European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

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2ND ENCEPP MEETING WITH CENTRES AT THE EMEA

MINUTES OF WORKING GROUP 3:

Inventory of EU data sources and methodological approaches for multi-source studies

18 April 2008

Chairperson: Miriam Sturkenboom

Present:
Bourke, Alison
Czeizel, Andrew E
de Carmo Campos, Ana
de Jong-Van den Berg, Lolkje
Fekete, Ferenc
Fourrier-Reglat, Annie
Furu, Kari
Garbe, Edeltraud
Lopalco, Pierluigi
MacDonald, Thomas
Malm, Heli
Moretti, Ugo
Roddam, Andrew
Scharnetzky, Elke
Shakir, Saad
Silman, Alan
Sturkenboom, Miriam *(Chair)*
Trifiro, Gianluca
Van Ganse, Eric
Van Staa, Tjeerd *(ENCIAG)*
Wong, Ian Chi Kei
Prilla, Stefanie *(EMEA)*
Slattery, Jim *(EMEA)*

Apologies: Bakker, Marian K; De Abajo Iglesias, Francisco *(ENCIAG)*

1. Introduction

The group discussed the different topics of the draft Mandate, approving, further defining, rejecting and/or amending different items. In addition, a document provided by the ENCIAG member Francisco De Abajo Iglesias prior to the meeting "Key elements of the EU Inventory of Data sources for PE/PV research" was discussed.

2. List of Questions

The following questions regarding the tasks and the organisation of the WG were put to the group for discussion:

1. Does the Working Group (WG) agree with the proposed mandate? *In principle, the group agreed to the overall mandate. Certain topics, however, were reworded and amended, as described below.*
2. Are there additional topics which need to be included? *This question was addressed during the discussions on the different topics of the draft Mandate (see chapter 3). As an additional topic, the group should also address ad-hoc data collection and the difficulties in data collection.*
3. Are there any possible conflicts of interest/issues which might preclude a specific topic being developed through a (successful) IMI proposal? *Not addressed.*

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4. Are there topics which overlap with other groups? If so, how should this be addressed? *The topic of data privacy and data protection overlaps with the scope of* WG 2. *Both WGs should liaise and exchange their views on this topic.*
5. How would the WG suggest prioritising the topics? *This question was not specifically addressed. However, discussions focused on the establishment of an Inventory of EU data sources.*
6. How will the topics be addressed (including suggestions for lead persons for topics if appropriate)? *Not addressed.*

3. Discussions on the draft Mandate

A draft Mandate for WG 3 by EMEA and ENCIAG was presented to the group. The group was asked to comment on and to amend the Mandate.

3.1 General comments

- It was suggested to change the name of the Working Group to "Inventory" or "Registry" of EU data sources. The name of the Register as such should be amended accordingly.
- The Working Group should also address the collection of data and pertaining difficulties
- As a general comment, the group asked for guidance by the EMEA on its role, the purpose of its work, and how the work of the group fits into ENCePP and the ENCePP structure.
- The aim should not be to develop a new scientific model for PE research but to identify and address existing gaps

3.2 Discussions on topics of the draft Mandate

1. *EU Inventory of data sources*
   - 1.a Define the elements that the EU inventory of data sources should have, according to different categories (e.g. Databases, Disease Registries, Exposure Registries, Case-control surveillance, etc)
   - 1.b Identify existing data sources useful for PE and PV research
   - 1.c Identify relevant areas of PE and PV not covered by the existing data sources in the EU
   - 1.d Explore ways to stimulate and support initiatives to create new data sources in EU member states

1.a) and 1.b)

It was found essential for the Inventory of data sources to firstly define the different types of available data sources (e.g. drug utilisation or disease linkable to drugs) and, in addition, the criteria to define a data source. Data sources with only few data should not be excluded.
A preliminary list of data sources was drafted:
- Automated databases
- Disease registries (teratogenic, cancer, etc)
- Drug Exposure registries
- Case-control surveillances
- Intensive monitoring systems

It was agreed that this list should be circulated and extended, including criteria to define the respective source.

For each data source, minimum information should be available in the inventory, including a description of the kind of data available and the type of coding used.

It was agreed that the document "Key elements of the EU Inventory of Data sources for PE/PV research" from the ENCIAG member Francisco De Abajo Iglesias should be used as a starting point for discussions to be circulated and amended after the meeting. The deadline for comments was set 25 April 2008. The following main comments were made at the meeting:

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- Initially, a list of all data sources available through the current ENCePP partners should be created to be extended at a later stage through an application process to register new sources. The chair or an appointed delegate should start the list to be extended by the other WG members.
- A (hyper)link to the registered sources, publications, studies, etc should be included
- Case-control surveillances systems should also be covered
- Initially, the identification of data sources should be inclusive. At a later stage, however, accreditation criteria should be applied in a peer-review process.

