European Medicines Agency

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The ENCePP Code of Conduct

FOR SCIENTIFIC INDEPENDENCE AND TRANSPARENCY IN THE CONDUCT OF PHARMACOEPIDEMIOLOGICAL & PHARMACOVIGILANCE STUDIES

Draft for public Consultation

The ENCePP Code of Conduct was adopted on --/--/---- by the European Medicines Agency (EMEA) and the participants of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP). The terms of the Code of Conduct will be reviewed periodically after its adoption.

Steps taken

Key elements of the Code of Conduct agreed by the ENCePP Working Group on *Independence and Transparency*	21 November 2008
1st draft Code of Conduct agreed by Drafting Group of the ENCePP Code of Conduct	8 May 2009
2nd draft Code of Conduct agreed by ENCePP Working Group on *Independence and Transparency*	17 June 2009
Final draft Code of Conduct approved by ENCePP Implementation Advisory Group	27 October 2009
Public consultation	*16 November 2009 – 5 January 2010*
Adoption of the Code	--/--/----

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1. Background

In recent years, the EMEA has concentrated on developing a more proactive approach to Pharmacovigilance as part of the European Risk Management Strategy[1]. ENCePP originates from the EMEA's endeavour to enhance the scientific and operational expertise and capacity in the fields of Pharmacoepidemiology and Pharmacovigilance across Europe and to improve pharmacoepidemiological research and post-authorisation safety surveillance of medicines by offering access to a robust network of resources.

The ENCePP Code of Conduct, referred to subsequently as the "Code" has been primarily developed by the ENCePP Working Group on *Independence & Transparency* and has been subsequently adopted by the ENCePP Plenary.

2. Rationale and Scope

Rationale

The aim of the Code is to maximise Transparency and to promote scientific independence throughout the research process of Pharmacoepidemiology and Pharmacovigilance studies. By applying the principles of Transparency and scientific independence, the Code aims to strengthen the confidence of the general public, researchers and regulators in the integrity and value of Pharmacoepidemiology and Pharmacovigilance research. This is in line with the EMEA's undertaking to increase and uphold Transparency in the Agency's activities.

Scope

The Code of Conduct sets out rules and principles for Pharmacoepidemiology and Pharmacovigilance studies, with an emphasis on non-interventional Post-Authorisation Studies (see also definitions of Post-Authorisation Study and Non-interventional Study in Annex 1). This includes - but is not restricted to - active surveillance studies, registries, drug-utilisation studies, and any other type of observational research. However, the definition of Pharmacoepidemiology and Pharmacovigilance studies may also include Clinical Trials (see Annex 1).
The Code does not include rules or guidance on methodological aspects or scientific standards to be used for specific studies or study types. Adherence to the rules will not guarantee validity or integrity of study data. However, knowledge of these rules and a documented commitment of applying them to a study will help regulators and other stakeholders in the assessment of the reliability of study findings.

The use of this Code is a requirement in order for a study to be presented as "ENCePP study" or to claim to be a "study performed in accordance with the ENCePP Code of Conduct for scientific independence and transparency" (see also Chapter 3 and 5 for further details).

Main principles

The Code has been conceived after consultation of both academic and commercial Investigators also taking into account regulatory requirements in Europe, and lays down rules and recommendations as regards:

- **scientific independence**, by ensuring best practice in the relationship between Investigators and Study Funders, including protocol agreement and publication of results;

[1] The European Risk Management Strategy (ERMS) is a joint effort between the EMEA and the Heads of Medicines Agencies (HMA) started in July 2002 aiming at strengthening the safety-monitoring in the EU/EEA of medicinal products for human use. More information is available at http://www.hma.eu/43.html.

- and **Transparency** throughout the research process.

3. Implementation of the Code in the context of "ENCePP Studies"

Adherence to the Code is one of the prerequisites for studies to qualify for the title "ENCePP Study" (see also Chapter 5). In short, all Pharmacoepidemiological and Pharmacovigilance studies can qualify as an "ENCePP study" provided that the (Primary) Lead Investigator belongs to an entity that is included in the ENCePP Inventory of resources and that the "CoRe requirements" are met as detailed below.

