EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP)

The ENCePP Study Concept

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) has been created by the European Medicines Agency with a view to strengthening the available expertise and resources in Europe in the area of pharmacoepidemiology and pharmacovigilance. Ultimately, the network's goal is to both facilitate and enhance the conduct of collaborative pharmacoepidemiology and pharmacovigilance studies. A key element of ENCePP is to uphold high standards throughout the research process based on the principles of transparency and scientific independence. To this end, the concept of an 'ENCePP study' is introduced to identify those studies which are conducted in accordance to the following general principles:

- A maximum level of transparency is provided as regards the use of agreed methodological standards in the study protocol, the development and agreement of the study protocol, and the communication of the results;
- The primary purpose of a study shall be to generate data of potential scientific or public health importance and not to promote the sale of a medical product;
- The design of the research shall not be aimed towards producing a pre-specified result;
- The contractual arrangements between investigators and the study funder should clearly define the research assignment and should address in sufficient detail critical areas of interaction, remuneration, protocol agreement, analysis of results and publication of results;
- Remuneration shall only be granted as specified in the research contract and shall not depend upon a particular study result;
- The results of a study shall always be published, preferably in a peer-reviewed journal, or made available for public scrutiny within an acceptable time frame, regardless of the (positive or negative) results and the statistical significance;
- Relevant information on the research process and results shall be publicly available;
- The study must be registered in the publicly accessible register of ENCePP studies prior to its start, thereby making publicly available information on the study including the expected timelines, and updating the register with the results (or references to publications) on study completion.

***CoRe* requirements**

- **Code of Conduct: Signed declaration and checklist**
- **Methodological Standards for ENCePP Study Protocols: Signed checklist**

The signed declaration and checklists and the study protocol must be provided to the ENCePP Secretariat before the study commences.

The original and final versions of the protocol will be made publicly available after the final study report.

- ***E-Register* of Studies**

The study must be included in the electronic register of studies before it commences.

In practice, all pharmacoepidemiological and pharmacovigilance studies can qualify as "ENCePP studies" provided that the (primary) lead investigator belongs to an entity that is included in the ENCePP Inventory of Centres and Networks and that the "CoRe requirements" are met.

In essence, investigators that accept to conduct an ENCePP study commit to a maximum level of transparency with regard to relevant information pertaining to their investigation. This includes publication of study findings regardless of their (positive or negative) results and granting access to relevant information of the study protocol.

ENCePP Study Seal

Provided all the CoRe requirements have been fulfilled and the ENCePP Secretariat has confirmed the receipt of all necessary documents, a study may *a-priori* be considered as an "ENCePP Study". A letter of confirmation will be dispatched and a corresponding "ENCePP seal" will be displayed in the electronic ENCePP Register of Studies which may also be used in connection with this study. The seal will make immediately recognisable to the general public that the study was conducted in adherence to the ENCePP research principles and methodological standards and through transparency and clarity of roles, will increase trust in the robustness of the research.

However, investigators are reminded of the ongoing obligations the ENCePP study seal places on the conduct of a study, namely to adhere to the entirety of the provisions of the ENCePP Code of Conduct throughout the research process. In particular, researchers are obliged to:

- Regularly update the entry of the study in the register.
- Provide the original and final versions of the protocol through the ENCePP Register of Studies. The ENCePP Secretariat will make both versions publicly available after the final study report unless they have previously been made available by the (primary) lead investigator.
- Make publicly available a clear summary of the main study results, whether positive or negative, including results from prematurely terminated studies according to the timetable agreed in the research contract. In addition, an abstract of the study findings shall be provided to the ENCePP Secretariat for publication within 3 months following the final study report.
- Make publicly available a full report of all results with a scientific or public health impact without unjustified delay.

Investigators of ENCePP Studies are obliged to inform the ENCePP Secretariat without delay if a study deviates from and/or no longer follows the rules of the Code. In this event the concerned study shall not be entitled to the "ENCePP seal" and thus the title "ENCePP study", unless its deviation is judged by the ENCePP Steering Group not to affect the standards expected of an ENCePP Study, including the principles of transparency and independence.

E-Register of Studies

The electronic ENCePP register of studies aims to provide a publicly accessible resource for the registration of pharmacoepidemiological and pharmacovigilance studies. Its purpose is to:

- Increase transparency
- Reduce publication bias
- Promote information exchange
- Facilitate collaborations within the scientific community
- Facilitate optimal use of pharmacoepidemiology and pharmacovigilance expertise in Europe by preventing unnecessary duplication of research.

Registration of studies in the electronic register is mandatory only for "ENCePP studies"; it is voluntary for all other studies.

For clinical trials conducted in the EU, registration in the EUDRACT database is a legal obligation. Additional registration of clinical trials in the ENCePP e-register is only obligatory for "ENCePP studies".

How to register an 'ENCePP Study'

Given that registration of studies in the electronic register is one of the three CoRe requirements to be met for a study to qualify as an ENCePP study, an interim solution has been developed pending finalisation of the database, enabling researchers to receive the ENCePP study seal.

