Deutsche
Forschungsgemeinschaft
German Research Foundation

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Response to the concept paper regarding the revision of the „Clinical Trials Directive“ 2001/20/EC

The Deutsche Forschungsgemeinschaft (German Research Foundation, DFG) generally welcomes the concept paper on the revision of the „Clinical Trials Directive 2001/20/EC” submitted by the DG SANCO on 09/02/2011. Many of the suggestions and recommendations from previous discussions and publications such as the Forward Look on Investigator Driven Clinical Trials by the ESF have been implemented into this concept paper. While the suggestions in the concept paper do address aspects of protection of clinical trial subjects and credibility of results quite well, we see a lack of suggestions that actively promote and support the conductance of investigator driven clinical trials as a necessary and important element of the medical innovation process and health care improvement. This should also be more actively pursued by the Commission and the European Parliament. To carry this discussion further, the DFG provides further consultation to the addressed items as follows. If implemented well, these improvements should lead to a significant reduction of the regulatory burden for investigator driven clinical trials without compromising patient safety. Following the implementation of these changes on the EU level, the transfer into national laws and guidelines will then also have to be carefully monitored to assure comparable standards and guidelines in all Member States.

Specific comments:

1.1 Single submission with separate assessment

CI No 1: We agree that a single submission would reduce the administrative burden for multinational trials. The basis for this would be a standardised set of documents and information as well as defined rules for biometrical and statistical planning, calculation of fair direct and indirect study costs, and interaction with industry as (co)sponsor that is accepted in all Member States. This should also include a streamlined electronic submission system. National trials might be submitted to national CTAs in local language directly, but should be based on similarly standardised documentation and compatible submission systems.

CI No 2: A single submission alone would not be sufficient to address the issue of diverging local assessments. A streamlined and coherent assessment would also be needed (see 1.2.)

1.2 Single submission with subsequent central assessment

CI No 3: From a scientist’s view, ethical appraisal across different European countries should be comparable and at first hand not require a national review. However, for voluntary participation of patients in clinical trials and for the acceptance of clinical trials by the public as a whole, national perspectives might still be important and should therefore be considered. We also agree that the sheer number of multinational clinical trials would be more difficult to handle by a centralised agency. Since national trials would still need a national assessment, national regulatory authorities would still be required. These should be closely linked with the authorization process for multinational trials to make sure they all accept and follow the same standards. In summary, a centralised assessment should not be supported and a coordinated assessment procedure (CAP, see 1.3) would be favoured.

1.3 Single submission with a subsequent “Coordinated Assessment Procedure”

CI No 4: The above mentioned catalogue is complete.

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CI No 5: We agree to include the aspects under a) to the CAP-procedure. The general risk-benefit assessment can be done under the CAP procedure and, while clearly part of an ethical assessment, does not necessarily need a national perspective, given that the regulatory rules as outlined above (see 1.1) have been authorised by all Member States. It might be considered to include insurance and indemnity issues under a) rather than c).

CI No 6: A consensus agreement should always be the primary option. If this is not possible, an “opt out” by individual Member States would be the preferred. If there are major ethical concerns seen by one Member State, participation of this state should not be enforced via a majority vote.

CI No 7: CAP should be optional for multinational trials. It should still be possible for national regulatory authorities to assess national trials in their national language, but compatible with and to comparable standards with CAP. Two optional but comparable procedures might thereby help to test the better solution in a somewhat competitive way.

CI No 8: The DFG welcomes this risk based approach and the general criteria for “type-A trials”. However, further specification or examples of what “insignificant additional risk” could entail would be necessary to allow a quick and reliable assessment with low bureaucratic burden.

2.1 Better adaptation to practical requirements and a more harmonised, risk-adapted approach to the procedural aspects of clinical trials

CI No 9: The current “one size fits all” approach has clearly shown not to be suitable for investigator initiated clinical trials. The DFG therefore welcomes a more graded, risk-adapted approach as also suggested in the Forward Look on Investigator-Driven Clinical Trials by the ESF. Under these conditions, the current scope might be maintained. Notwithstanding, the border between interventional and observational trials should be clarified to achieve the same scope in all national laws and guidelines.

CI No 10: Yes, the criteria and standards for conducting clinical trials should be the same regardless of the nature of the sponsor. It should be the type of trial and the inherent patient risk that should be the guiding principle for the standards and regulations of such trials. However, care has to be taken to reduce the overall regulatory and bureaucratic burden for scientists to foster scientific innovation.

CI No 11: Yes, we agree with this appraisal. Inclusion in the annex would allow better fine tuning and adaptation by the commission by a delegated act, which would not be possible if included in the basic legal act. However, before implementing this, clear examples should be provided that this indeed leads to improvements.

CI No 12: No further rules are needed.

CI No 13: This clarification is welcome. Still, also IMPs should be subject to a risk adapted, proportionate regulatory regime.

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CI No 14: Both options would be viable with the first one being more practical and speedy in the process of establishing a clinical trial. The costs for the optional indemnisation by Member States will carry only a small financial risk according to the figures in the annex and the necessary funds required will be much less than what would be spent by public funding agencies on insurance costs.

CI No 15: If a true harmonisation can be achieved and the responsibility issues are defined separately from the liability issues, then the single sponsor solution might be viable in the long term. Until then, other, shared-sponsorship models should be supported as well, otherwise investigator driven clinical trials in the academic setting might not be feasible. Therefore, shared-sponsorship models should be supported now and the implementation of the responsibility issues on the national level have to be carefully monitored. Only when true harmonisation has been achieved will the single-sponsorship model become viable.

CI No 16: Yes, we agree with the appraisal.

CI No 17: Yes, we agree with this appraisal. Conductance of clinical trials according to GCP should be a basic requirement for all clinical trials. This should, however, take into account different types of trials (e.g. observational, interventional; low-risk, high-risk) where the general GCP-requirements should be adapted accordingly.

CI No 18: No further comments or quantifiable data.