CoRe requirements

- *Co*de of Conduct: Signed declaration and checklist
- Methodological *R*esearch Standards: Signed checklist[2]

The signed declaration and checklists and the Study Protocol must be provided to the ENCePP Secretariat before the study commences and will be made publicly available.

- *e*-Register of Post-Authorisation Studies[3]

The study needs to be included in the electronic ENCePP Register of Post-Authorisation Studies before it commences.

4. Legal framework & approved guidelines

In addition to the rules and principles laid down in the ENCePP Code of Conduct, studies performed in line with the Code need to comply with relevant legislation, as applicable. Specifically, the Declaration of Helsinki[4] and the provisions on processing of personal data and the protection of privacy as outlined in of Directive 95/46/EC and Regulation 45/2001 of the European Parliament and of the Council need to be followed.

In case of interventional research, the Clinical Trials' Directive (Directive 2001/20/EC) applies.

As Post-Authorisation Studies are carried out with authorised medicinal products, relevant European and national legislation applies. Specifically, Marketing Authorisation Holders will need to comply with Directive 2001/83/EC and Regulation (EC) No 726/2004 of the European Parliament and of the Council.

This Code should not be considered as a stand-alone document but should be read in conjunction to other relevant guidance. Notably, this Code takes into account the ISPE's Guidelines for Good Pharmacoepidemiology Practices (ISPE GPP, Revision 2, 2007) and refers to relevant parts thereof, as appropriate. Other relevant guidance including Volume 9A of the Rules Governing Medicinal Products in the European Union - Pharmacovigilance for Medicinal Products for Human Use, the STROBE Statement (Guidelines for Reporting Observational Studies), the Guidelines for Good Clinical Practice (Commission Directive 2005/28/EC) and the International Guidelines for Ethical Review of Epidemiological Studies of the Council for International Organizations of Medical Sciences (CIOMS) should be taken into account when conducting pharmacoepidemiological studies.

[2] The Checklist for Methodological Research Standards is currently released for public consultation at http://www.encepp.eu.
[3] The electronic ENCePP Register of Post-Authorisation Studies is currently under development.
[4] World Medical Association declaration of Helsinki (see also chapter 15)

5. Application of the Code and Compliance

Studies performed in accordance with the rules laid down in this document shall be eligible to be considered as "studies performed in accordance with the ENCePP Code of Conduct for scientific independence and transparency". In publications, the section 'conflicts of interests' should make reference to the Code. In addition, adherence to the Code is one of the prerequisites for studies to qualify for the title "ENCePP Study" (for details on the requirements of "ENCePP studies" see Chapter 3).

The (Primary) Lead Investigator of the study must complete the checklist (Annex 2) and sign the declaration that he will comply with the provisions of the Code (Annex 3). Originals of the signed checklist and declaration together with a copy of the agreed full Study Protocol shall be provided to the ENCePP Secretariat, who will archive them for no less than five years after the termination of the study, check the documentation for completeness and confirm the *a priori* eligibility of the study to be considered as "study performed in accordance with the ENCePP Code of Conduct for scientific independence and transparency". The declaration, the checklist and the Study Protocol will be made publicly available on the ENCePP webpage.

At the same time, the (Primary) Lead Investigator should ensure that the funding contract makes appropriate reference to the Code. By signing the funding contract the Funder commits to abide by the rules of the Code (see also Chapter 8).

Investigators and Funders who, for a particular study, make use of the claim "ENCePP Study" or "studies performed in accordance with the ENCePP Code of Conduct for scientific independence and transparency" commit to adhere to the rules of this Code throughout the research process including the publication of the research results.

Withdrawal and Breach

In case the (Primary) Lead Investigator decides to deviate and/or no longer follow the rules of the Code, he should inform the ENCePP Secretariat without delay. The ENCePP Secretariat may subsequently request the (Primary) Lead Investigator to cease using the title "ENCePP Study" or making reference to the study as "study performed in accordance with the ENCePP Code of Conduct for scientific independence and transparency". If the ENCePP Secretariat is not informed before the implementation of such a decision, the deviation from the provisions of the Code may be considered as a breach of the declaration (Annex 3).