The following steps have been put in place whilst the development of the database is being finalised:

1. Investigators who wish to register their studies should fill in the "Data Entry Form" (available for download from the ENCePP website) and send it by email to the ENCePP Secretariat. This needs to be done before the study starts.
2. The original signed declaration, the checklist of the Code of Conduct and checklist of methodological standards should be sent to the ENCePP Secretariat (c/o EMA, 7 Westferry Circus, London E14 4HB, United Kingdom) before the study commences.
3. A copy of the study protocol should also be submitted at this stage, either electronically (preferably as PDF file) or by post.
4. Upon receipt of the documents, the ENCePP Secretariat checks for completeness of the "Data Entry Form", the signed declaration and checklists, and assigns a provisional registration number to the study.
5. The ENCePP Secretariat dispatches a letter signed by the Chair of the ENCePP Steering Group, confirming *a priori* eligibility of the study to be considered as an "ENCePP study" and places the ENCePP study seal in the log of ENCePP study applications.
6. The ENCePP Secretariat maintains a log of ENCePP study applications received during the interim phase. This log is published on the ENCePP website, and updated whenever new studies are added, or if the status of a study is changed.
7. By clicking on individual entries included in the log it is possible to access pdf-versions of the related documentation (signed checklists, signed declaration, data entry form and any other information relevant to the study). This complies with the transparency requirements laid down in the Code of Conduct.

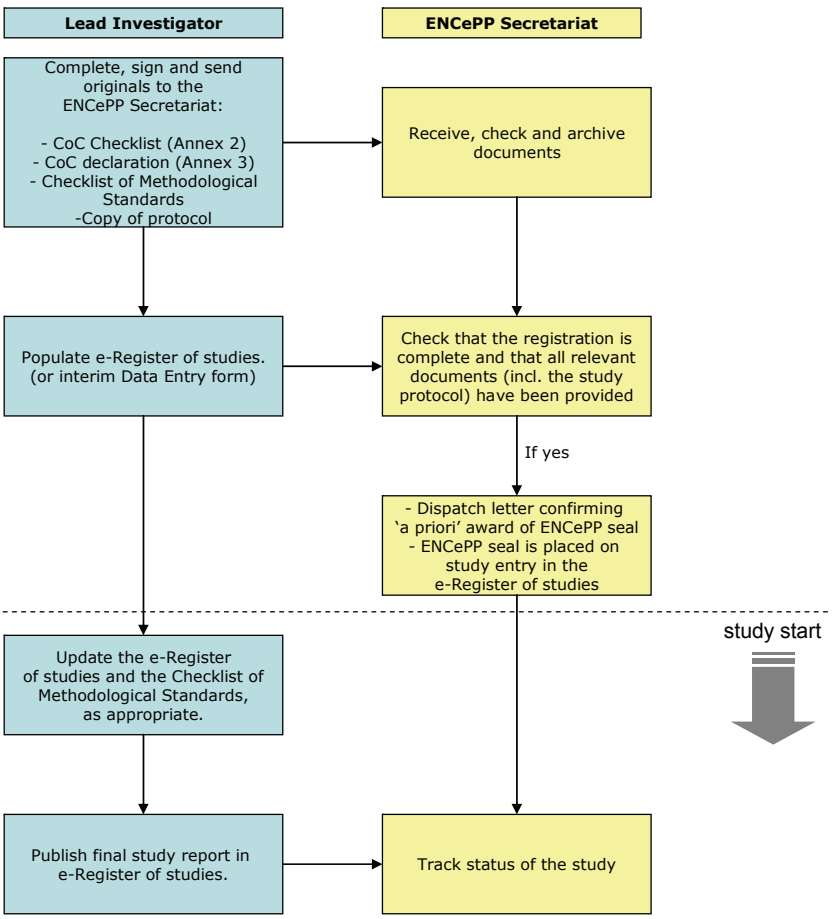
Any information and documents placed on the register during the interim phase will be migrated to the finalised database by the ENCePP Secretariat. Investigators will then be requested to check the migrated information for accuracy.

How to register Non-ENCePP studies

The electronic register of studies, once available, will be open to register all pharmacoepidemiological and pharmacovigilance studies regardless of whether there is an application for the ENCePP study seal or the research centre participating in the ENCePP network.

Investigators who only wish to register their studies, i.e. no request is made for an ENCePP study seal, need to submit a completed data entry form and any other relevant document they wish to make publicly available. There is no obligation to adhere to the ENCePP Code of Conduct or comply with the Checklist of Methodological Standards for ENCePP Study Protocols. However, investigators are required to regularly update the entry of their studies in the register.

ENCePP Study Process Flow Chart



The above flow chart represents the simplified process of applying for the ENCePP study seal and complying with the underlying requirements. Of note, the rules and provision of the Code of Conduct need to be followed in their entirety.

Further information can be found on the ENCePP website at:
www.encepp.eu