Comments from Les Laboratoires Servier

SANCO/C/8/PB/SF D(2011) 143488

REVISION OF THE 'CLINICAL TRIALS DIRECTIVE' 2001/20/EC
CONCEPT PAPER SUBMITTED FOR PUBLIC CONSULTATION

1. COOPERATION IN ASSESSING AND FOLLOWING UP APPLICATIONS FOR CLINICAL TRIALS

Preliminary appraisal: A single submission would greatly reduce the administrative work of sponsors for submission of documentation to the Member States concerned.

Consultation item n°.1: Do you agree with this appraisal? Please comment.
Les Laboratoires Servier do not agree with this appraisal because even if there will be one application dossier for submission, we will always have independent assessments by each Member State. So first, application dossier will be the same then could change in one Member State after questions, leading to some difficulties in a further international amendments managing.

Preliminary appraisal: A separate assessment would insufficiently address the issue set out above. The difficulties created by independent assessments would remain.

Consultation item n°.2: Do you agree with this appraisal? Please comment.
We do not agree with an independent assessment by each Member State because a separate assessment does not resolve the difficulties created.

Preliminary appraisal: A central assessment is not appropriate for clinical trials approval and would, as regards clinical trials, not be workable in practice for some reasons.

Consultation item n°.3: Do you agree with this appraisal? Please comment.
A central assessment will not be appropriate for clinical trials approval for the following reasons provided in the concept paper:

- this option would insufficiently take account of ethical, national, and local perspectives. For these aspects, a parallel, national, procedure would have to be established in any case.
- The sheer number of multinational clinical trials per year would make centralised assessment very difficult. To this would add all substantial amendments of the clinical trials.
- The involvement of all Member State is not needed, as very few clinical trials are rolled out in more than five or six Member States.

Preliminary appraisal: The CAP could offer a sufficiently flexible approach. It allows for a joint assessment without a cumbersome committee structure. It would allow national practice

to be taken into account. It would respect that, as a basic rule, ethical issues clearly fall within the ambit of Member States.

Only the aspect under point a) would be suitable for the CAP. In particular, the aspects under b) and c) are not suitable for the CAP as they relate to ethical issues (as is the case for b) or to local expertise (as is the case for c).

Consultation item n°.4: Is the above catalogue complete?
Yes

Consultation item n°.5: Do you agree to include the aspects under a), and only these aspects, in the scope of the CAP?
Yes and it will be important to avoid to submit a national dossier for these aspects. Additional national requirements should not be permitted and there should be no expectations for additional 'country-specific' documents or translations.

Comment : the responsibilities of the 'Reporting Member State' would need to be clearly defined, and also the proposed process for deciding the Reporting Member State.

Disagreement with the assessment report

Consultation item n°.6: Which of these approaches is preferable? Please give your reason.
The Member States concerned could vote on the issue and decide by simple majority: this seems to be the preferable approach. This approach could permit an "European approval" without different application in the Member States concerned by the clinical trial application. Furthermore, the last option, i.e. to refer to the Commission or the Agency seems not to be really applicable because of the numerous of clinical trials and could lead to a lost of time in the assessment of the trial.

Mandatory/optional use

Consultation item n°.7: Which of these three approaches is preferable? Please give your reasons.
The first option (mandatory for all) will be the preferable approach because in case of a single country clinical trial with the possibility of extending the clinical trial to an additional Member State after the trial has been authorised, a joint assessment would avoid divergence between Member States involved.

Tacit approval and timelines / Pre-assessment

Consultation item n°.8: Do you think such a pre-assessment is workable in practice? Please comment.
Yes such a pre-assessment will be workable in practice but terms and conditions should be specified in order to avoid a lot of questions regarding the scope of this pre-assessment. Furthermore, the requirements should be determined in case of marketed product used outside conditions of the SmPC (e.g. new indication).

With this assessment, the timelines could be shortened. But which rules will be provided?

