European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

Response to:

Concept paper of 9 February 2011 submitted for public consultation by the European Commission on the

REVISION OF THE "CLINICAL TRIALS DIRECTIVE" 2001/20/EC

Submitted by the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP)

13 May 2011

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Introduction

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) aims to further strengthen post-authorisation medicines research in Europe, thereby contributing to public health promotion and protection. The Network is currently comprised of more than one hundred centres, networks and data sources across seventeen European countries. The European Medicines Agency (EMA) provides the secretariat for the Network.

ENCePP welcomes the proposals for revision of the 'Clinical Trials Directive' 2001/20/EC and acknowledges the helpful nature of some of the initiatives in the relevant paper submitted for public consultation by the European Commission. The following are the ENCePP agreed responses to the topics that are considered most relevant to the Network among the consultation items in the paper.

ENCePP Responses

- **Concept of 'type-A' clinical trials (Consultation item no. 8).**

The paper introduces the concept of 'type-A-trials' i.e. clinical trials in which the expected risk for the subjects enrolled is low and where the assessment in a coordinated assessment procedure is largely limited to issues of reliability of data. ENCePP considers this to be in line with the general proposal to introduce harmonised risk-graded requirements for all clinical trials that fall within the scope of the Directive. ENCePP, however, wishes to state that it is paramount that the introduction of a sub-categorisation within clinical trials *per se* should not have any implications for 'non-interventional trials' and should not lead to any blurring of the boundaries between the two entities or enlargement of the scope of the Clinical Trials Directive. This requires that particular attention should be paid to clearly defining what constitutes a 'non-interventional trial' falling outside the scope of the Directive as distinct from an interventional clinical trial falling within the scope.

- **Definition of 'non-interventional trials' (Consultation item no. 9).**

ENCePP suggests the following recital to better explain the distinction between interventional and non-interventional trials:

"Experience has shown that the current definition of a non-interventional trial is open to interpretation and studies have been erroneously classified as interventional trials in the past. This is a hindrance to public health research and there is a need to amend the definition.

The classification of a study as a non-interventional trial should be scientifically-based and determined by the methodological instruments involved. This approach will readily determine whether a study is a systematic assessment of events that unfold without interference in their course. Such an observational study is clearly distinct from a trial, which implies an element of intervention either in terms of treatment with a medicinal product itself or in terms of the diagnostic and monitoring procedures applied in the context of the overall therapeutic strategy being followed.

If the methodologies involved, however, require prospective data collection or suggest an element of intervention, further consideration should be given as to whether a trial should be classified as non-interventional as distinct from interventional, the latter falling within the scope of the Clinical Trials Directive. In this case, if treatment with the medicine has already commenced, or if treatment that will happen is not assigned *a priori* in a protocol, and the therapeutic strategy within which the treatment is prescribed, including the related diagnostic or monitoring procedures applied, can be considered as current clinical practice, then the trial should be classified as non-interventional."

A non-interventional trial may, therefore, be defined as:

"A trial with monitoring of patients and/or prospective data collection, where the medicinal product(s) is (are) prescribed independently to the inclusion of the patient in the trial and as part of a therapeutic strategy which is applied according to the current clinical practice. The therapeutic strategy, including related diagnostic and/or monitoring procedures, shall not be influenced by inclusion of the patient in the trial."

- **Excluding clinical trials by academic-commercial sponsors from the scope of the Clinical Trials Directive (Consultation item no. 10).**

ENCePP supports the appraisal that proportionate requirements would apply independently of the nature of the sponsor.

- **Streamlining of the rules for conducting clinical trials (Consultation items no. 11 and no. 12).**

ENCePP supports the proposal for more precise and risk-adapted rules for the content of the application dossier and for safety reporting by means of sufficiently detailed provisions on these topics being included in Annexes to the basic legal act. ENCePP suggests the Commission, in drawing up these Annexes, also takes account of the implementing measures linked to the new pharmacovigilance legislation, especially the minimum requirements for data quality therein. In addition, ENCePP seeks to ensure robustness and reliability of data for post-authorisation monitoring of medicines through its activities including development of the ENCePP Code of Conduct and its work on methodological standards. It is acknowledged that these initiatives are of a voluntarily nature and do not have any legal basis. The Commission is, however, encouraged to take the principles that underlie the documents developed by ENCePP into consideration when it comes to detailing provisions that will ensure data reliability and robustness for medicines research, including the guidance for the new legislation.

- **Single sponsor for clinical trials (Consultation item no. 15).**

In terms of maintaining the concept of a single sponsor, while ENCePP seeks to facilitate research by consortia or networks, it is hard to argue against the requirement for a person who can ultimately and authoritatively inform the national competent authority about the clinical trial and ENCePP agrees with the appraisal laid out in the concept paper, accordingly.

Conclusion

ENCePP welcomes the opportunity to comment on the proposed revision of the Clinical Trials Directive and considers the following as key points:

1. If 'type-A trials' are introduced, the concepts involved should only be applied to interventional clinical trials falling within the scope of the Directive and clearly separate to non-interventional trials falling outside the scope of the Directive, by definition.

2. The definition of non-interventional trials should be scientifically based and take account of the methodological instruments applied.