Template for comments

Date: 11 January 2010	Document Title**:** Assessment of the Functioning of the clinical trial directive "2001/20/EC"

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Page	Chapter No./ Annex (e.g. 3.1)	Paragraph/ Figure/Table/Note (e.g. Table 1)	Question	Response
10	2.5.	Consultation item No1	Can you give examples for an improved protection? Are you aware of studies/data showing the benefits of Clinical Trials Directive?	No.
12	3.1	Consultation item No 2	Is this an accurate description of the situation? What is your appraisal of the situation?	This is in our opinion a correct description of the situation. Competent Authorities can come back with many different questions and divergent opinions.
14	3.2	Consultation item No 3	Is this an accurate description? Can you quantify the impacts? Are there other examples for consequences?	Yes, this is an accurate description. Indeed, a doubling of resources seems an adequate estimate. An indirect consequence is the development of country specific amendments resulting from different requests from the NCAs.
16	3.3	Consultation item No 4	Can you give indications/quantifications/examples for the impact of each option? Which option is preferable? What practical/legal aspects would need to be considered in	Community wide streamlining would be preferred to ensure significant changes. Member States might have specific processes in place endorsed by local legislation which they do not feel need to be changed. When opting for the community wide streamlining the impact will be more significant.

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			further detail?	Within the Streamlining option, different degrees are suggested to be considered. The option of an authorization of a clinical trial of the entire Community by one body, seem to be the preferred option. This will not only ensure there is truly one assessment process and thus ensure consistency across submission, assessment, questions and reply as well as to approval. This One Body option would be most transparent. However, it might complicate assessment for (academic non-commercial) sponsors who engaging in local clinical trials. For this reason, it could be considered that the One Body will not assess the local (one Member State) assessments. For international organized Pharma mainly executing international clinical trials, this assessment process will have similarities to the Marketing authorization process. One concern to such a more significant change would be the impact on timelines of the assessment. There will be an impact on resource for this One Body with the risk of increasing assessment times. Especially upon implementation of such a new process. Another advantage of One Body would be that the overlap with the EC will be decreased although the ECs could take on the "responsibility" of ensuring local legislation will be covered in the clinical trials submitted. This local legislation could also be an obstacle in implementing of this option. It is very important to clearly define what the different responsibilities are between CA and EC and on which part of the submission they can comment in order to avoid these bodies to make divergent comments to the same part of the submission. This would help a lot to reduce further discussion after submission.
17	3.4	Consultation item No 5	Can you give indications/quantifications/examples for the impact of each option? Which option is preferable? What practical/legal aspects would need to be considered in	The 'one-stop shop' would be the preferred option. Strengthening the network between ECs seems to have no clear advantage.

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			further detail?	
20	4.1	Consultation item No 6	Is this an accurate description of the situation? Can you give other examples?	This is a correct description of the situation. One other example of a divergent opinion between the member states is the definition of an IMP and non-IMP. In addition, there are different requests on comparative tables (as is currently obligatory in France) for the IMPD and IBs as compared to the previous version.
20	4.2	Consultation item No 7	Is this an accurate description? Can you quantify the impacts? Are there other examples for consequences?	Yes, the description is accurate. Further examples of consequences are time delay, too complicated trials and country specific amendments.
21	4.3	Consultation item No 8	Can you give indications/quantifications/examples for the impact of each option? Which option is preferable? What practical/legal aspects would need to be considered in further detail? In particular, are the divergent applications really a consequence of transposing national laws, or rather their concrete application on a case-by-case basis?	There should ideally be a centralized, uniform approach to reporting SUSARs into a single database. Rational: This would ensure one consistent, more efficient process. If all NCAs and ECs concerned are given the appropriate access to or are forwarded the appropriate SUSAR reports, this would be a significant improvement.
22	5.2.1	Consultation item No 9	Can you give examples for an insufficient risk-differentiation? How	Do not categorize clinical trials into risk categories (eg low, medium and high). Processes would need to be set up to for decision making. Parallel running of these

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			should this be addressed?	risk category processes would provide unnecessary burden and complexity.
22	5.2.2	Consultation item No 10	Do you agree with this description? Can you give other examples?	No comments
23	5.4.1	Consultation item No 11	Can a revision of guidelines address this problem in a satisfactory way?	Reduce costs. IMP should be looked at on a more case by case basis.
23	5.4.2	Consultation item No 12	In what areas would an amendment of the Clinical Trials Directive be required in order to address the issue? If this was addressed, can the impacts be described and quantified?	No requirements to submit information (apart from the ICF) in another language than English; no additional requirements for local forms, certificates, specific forms etc.
24	5.4.3	Consultation item No 13	Would you agree to this option and if so what would be the impact?	No. If the CTD was set up for the safety of patients, there should be no exemption for academics on the requirements. One may exempt the academic centers from the fees.
26	6.2	Consultation item No 14	In terms of clinical trials regulation, what options could be considered in order to promote clinical research for paediatric medicines, while safeguarding the safety of the clinical trial participants?	It could be considered to emphasize more on PK/PD studies in the younger patient population.
26	6.2	Consultation item No 15	Should this issue be addressed? What ways have been found in order to reconcile patient's rights and the	This issue should indeed be addressed. As stated in the consultation document the Declaration of Helsinki (referenced #46) already has statements around enrollment of physically or mentally incapable patients giving consent (if unable to give informed

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			peculiarities of emergency clinical trials? Which approach is favourable in view of past experiences?	consent as soon as possible). Similarly the CTD could address this issue. The cases under discussion should be limited to cases where the patient is incapable to provide prior consent due to the illness under investigation or related to the illness under investigator. The approach that would be favorable is that regulations would permit enrollment without prior informed consent in these cases which are clearly described in the protocol and that each case is documented upon enrollment without the prior consent. This process (and the protocol describing it) should be approved prior to CA and/or EC. It would be suggested that the process and not every individual case is endorsed by EC. This process approval would ensure consistency across different institutions running the trial.
29	7.1	Consultation item No 16	Please comment? Do you have additional information, including quantitative information and data?	The only comment I have here is that it sounds most logic to me that the only way this (sh)could be addressed is by mandating that the trials being used for submission of a marketing application should follow international/global acceptable standards like ICH-GCP. A clock stop would not be acceptable. But same standards should be applied in EU and non-EU countries.
31	7.3.6	Consultation item No 17	What other options could be considered, taking into account the legal and practical limitations?	Trials should always be multinational with at least one European country.
32	7.3.6	Consultation item No 18	What other aspect would you like to highlight in view of ensuring the better regulation principles? Do you have additional comments? Are SME aspects	No comments

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			already fully taken into account?	