EUROPEAN COMMISSION
Health and Consumers Directorate-General
Public Health and Risk Assessment
Pharmaceuticals

Issue **Comments of National Committee on Medical Research Ethics on the revision of the "Clinical Trials Directive" 2001/20/EC; concept paper submitted for public consultation**

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The National Committee on Medical Research Ethics in Finland (TUKIJA) appreciates the consultation which is based on the initiative of the Commission to propose a revision of the "Clinical Trials Directive" (CTD).

Major Comments

Commission criticizes that CTD is applied differently in the different Member States. CTD does not provide any mechanism whereby the application for the clinical trial is submitted jointly to all Member States concerned, nor does it require that Member States concerned work together to assess or follow up the request for authorisation. All clinical trials are currently assessed independently by the various Member States concerned.

TUKIJA would like to see the current situation of assessment procedures as a starting point in the future too. With some minimal changes the CTD provides a clear and relevant legal framework across the EU. In other words TUKIJA does not support the centralisation of the authorisation process. There are three main reasons for this conclusion:

1. At the Member State level clinical trials on medicinal products consist of large variety of local and national actors and institutions, e.g. investigators, supporting staff, research subjects, research centres, the authorities etc. To be able to formulate a clear and understandable insight on what an individual trial may actually mean for national and local infrastructure, what are the relevant preconditions (language; health care system; medical standards; cultural traditions and variations etc.) to be taken into account, and what are the foreseeable benefits of an individual trial, the evaluation of the entire research proposal must be done independently by each Member State concerned. In addition the principle of subsidiarity requires that the administrative and organizational matters ought to be handled by the local authorities.

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2. It is mentioned in the consultation paper that identical information directed to several Member States creates unnecessary administrative costs. However, this statement is not offered any justification whatsoever. TUKIJA believes that as an additional level of assessment procedure, CAP does not minimise duplication and reduce administrative burdens in general. In fact, it can create both additional costs and delays in application process. CAP is clearly an extra administrative tier because some part of the authorization must be done at the national level anyway. The CAP may even hamper the understanding of the respective roles and responsibilities of both the national authorities and the separate Member States. It is not discussed in the consultation paper what kind of implications the CAP might have for the responsibilities of the national competent authority and for the ethics committee. One of the benefits of the implementation of the current CTD is the greater understanding of the roles of both authorities. TUKIJA believes that excessive harm can be done to the coordination between the authorities by leaving these clarifying elements out of the scope of the revised Directive.
3. Any attempts to limit the independence of the ethics committees should be avoided. Competent authorities and ethics committees have clearly separate roles in protecting the patients. Overlap in the scope of the assessment is not necessarily a disadvantage. If anything, it gives the best possible guarantee of local and cultural variations to be taken into account properly.

Chapter 1.1 (items 1 and 2) Single submission with separate assessment

Single submission may reduce the administrative work of sponsors. However, it easily multiplies the work of authorities. It might be difficult to work within a reasonable timelimit if the authorities do not have direct contacts or communication with the sponsors.

Chapter 1.2 (item 3) Single submission with subsequent central assessment

This option is clearly not feasible, therefore TUKIJA agrees with the Commission.

Chapter 1.3 (items 4 -8) Single submission with CAP

CAP is clearly an extra administrative burden because some part of the authorization would be done at the national level anyway. What would "joint assessment" mean and include? Is ethical evaluation intended to be included in the concept of "joint assessment"? Ethical evaluation of clinical trials must remain under the jurisdiction of the individual Member States.

It is stated in the consultation paper that ethical issues clearly fall within the ambit of Member States. Later on it is presented that there are three areas of the CAP, which are to be considered in the clinical trials application. One of these areas is "Ethical aspects related to informed consent, recruitment and reward". TUKIJA would like to remind that there are several ethical aspects in every clinical trial, which are not

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limited to recruitment. The ethics committees must evaluate whether trials have been planned in an ethically acceptable manner so as not to cause unnecessary harm or risks to potential research subjects. An assessment of the scientific rationale (study design, risk-benefit aspects, study objectives etc.) is therefore an essential duty of the ethics committee. To be able to fulfil their duty, ethics committees must have a clear and comprehensive insight of the complete clinical trial.

Under paragraph 1.3.2 the Commission suggests that individual Member State may have a right to "opt out" under the CAP, on the basis of a "serious risk to public health" or "safety of the participant". From the TUKIJAs point of view, the justification for not approving an individual clinical trial can vary in a way that cannot be determined beforehand.

The Commission suggests (1.3.4) that evaluation timelines could be shortened where the risk to the trial subjects is low and where the assessment in the CAP is limited largely to issues of reliability of the data. Furthermore, these so-called type A- trials could be identified in a pre-assessment. TUKIJA does not see it conceivable to shorten the timelines of ethical evaluation. Typically ethics committees have meetings once a month and the members work on a voluntary basis. These preconditions have to be taken into account when considering any revisions to the CTD. TUKIJA considers the operative timeframes sufficient.

Chapters 2.1 and 2.2 (items 9, 11 and 12): The scope of the CTD and safety reporting

As far as the definition of the non-interventional trials is concerned, TUKIJA agrees with the view of the Commission that the scope of the present CTD is appropriate and functional.

TUKIJA finds it advisable to concentrate the reporting requirements only to NCA since the NCA oversees all the usage of medicinal products. Ethics committees are not in a position to actively monitor the safety data of the clinical trials. This kind of change to the CTD would significantly minimize the administrative burden of the safety reporting procedures.

Chapter 2.4 (item 14): Insurance/indemnisation

With regard to this issue, the Commission offers two policy options to be considered: removing insurance /indemnisation requirements for low-risk trials and establishing optional indemnisation by Member State. In latter case the reasoning seems inconsistent with what the Commission has stated earlier in the same chapter. To start with Commission argues that the costs of the insurance would restrain research but later on it estimates that the burden on the national budgets would be minimal.

By removing the insurance/indemnisation requirements one cannot remove the responsibility for the safety and well-being of the participants. In the case of the possible damage the liability for damage might be inconvenient process both for the participant and for the sponsor/investigator.

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Chapter 2.6 (item 16) Emergency clinical trials

Also the patients in medical emergency situations have a right to receive evidence-based medicine of the highest standards. In certain precondition emergency trials can be justified without free and informed consent of the research subjects or her /his legal representative.

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