to studies on pharmacoconomics and the Checklist of Methodological Research Standards would not apply. This should be fed back to WG 1 to further explore what work should be done relating to methodological aspects in this area.

Issue 2: Investigators from pharmaceutical industry - What is the ENCePP position on conduct of studies by industry?

It was confirmed that companies that do not fulfil the criteria for the Inventory of research centres and networks, i.e. provision of service to others and main focus on pharmacoepidemiology and pharmacovigilance research, cannot become part of ENCePP. Industry is not a service provider whilst CROs are. Therefore, studies conducted solely by a company would not meet the 'ENCEPP study' criteria. This should be communicated more clearly. VS highlighted that the exclusion of Industry studies could be perceived as downgrading the quality of these studies though potentially conducted by highly qualified researchers. To address this concern, it was proposed to invite EFPIA to present a proposal about the interface of industry research and ENCePP at a future SG meeting.

Issue 3: Publication of study protocol - Discussion of pros and cons of full transparency vs. publication of protocol synopsis.

Following an extensive discussion on the pros (full transparency and scrutiny) and cons (intellectual property right/copyright) of publishing the full protocol before the study start the majority of SG members decided that the Code should require investigators to publish a synopsis giving sufficiently detailed information before the study start. At the same time – i.e. before study start - the full protocol should be provided to the EMA to be released for public scrutiny only once the study is completed. The publication of the full protocol before study start or at any point during the conduct of the study should be optional.

The synopsis should follow ICH requirements, i.e. be a list of minimum required information in a standardised format.

Issue 4: Availability of data and results - Need to further specify disclosure of study data and publication of results.

There are a number of factors to be taken into account including licences for studies with existing data, embargo policies of some journals, intellectual property of data and possibility of fraud and lack of reproducibility. The SG agreed that the requirement to make available all non-identifiable study data might be unreasonable and anyway is a rather vague requirement. It was proposed to implement the concept of an audit trail in addition to require making available the analytical data set. Details on excluding certain data should be provided. As a second step the meaning of the term 'study data' should be defined accordingly. Furthermore, it was agreed that the concept of audit and inspection will be discussed at a future meeting.

Issue 5: Scope of Code.

The SG agreed that the existing text should not be changed.

Issue 6: Network partnership criteria.

The SG agreed that the development at some type of accreditation for centres in ENCePP should be explored; however, this should be done at a later point in time.

Issue 7: Study auditing and assessment - Feasibility of validation and monitoring of ENCePP studies.

The SG agreed that this should not be included in the Code. Policing of compliance with the provisions of the Code might be envisioned in the future.

## **MRS Checklist**

Issue 1: Follow up of incomplete protocols.

There will not be a follow-up at this point in time. However, the issue of enforcement or policing function of ENCePP vis-à-vis a self declaration code should be considered in future discussions.

Once all comments have been reviewed, a final version of the documents will be put to the respective WGs for review and then put forward to the SG for adoption. PA emphasized that the decisions of the SG should be considered final and discussions should not be re-opened in the WGs. The finalisation of the Code and the MRS checklist are prerequisites for the launch of the first ENCePP studies. The aim is to adopt the final version of the Code at the SG meeting in May 2010. To facilitate the proposed timeline, an additional Vitero meeting will be organised during March or April to address remaining issues of the present agenda and further issues coming up during the review of the comments received.

JL proposed to include a firm revision date for both documents which was agreed by the group.

YM suggested including a performance measure on the process itself.

## **7. Future Direction of ENCePP**

PA initiated a short brainstorming session encouraging SG members to come up with topics for future discussion by the Steering Group.

The following topics were raised:

- New Pharmacovigilance legislation as the scope of Pharmacovigilance has been widened, including also meta analysis etc.
- Evaluation of added value of the ENCePP study concept compared to the added bureaucratic burden (performance measures); measures of success of ENCePP; quality evaluation & assurance
- Funding of academic research / independent studies
- Audit / appeal / policing
- Multiple analysis
- Regulatory interface
- Outreach / dissemination to other stakeholders
- Repository of Conflict of Interest declaration
- Quality of studies: basis for better decision-making
- Dialogue with medical journals
- Accreditation of centres
- Strategy – safety issues in Europe: Explore in a pilot phase how ENCePP can react to a particular problem
- Peer review
- Publication / communication of ENCePP output
- Data privacy & protection

## **8. Work Plan 2010**

### **8.1. Discussion of draft Work Plan 2010**

Due to time pressure this item was only discussed very briefly. PA explained that the main deliverables of the current draft work plan were those that had not been achieved in the ambitious 2009 work plan and have therefore been carried over. The work plan would be reviewed in detail at the next SG meeting, but was adopted in principle.

SB very briefly explained the concept behind the EMA debate planned to take place in August 2010 during the ICPE in Brighton. The concept paper will be circulated to the SG.

### **8.2. Review of WG priorities for future activities**

Due to time pressure, this agenda item was postponed for discussion at the next SG meeting.

### **8.3. ENCePP Info Day**

HF briefly explained the concept of the ENCePP Info Day, chiefly aimed at industry and initially planned to take place end of June 2010.

#### **Post-meeting note:**

The date has been postponed to October 2010 due to time constraints.

The concept of this outreach meeting to promote ENCePP studies was agreed by the SG.

## **9. General discussion / Issues raised by ENCePP Partners**

Due to time pressure, this agenda item was postponed for discussion at the next SG meeting.

## **10. Summary of Discussions & Next Steps**

*Ad 4.2 Election of SG Vice Chair:*

At this point of the meeting, Ingemar Persson was proposed as Vice Chair; this proposal was unanimously endorsed by the SG.

PA concluded the meeting by thanking everyone for their active attendance. The minutes of the meeting will be circulated and made public as soon as possible.

#### **Action Points arising from the discussions:**

- HF to contact Prof. Milan Kriška to find out more information on the proposed meeting in May 2010 (see post-meeting note in chapter 4.3).
- ENCePP Secretariat to look into bringing forward the timing of the proposed Vitero meeting in September 2010.
- NM to provide a copy of his correspondence with ICMJE to the ENCePP Secretariat.
- SG members to draft a definition for 'study data'.
- ENCePP Secretariat to organise a Vitero meeting in March/April to discuss revised versions of CoC and MRS Checklist (see below for a confirmed date).

#### **Next meetings:**

- Vitero meeting: 19 March 2010, 14.00-16.00
- Face-to-face meeting: 7 May 2010, 9.30-16.00

- Vitero meeting: 16 September 2010, 14.00-16.00
- Vitero meeting: 2 December 2010, 14.00-16.00

**Annexes:**

- Presentations (see hyperlinks in text)