EUROPEAN SCIENCE FOUNDATION
SETTING SCIENCE AGENDAS FOR EUROPE

European Medical Research Councils (EMRC)

Comment on the consultation paper: revision of the clinical trials directive 2001/20/10

Introduction

The European Science Foundation (ESF) is an independent non-governmental organisation, the members of which are 78 national funding agencies, research performing agencies, academies and learned societies from 30 countries. European Medical Research Councils (EMRC) is the membership organisation for all the Medical Research Councils in Europe under the ESF.

The European Medical Research Councils of the ESF welcomes the "Concept paper for the revision of the Clinical Trials Directive (CTD) 2001/20/EC" submitted by the DG SANCO on 9 February 2011 and is grateful for the opportunity to comment on this paper. We appreciate that many suggestions and recommendations from previous meetings with experts as well as publications such as the Forward Look on "Investigator Driven Clinical Trials" from EMRC have been taken into account. We also thank you for giving us the opportunity to provide feedback during the stakeholder meeting on 31 March 2011. Please find below detailed comments on the different consultation items and some general remarks and suggestions for the revision of the CTD.

1) **Summary of feedback and comments on the consultation items**

Consultation item no. 1:

The idea of a single submission is highly appreciated.

Comments and suggestions:

- A coordinated submission will only be beneficial if no additional submissions are required by member states. However, we would like to see a clear proposal from the Commission as to how a single portal submission for multinational trials would work in practice.
- The single EU portal should be a single entry portal where all documents have to be uploaded and sent for submission. The procedures of submission have to be clearly defined, the content of the file should be well structured. Central submission should be a standardised set of documents with clear and defined requirements. Mechanisms for ethics committee (EC) submission have to be compatible with the authorisation procedure. National trials might be submitted to national competent authorities (NCA), but should be based on similarly standardised documentation and compatible submission systems.

Consultation item no. 2:

We agree that a single submission alone would not be sufficient to address the issue of diverging local assessments. A streamlined and coherent assessment is also needed- the idea of streamlining and coordinating the assessment procedure is highly appreciated.

Consultation item no. 3:

We agree that a central assessment would delay the procedures and be more cost intensive. Therefore a coordinated assessment procedure seems to be the better option.

Consultation item no. 4:

Is the above catalogue complete?
The above mentioned catalogue is complete.

Consultation item no. 5:
Do you agree to include the aspects under a), and only these aspects, in the scope of the CAP?

The idea of a CAP is very much appreciated. However, until there is more detail as to how it will operate in practice it is difficult to comment on whether this would lead to a reduction in time and cost. We would therefore appreciate seeing a draft of the proposal.
Comments and Suggestions:

- A proportionate approach involving a risk-benefit assessment could be incorporated in CAP. Please see consultation item 11 for further detail on risk-benefit assessment
- To streamline the ethical assessment of multinational protocols a national assessment for information, informed consent, personal data protection, investigation site and investigator capabilities and an EU-wide assessment of protocol design and methodology could be useful.
- We would encourage interactions between Ethics Committees between member states to increase consistency, share best practice and improve efficiency. It is vital that any duplication of functions of Ethics Committees and NCAs is avoided.
- Insurance and indemnity issues, currently under item c), could be incorporated in CAP under a).
- The submission procedure and administrative burden of CAP should be further clarified as part of an impact assessment. Further detail is required on how the central CAP and national systems, e.g. parts of the ethics assessments, will be coordinated.

Consultation item no. 6: *Disagreement with the assessment report*

The "opt out" option of Member States seems the preferable option- vote and commission decision would delay the initiation of a clinical trial. What happens if a trial is extended to other member states should be clarified.

Consultation item no. 7:

We are in favour of option 2, which is a harmonised approach for multinational clinical trials and would leave more flexibility for national trials. The option for national trials to be assessed by national competent authorities should be maintained, although this should be compatible with and have comparable standards to CAP.

Consultation item no. 8: Pre-assessment: *Tacit approval and timelines*

We welcome the concept of pre-assessment of „type A" trials and anticipate this will result in reduced timelines to clinical trial initiation.

Other comments and suggestions:

- More detail is required on the risk-benefit pre-assessment (see consultation item 11)
- Further specification or examples of what "insignificant additional risk" could entail is necessary for quick and reliable assessment.
- More detail is required on who does the pre-assessment of type A trials,
- How much time can be saved with this procedure should be quantified.

Consultation item no. 9:

We are against enlarging the scope of the Directive. The idea to implement a more risk-adapted approach is welcomed. However, we request the Commission to provide more detail on the proportionate approach outlined and the mechanism for harmonising this across member states. We would appreciate seeing a draft of the risk-based approach

Consultation item no. 10:

We agree with this appraisal.

Consultation item no. 11: More precise and risk-adapted rules for the content of the application dossier and for safety reporting

We agree with the concept laid out by the Commission, but would like to see a more detailed proposal. Stratification of clinical trials according to risk and risk-adapted rules for the application, insurance and safety reporting is required. The proposed trial risk classification needs to be clear and well defined. However, it should be noted that detailed provisions could add to the bureaucratic burden and cost of trial conduct, if an appropriate proportionate approach is not developed alongside this.

The research and patient community should be given the opportunity to comment on the development of the risk-based approach and categorisation. Examples of the types of trials that need to be taken into account when developing a proportionate risk-based approach include:

- Trials involving patients with terminal diseases. The potential benefit of a treatment for this patient group is likely to be greater than trials involving healthy individuals – the participants may accept different levels of risk.
- Trials of drugs in unlicensed indications e.g. in cancer patients and children, often pose a similar risk as standard care. Similarly post-market authorisation studies would benefit from a similar risk-based approach.

Consultation item no. 12: Are there other <u>key aspects</u> on which more detailed rules are needed?

No further comments.

Consultation item no. 13:

This clarification is welcome. IMPs should be subject to a risk adapted, proportionate regulatory regime.

Consultation item no. 14: insurance/indemnisation:

Both options are viable. The first solution would be more practical and could increase the speed in which a clinical trial could be established. The costs for the optional indemnisation by member states will carry only a small financial risk according to the figures in the annex.

Consultation item no. 15: Single sponsor

- If true harmonisation can be achieved and the liability issues are defined separately from the responsibility issues, then the single sponsor solution might be viable. Until then, other models (co-sponsorship) should be possible - otherwise investigator driven clinical trials in the academic setting might not be feasible.
- In order to facilitate collaboration with non-EU countries there must be a possibility for multiple sponsorship. For example, a US institution cannot act as a sponsor in Europe according to their rules, which makes EU partners very difficult to collaborate with in trials driven by American collaborative-groups.

Consultation item no. 16: emergency clinical trials

We agree with this appraisal

Consultation item no. 17: clinical trials in the third countries

We agree with this appraisal

2) General comments

- There is a general need for simplified application forms.
- Harmonisation of EC and NCA approval is required. If EC approval is conducted at a national level, clear rules have to be defined on their remit to avoid duplication of function.
- Stakeholder and patient involvement is necessary, in the development of the proposed risk-based proportionate approach to clinical trial authorisation and ongoing assessment.
- Further clarification of the Directive's definitions is needed.
- Assessment of the regulatory costs of CAP is required. Reductions in cost are urgently needed for academic-led trials.
- We would appreciate seeing a draft of the revised Directive and the risk-based proportionate approach to comment on how the ideas laid out in this consultation paper would work in practice.

We hope you find our comments useful. We would be happy to provide any further information or a representative to discuss the response further, as required. Please contact Dr Kirsten Steinhausen (ksteinhausen@esf.org, tel. 0033388762184).

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