In the event of a breach of the declaration, the concerned study shall be deprived of the title "ENCePP study" or "study performed in accordance with the ENCePP Code of Conduct for scientific independence and transparency".

In case of either a voluntary withdrawal or a deprivation for breach, the ENCePP Secretariat may identify the respective studies in the annual reports and on the ENCePP website.

6. General Provisions

ENCePP Studies should comply with the highest possible standards for independent and transparent research. By agreeing to follow the Code, Investigators and Study Funders commit to adhere to the following general principles:

- 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 medicinal product;
- The design of the research shall not be aimed towards producing a pre-specified result;

- A contract shall be concluded between the Investigator and the Funder clearly defining the assignment and addressing in sufficient detail critical areas of their interaction, remuneration, protocol agreement, analysis of results and publication of results;
- Remuneration shall only be granted as specified in the contract and shall not depend on the study results;
- The results of a study shall always be published or made available to public scrutiny within an acceptable time frame, regardless of the (positive or negative) results and the statistical significance;
- Relevant information on the research contract, process and results as specified in this Code shall be publicly available.

7. Ensuring Transparency

A maximum level of Transparency with regard to any information pertaining to the research process - including the disclosure of the Study Protocol and any revisions thereof - and the publication of study findings should be ensured. Open access to this information should be provided to regulators, health care professionals and the scientific community, as well as, patients and the general public.
The following means to ensure transparent research are addressed by the Code:

- Registration of the study in the ENCePP Register of Post-Authorisation Studies prior to the study start, and thereby making publicly available information on the study including the Study Protocol, the expected timelines and the results on study completion;
- Accurate and detailed documentation of all steps throughout the research process, especially any changes to/deviations from the original Study Protocol and the justification thereof;
- Agreement to make available on request any information including the content of the funding contract, reports from independent reviewers, non-identifiable study data, all interim and final study findings irrespective of positive or negative results; this includes the publication of the results aiming at the highest possible level of scrutiny;
- State in advance and in publications the affiliations of the Investigators and any potential Conflicts of Interest.

8. Funding Contract

The contractual arrangement between the (Primary) Lead Investigator or the Coordinating Study Entity and the Funder should be signed in a legally binding manner prior to the first step in the research process subject to the assignment.

The funding contract shall specifically refer to the ENCePP Code of Conduct and shall include the statement “The parties to this agreement and individuals acting on their behalf hereby commit to adhere to the rules of the ENCePP Code of Conduct in their entirety”. The relevant version of the Code at the time of the signature of the funding contract should be annexed to the contract for reference.

The following aspects should be addressed in the funding contract:

- The main objectives and a brief description of the intended methods of the research which is subject to the contract. The name of the study and a clear assignment of tasks and responsibilities should be stated.

- The amount of the financial support and the payment scheme.
- Ownership of and access to the data produced during the study. The provisions on data ownership addressed in Chapter 11 shall apply.
- A communication strategy for the interim and final results should be included. Plans for publication should be stated. The contract should provide for the rights and obligations as detailed in Chapters 9 and 13.

In case of complaints from Third Parties questioning the compliance of a particular ENCePP Study or a study claiming to be a "study performed in accordance with the ENCePP Code of Conduct for scientific independence and transparency" with the provisions of this Code, the ENCePP Secretariat may request to see the funding contract to verify it is not in breach of the Code.

9. Rights & Obligations of the Investigator and the Study Funder

The (Primary) Lead Investigator shall be responsible for the content of the assigned research project including the design of the protocol, the conduct of the study, the analysis and interpretation of the study results and the preparation and publication of the study outcome. All those contributing to the development of the Study Protocol and their roles in doing so should be specified in the Study Protocol. Any Conflict of Interest among the Investigators should be declared and be made publicly available. The (Primary) Lead Investigator shall keep the Funder informed about the study progress in terms of recruitment, where relevant, and data collection, any modification of the protocol and the reasons for it, but should not communicate preliminary results. The final study results and interpretations of the findings in advance of publication could be provided for comment within a time limit specified in the contract.

Detailed provisions on the reporting and publication of the study results can be found in Chapter 13.