2. BETTER ADAPTATION TO PRACTICAL REQUIREMENTS AND A MORE HARMONISED, RISK-ADAPTED APPROACH TO THE PROCEDURAL ASPECTS OF CLINICAL TRIALS

Preliminary appraisal: Rather than limiting the scope of the Clinical Trials Directive through a wider definition of 'non-interventional trial', it would be better to come up with harmonised and proportionate requirements which would apply to all clinical trials falling within the scope of the present Clinical Trial Directive.

Consultation item no. 9: Do you agree with this appraisal? Please comment.
We do not agree to broaden the definition of 'non-interventional' trials, excluding more studies from the scope of the Clinical Trials Directive: this would limit the impact of the Clinical Trials Directive. Moreover, this would also undermine past and future efforts to harmonise Clinical Trial legislation.

Preliminary appraisal: Rather than limiting the scope of the Clinical Trials Directive, it would be better to come up with harmonized and proportionate requirements for clinical trials. These proportionate requirements would apply independently of the nature of the sponsor ('commercial' or 'academic/non-commercial').

Consultation item no. 10: Do you agree with this appraisal? Please comment.
We do not agree to exclude clinical trials by 'academic/non-commercial sponsors' from the scope of the Clinical Trial Directive. If they were excluded from the scope of the Clinical Trials Directive, Member States would be responsible for regulating these trials via national laws. This would introduce differences in trial subject protection in the EU.

Preliminary appraisal: This approach would help to simplify, clarity, and streamline the rules for conducting clinical trials in the EU by providing one single, EU-wide, risk-adapted set of rules.

Consultation item no. 11: Do you agree with this appraisal? Please comment.
This kind of Annexes to the basis legal act would help to simplify, clarify and streamline the rules for conducting clinical trials in the EU but these texts need to be transposed in national laws leading to some potential divergences between each Member State as well as to some time gaps for transposition between each Member State.

Consultation item no. 12: Are there other key aspects on which more detailed rules are needed?
No.

Preliminary appraisal: This combined approach would help to simplify, clarify, and streamline the rules for medicinal products used in the context of a clinical trial.

Consultation item no. 13: Do you agree with this appraisal? Please comment.
This combined approach would help to simplify, clarify, and streamline the rules for medicinal products used in the context of a clinical trial and refers to the "VOLUME 10 - GUIDANCE ON INVESTIGATIONAL MEDICINAL PRODUCTS (IMPS) AND 'NON INVESTIGATIONAL MEDICINAL PRODUCTS' (NIMPS) (REV. 1, MARCH 2011)".

Preliminary appraisal: Both policy options could be a viable solution

Consultation item no. 14: Which policy option is favourable in view of legal and practical obstacles? What other options could be considered?
None policy option is favourable in view of legal and practical obstacles.

Preliminary appraisal: In view of the above, option 1 may be preferable, provided that.

- *It is clarified that the 'responsibility' of the sponsor is without prejudice to the (national) rules for liability; and*
- *It is ensured that the regulatory framework for clinical trial in the EU is truly harmosised (see point 2.2).*

Consultation item no. 15: Do you agree with this appraisal? Please comment.
We agree to maintain the concept of a single sponsor who is 'responsible' for the trial vis-à-vis the national competent authority and the Ethics Committee.

Preliminary appraisal: This could be a viable option in order to address this type of research and bring the regulatory framework in line with internationally-agreed texts.

Consultation item no. 16: Do you agree with this appraisal? Please comment.
We do not agree with this appraisal because it seems not really applicable according the recent legislation approved in this area. Otherwise, the application conditions should be clearly specified and determined.

3. ENSURING COMPLIANCE WITH GOOD CLINICAL PRACTICES IN CLINICAL TRIALS PERFORMED IN THIRD COUNTRIES

Consultation item n°.17: Do you agree with this appraisal? Please comment.
Regarding the point about the registration of the trial in the EU clinical trials database EudraCT and the publication of the results via the public EU-database EudraPharm, we would prefer to continue to use the public website such as "ClinicalTrials.gov" and "ControlledTrials.com". Clinical studies are already conducted in accordance the Good Clinical Practice as specified in the clinical study protocol and the study report.