1.c)

Areas not or not sufficiently covered by existing data sources were listed:
- In-hospital data (hospital-drug exposure studies)
- Data for drug use in nursing homes
- Neonatal data
- Data for OTCs
- Data for medical devices/diagnostic products

2. *Methodological approaches for multi-site studies*
   - 2.a Discuss operational approaches for organising, initiating and performing observational safety studies through ENCePP, as well as large simple randomised clinical trials.
   - 2.b Explore ways of performing multi-source studies (e.g. combining data, using common protocols)
   - 2.c Identify major heterogeneities in available data sources and develop solutions to facilitate the conduct of multi-source studies
   - 2.d Develop training programs

2.a) and 2.b)

The group agreed that it was not possible to harmonise databases and simply combine data sets from different data sources, which were created for different purposes, routinely using different coding systems and having different established structures. The combination of data in a single data base would require a low common denominator and therefore important available information would be lost. An alternative and feasible approach for studies based on data sets from more than one data source would be to apply a common protocol using similar definitions. Efforts to combine data sets from different data sources should focus on algorithms to translate between the sources. Through ENCePP, future data source owners should be encouraged to use a common coding system. ENCePP could give general recommendations on best practices for establishing and running data sources with a focus on facilitating the merging of data for multi-source studies.

The organisation of multi-source studies requires 3 steps:
- Identification of relevant data sources/data sets
- Identification of participating centres with the sufficient capacities, resources, expertise, etc
- Feasibility assessment including an estimate of the costs/budget involved

For studies to be carried out through the ENCePP network the group felt that a transparent procedure allowing all centres to compete in a fair and open way should be used. Once the work has been allocated, a scientific body within ENCePP could provide advice/assistance with regard to the design of such studies and identify appropriate data sources upon request. An ad-hoc consortium could be formed to give scientific advice and to support the research group by finding the best resources and the best methodology to address a certain research question. For this purpose it would be helpful to create a profile for each ENCePP participant (see WG 4). However, this procedure needs to be further developed.

It was found useful for the group to run through typical research requests in order to further develop this aspect.

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2.c)

Due to time constraints, this topic was deleted from the agenda. However, it was suggested to address the heterogeneity of data sources in PhD projects.

2.d)

It was agreed that the owners of every data source would be happy to participate in a training programme on PV and PE research. The training activities should include:
- Exchange of (young) researchers
- Funding of PhD students
- Interactive, relevant training courses

A strategic approach would be needed including a programme for students and young professionals. An expert committee in ENCePP should be established to further develop the training.

3. *Data Privacy restrictions for PE/PV research*
   - 3.a Develop approaches to overcome differences in national legislation on data privacy in order to facilitate multi-national database studies, taking into account legal advice.
   - 3.b Develop common rules to protect patients' and providers' rights with respect to data confidentiality

In general, it should be clear and well publicised that data privacy is ensured throughout ENCePP. All ENCePP members will need to give their consent to comply with the ENCePP rules on ethical issues.

3.a)

Data should be kept and processed locally/nationally rather than creating a single EU database, and processed according to the local/national regulations in force. The combination of data should be addressed on a case-by-case basis. However, based on experience from ongoing projects, the approaches used to address individual research questions should be compiled. It was found that one has to comply with the diverse national regulations and that there would be no possibility to circumvent them. Information on the restriction on the different data sets could be provided through the ENCePP Registry of data sources.

3.b)

It was suggested to extend the topic of data privacy to other type of data, e.g. physicians', pharmacists', and hospital data. Also, the interests and rights of the researchers should be protected.

3. *Input to the design of the ENCePP web page*

Not addressed.

4. Future organisation

At the end of the meeting, Miriam Sturkenboom was asked to keep the position of the chair of the WG. Miriam accepted but indicated that the decision might need to be revised due to a possible conflict of interest.

The "Key elements of the EU Inventory of Data sources for PE/PV research" were circulated and comments from WG members were provided by 25 April 2008. An amended document will be forwarded to all WG members to be discussed and further elaborated. Together with the chairperson and the ENCIAG representatives, the need and timing of further meeting/TCs, as well as a date for the next meeting, will be discussed.

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ANNEX – Amended Mandate of ENCePP Working Group 3

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Working Group 3

Scope	***Inventoy of EU data sources and methodological approaches for multi-source studies***
Chair: **Rapporteur(s):** **ENCIAG:**	Miriam Sturkenboom Jim Slattery (EMEA), Stefanie Prilla (EMEA) Dr. Francisco de Abajo Iglesias, Dr. Tjeerd Van Staa
Mandate	*EU Inventory of data sources* ▪ Define the elements that the EU inventory of data sources should have, according to different categories (e.g. Databases, Disease Registries, Exposed Registries, Case-control surveillance…) ▪ Identify existing data sources useful for PE and PV research ▪ Identify relevant areas of PE and PV not covered by the existing data sources in the EU ▪ Explore ways to stimulate and support initiatives to create new data sources in EU member states *Approaches & processes for interoperability and sharing of European epidemiology data sources* ▪ Discuss operational approaches for organising, initiating and performing of observational safety studies through ENCePP, as well as large simple randomised clinical trials. ▪ Explore ways of performing multi-source studies (e.g. combining data, using common protocols) ▪ Develop training programs *Data Privacy restrictions for PE/PV research* ▪ Develop approaches to overcome differences in national legislation on data privacy in order to facilitate multi-national database studies, taking into account legal advice. ▪ Develop common rules to protect patients' and providers' rights with respect to data confidentiality *Input to the design of the EMEA web page*

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