Registration of Studies

The (Primary) Lead Investigator on behalf of the Coordinating Study Entity undertakes to register the study before it commences in the electronic ENCePP Register of Post-Authorisation Studies[5]. Information on the study including the Study Protocol and information on the researchers, the (Primary) Lead Investigator and the team of Investigators if applicable, their affiliations, the Coordinating Study Entity and all research institutes and study sites involved as well as the Funder, will be made publicly available through the ENCePP webpage.
The Register should be regularly updated as appropriate.

10. Development of the Study Protocol

The protocol shall be developed before the study commences by individuals with appropriate scientific background and experience. The funding contract should refer to a clear protocol taking into account the elements of the *Checklist of Methodological Research Standards* (also see Chapter 4). Any amendments or updates from study start need to be duly justified and should be documented in a traceable and auditable way. Changes for reasons such as marketing and/or advertising strategies shall not be acceptable.

The protocol must be designed to ensure scientifically valid and sound results are generated independently from any potential conflicting interest of the Funder or the researcher. To

[5] The electronic ENCePP Register of Post-Authorisation Studies is currently under development.

achieve this aim, the protocol needs to pre-define certain information before the study starts as outlined in the *Checklist of Methodological Research Standards* including a timetable for the study progress and completion of the study describing milestones (e.g. interim reports) and deadlines.

Any deviation from the initial protocol should be duly justified and documented including the date of the change. Particularly, any changes after the start of data collection, especially after the first results have become available, shall be identifiable and reported as such in publications and the ENCePP Register of Post-Authorisation Studies and this should be considered for the purpose of the interpretation of the findings. This includes objectives or endpoints added or amended after the study start that are based on (initial) findings.

Protocol Agreement

The funding contract between (Primary) Lead Investigator or Coordinating Study Entity and the Study Funder shall specify the negotiation procedure to achieve agreement on the Study Protocol. If the development of the Protocol is part of the assignment, the Investigator shall write the Protocol within the remits of the assignment. Involvement of the Funder in the design of the protocol is permitted but any involvement shall be specified in the contract and information on the degree of the Funder's involvement shall be made publicly available together with information on all parties involved in the writing and adoption of the Protocol.

Irrespective of the origin of the Study Protocol, the (Primary) Lead Investigator shall have final responsibility for its content. It is recommended to subject the Protocol to an impartial peer-review before its final adoption.

Availability of the Study Protocol

The full Study Protocol[6] shall be made publicly available through the ENCePP Register of Post-Authorisation Studies. In case of amendments to the Protocol, the former version or the information on the concerned elements should be replaced without delay by the new version/information including the date of the amendment and a summary of the main changes should be provided.

11. Data Ownership and Access to Data

The (Primary) Lead Investigator and Study Funder shall agree on data ownership in the funding contract (see Chapter 7). Intellectual ownership by the parties directly involved in the planning and conduct of the study as well as the analysis and interpretation of the study data should be taken into account and should be provided for in the contract. As regards the relation between data ownership and publication of results please refer to Chapter 13.

Both the Study Protocol and the funding contract should address rules for access to raw data, processed data and final results generated under the study. Any identifiable data should be maintained under secure conditions in line with data protection legislation (see also Chapter 4).

The (Primary) Lead Investigator should ensure that all data collected and generated in a study are recorded in an accurate way that allows access e.g. for the purpose of verifying the published results at all times whilst ensuring personal data protection.

[6] For the purpose of the Code, a *full* Study Protocol is a version of the Protocol which includes enough detail in order to answer all questions in the Checklist of Methodological Standards (also see Chapter 4).

12. Study Conduct

Any step in the research process shall follow the agreed procedures laid down in the Study Protocol and shall be directed towards the generation of sound and valid findings. The Investigator shall be responsible for the conduct of the study within the remits of his assignment, including the data collection and analysis, the interpretation of the study results and the preparation and publication of the study outcome.

All parties to be involved in the conduct of a study shall declare existing direct or indirect interests of a commercial, financial or personal nature. Any party with a financial interest in the results of a study should not actively participate in the conduct of the study except for providing expert advice on requests of the (Primary) Lead Investigator.

Data Analysis

A detailed statistical analysis plan shall be described in the Study Protocol. Any deviations from the analysis plan should be clearly documented and a reasonable scientific justification should be provided (also see chapter 10.).

Outcomes resulting from changes to the analysis plan after data analysis has begun, e.g. formation of new sub-groups based on knowledge of (initial) study results may not be used for the purpose of verifying or rejecting a hypothesis of a causal association. In any case, all changes need to be documented and shall also be indicated in communications on the study results.

Study Steering Group

If a steering group or a scientific oversight committee is foreseen for the purpose of providing scientific advice and guidance and/or to oversee the conduct of the study, the members of this steering group shall declare existing direct or indirect interests of a commercial, financial or personal nature and should only be appointed if no Conflict of Interest exists.

Other parties and stakeholders including the Study Funder, if they have a Conflict of Interest, may only participate in meetings of the steering group as invited observers. Observers may be consulted by the members of the steering group on specific questions; however, any decision-making steps should take place in the absence of observers. The Study Funder may only be represented by a person with proven expertise and scientific knowledge in the area of the research.

The composition of the steering group including observers participating in its meetings should be made publicly available.

13. Publication/Reporting of Study Results

A dissemination and communication strategy should be pre-defined as part of the funding contract. Any deviation should be duly justified.

A clear summary of the main results of a study including results from pre-maturely terminated studies, whether positive or negative, should always be made available to the public according to the timetable agreed in the Study Protocol. In addition, an abstract of the study findings shall be provided to the ENCePP Secretariat for publication on the ENCePP webpage within 3 months after the final study report. The (Primary) Lead Investigator may ask the ENCePP Secretariat to delay the publication of this abstract for a limited period based on ongoing response to peer-review comments.

A full report of all results with a scientific or public health impact must be made publicly available without unjustified delay. In case of a (suspected) public health impact, relevant legal provisions shall be followed and the respective regulatory authority(ies) shall be informed forthwith and in advance of publication.

The outcome of a study shall always be presented in an objective and truthful manner providing a comprehensive and accurate description of the findings. In no way shall the interpretation and presentation of the results be aimed towards any commercial, financial or personal interests. As for the content of the report(s), it is recommended to follow the ISPE GPP and the STROBE statement.

If necessary, the published results shall be updated, e.g. in case of re-analyses or additional analyses, including an explanation for the update. Presentations to a limited audience at meetings will not suffice as the only or main means of communication.

The (Primary) Lead Investigator should have the right to independently prepare publications of the study results irrespective of data ownership (see also Chapter 11). The Study Funder shall be entitled to view the final results prior to the publication and to comment on the results and interpretations of the findings in advance of publication within a reasonable time limit, e.g. one month, as agreed in the funding contract and without unjustifiably delaying the publication. Requests that interpretation of the results or their presentation be changed must be based on sound scientific reasons. The Investigator is free not to take the comments of the Funder into account and the Funder may only require that the presentation of the results be changed to delete Confidential Information (see also Chapter 14). Any comments of the Funder should be made publicly available.

In line with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals by the International Committee of Medical Journal Editors (2009), the authors of the study should be those individuals who have made substantial intellectual contributions to the research. As is usually demanded by respected peer-reviewed journals, information on the actual role of all authors and the Study Funder should be provided. In addition, affiliations and Conflicts of Interest should be disclosed. The responsible author shall accept responsibility for the overall conduct of the study and the accuracy and integrity of the data presented (even if medical writers have been involved) as well as for any conclusions drawn from the data.

Scientific Review

The study results and any publications and/or communications thereof should be peer-reviewed by independent experts regardless of whether a steering group has been established.

The report(s) of the reviewer(s) should be documented. If the reviewer(s) recommend(s) changes, the (Primary) Lead Investigator should either revise the results and publications thereof or provide a rationale why the original version should be retained. The reports and related information e.g. regarding the implementation of the reviewers' recommendations should be made available upon request.

14. Confidentiality

A maximum level of Transparency with respect to regulators and health care professionals as well as patients and the general public should be strived for regarding any information pertaining to the research process, including the disclosure of the Study Protocol, and any revisions thereof, and the publication of study findings.

As information which constitutes Confidential Information depends on the actual research topic as well as the nature and relationship of the parties who contribute to a study, the exact

definition should be agreed on a case-by-case basis but in any event in advance before the study commences, in the funding contract or a separate agreement between the relevant parties. In any event, any data produced during the study shall not be regarded as Confidential Information. To this end, it is recommended that Investigators and Funders enter into appropriate confidentiality agreements.

15. References

Checklist of Methodological Research Standards for ENCePP Studies, currently a draft is released for public consultation at http://encepp.eu.

Commission Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products (Official Journal L 91, 9/4/2005 p.13-19), available at http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2005:091:0013:0019:en:PDF.

Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (Official Journal L 121, 1/5/2001 p. 34 - 44), available at http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol1_en.htm.

Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (Consolidated version: 30/12/2008), available at http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol1_en.htm.

Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data, available at http://ec.europa.eu/justice_home/fsj/privacy/law/index_en.htm.

Guidelines for Good Pharmacoepidemiology Practices (GPP), International Society for Pharmacoepidemiology, (Revision 2: April 2007), available at https://www.pharmacoepi.org/resources/guidelines_08027.cfm.

International Ethical Guidelines for Epidemiological Studies, The Council for International Organizations of Medical Sciences (CIOMS), 2009, ISBN 92 9036 081 X, superseding the 1991 International Guidelines for Ethical Review of Epidemiological Studies which are available at http://www.cioms.ch/frame_1991_texts_of_guidelines.htm.

Regulation (EC) No 45/2001 of the European Parliament and of the Council of 18. December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data, available at http://ec.europa.eu/justice_home/fsj/privacy/law/index_en.htm.

Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (Consolidated version : 6/7/2009), available at http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol1_en.htm.

STROBE statement: von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. **The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies.** J Clin Epidemiol. 2008 Apr;61(4):344-9.

Uniform Requirements for Manuscripts Submitted to Biomedical Journals by the International Committee of Medical Journal Editors (ICMJE), 2008, available at http://www.icmje.org/urm_main.html.

Volume 9A of the rules governing medicinal products in the European Union: Guidelines on Pharmacovigilance for Medicinal Products for Human Use (September 2008), available at http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol9_en.htm.

World Medical Association Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Subjects, 1964, last amended 2008, available at http://www.wma.net/en/30publications/10policies/b3/index.html.

Annex 1 (Definitions)

Definitions

ENCePP Study

Pharmacoepidemiological and Pharmacovigilance studies performed taking into account relevant methodological research standards as agreed by ENCePP and in line with the rules and requirements for the independent and transparent conduct of pharmacoepidemiological and Pharmacovigilance research laid down in the ENCePP Code of Conduct, and whose (Primary) Lead Investigator belongs to an entity that is included in the ENCePP Inventory of resources.

ENCePP Code of Conduct

A set of rules and principles laying down the responsibilities and good practices to guide the interaction between research centres, pharmaceutical industry and regulators, as well as rules and principles for the conduct of pharmacoepidemiological and pharmacovigilance studies to be followed throughout the research process in order to maximise Transparency and scientific independence.

Post-Authorisation Study

Any study conducted with an authorised medicinal product.

Non-interventional Study

Based on Directive 2001/20/EC, in a non-interventional study the assignment of the patient to a particular therapeutic strategy is not decided in advance by a trial protocol but falls within current practice and the prescription of the medicine is clearly separated from the decision to include the patient in the study. No additional diagnostic or monitoring procedures shall be applied to the patients and epidemiological methods shall be used for the analysis of collected data.

Study Protocol

A document that describes the objective(s), design, methodology, statistical considerations and organisation of a study. The term protocol refers to the initial protocol, successive versions of the protocol and protocol amendments.

Lead Investigator

A person with the scientific background and experience required for the conduct of a particular pharmacoepidemiological or Pharmacovigilance study. The Investigator is responsible for the conduct of a study at a study site.

Primary Lead Investigator

If a study is conducted at several study sites by a team of Investigators, the (Primary) Lead Investigator is the Investigator who has overall responsibility for the study across all sites.

Coordinating Study Entity

A legal person, company, institution or organisation which takes responsibility for the initiation and/or the management of a study. The Coordinating Study Entity can be a Contract or an Academic Research Organisation and can be identical with the Study Funder. The

(Primary) Lead Investigator is the person authorised to represent the Coordinating Study Entity.

Study Funder

A legal person who provides the financing for a study. The Funder can be the originator of the research question and is identical with the client in Contract Research.

Contract Research

Outsourced research, including either the complete research process or specific steps therein, such as the design of a protocol, data collection that is conducted by an independent contractor on behalf of a Funder.

Pharmacoepidemiology

The study of the utilisation and effects of drugs in large numbers of people. To accomplish this study, Pharmacoepidemiology borrows from both pharmacology and epidemiology.

Pharmacovigilance

The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems.

Clinical Trial

Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy.

Transparency

Transparency is based on openness, communication and disclosure of or making available information whilst respecting the protection of both personal data as well as commercially confidential information. Research may be labeled as (partly) transparent if some or all relevant aspects of the research are open in the sense of open access to information on the research process and data thereby facilitating an objective assessment of the quality and independence of the research and validity of the research results.

Conflict of Interest

In the context of this document, Conflicts of Interest include any direct or indirect interests of a commercial, financial or personal nature other than purely scientific motivation which might compromise the impartiality of the persons contributing to a study and may have an effect on relevant decisions including the choice of the study design, interpretation of data, and publication of results etc.

Confidential Information

Confidential Information means all information, facts, data and any other matters communicated between the Investigator(s), the Coordinating Study Entity and the Study Funder in the framework of the study undertaken which are clearly identified or marked as being confidential at the moment of their disclosure.

For the purpose of this document, Confidential Information shall be understood as information which may not be disseminated without the direct or indirect approval of the owner of such information as agreed between the above mentioned parties. This especially

includes commercial or financial information other than information on the identity of the Study Funder or information related to patents or copyrights. Data derived from a study shall reasonably be treated confidentially only in relation to data privacy law.

Annex 2 (Checklist)

Checklist of the ENCePP Code of Conduct

(To be developed once the Code has been finalised)

The Checklist will capture the key elements of the Code and require applicants to respond to questions regarding the compliance with the rules of the Code. All questions must be answered. In certain cases it might also be necessary to provide supporting documents in support of the answers given. The Checklist should be signed by the (Primary) Lead Investigator thereby declaring upon honour the answers in relation to the company or organisation that he/she represents.

Annex 3 (Declaration)

Declaration

The (Primary) Lead Investigator and a person authorised to sign on behalf of the Coordinating Study Entity hereby declare for the purpose of conducting the study <include study name and identifier/registration no.>

- to follow the rules and principles for the independent and transparent conduct of pharmacoepidemiological and Pharmacovigilance research of the ENCePP Code of Conduct of --/--/---- <include revisions>;
- to inform the ENCePP Secretariat, without delay, of any change or decision to change which constitutes a deviation from the provisions of this Code.

It is of note that the (Primary) Lead Investigator and the person authorised to sign on behalf of the Coordinating Study Entity may be identical.

Name of (Primary) Lead Investigator :

_____

Date: xx/yy/zzzz

Stamp and signature:

Name of the Coordinating Study Entity:

_____

Address:

_____

_____

Name of person authorised to sign on behalf of the Coordinating Study Entity [if different from (Primary) Lead Investigator]:

_____

Date: xx/yy/zzzz

Stamp and signature:

Mandatory supporting documentation to be provided in support of the above declaration:

- **Identification of the (Primary) Lead Investigator**
- **Identification of the Coordinating Study Entity**
- **Identification of the Study Funder**

Of note, in order to comply with this obligation it might be sufficient to submit the Study Protocol provided that the above mentioned persons and entities are clearly identified.

Applicants are requested to note that supporting documents provided must relate to legal persons and/or natural persons including, where considered necessary by EMEA, directors or any person with powers of representation, decision-making or control in relation to the candidate.

If there is any doubt about the mandatory documentation required, it is strongly recommended that the ENCePP Secretariat is contacted for clarification since failure to provide the correct documents may lead to elimination from the procedure.

The (Primary) Lead Investigator should also sign and date the Checklist (Annex 2). EMEA is unable to accept electronic signatures and will not accept photocopies of the completed declaration.