2019

Submission of comments on 'Questions and answers on Data Monitoring Committees Issues ' (EMA/…/…)

Name of organisation or individual
Arbeitskreis Medizinischer Ethik-Kommissionen in der Bundesrepublik Deutschland e.V (Association of Medical Ethics Committees in Germany)

Please note that comments will be sent to the relevant **ICH EWG** for consideration in the context of Step 3 of the ICH process.

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)

The Association of Medical Ethics Committees in Germany represents all Ethics Committees in Germany that are involved in the assessment of clinical trials with medicinal products and medical devices. We appreciate that the EMA has initiated a public consultation on the draft ‚Questions and answers on Data Monitoring Committees Issues' . This offers the chance to contribute to the further improvement of this document.

General comment:

The Q&A paper should start with a clear definition of the term DMC so that everybody knows what it is. We suggest to use the definition as used in the Guideline on Data Monitoring Committees (EMEA/CHMP/EWP/5872/03 Corr):
„Data Monitoring Committees A Data Monitoring Committee is a group of independent experts external to a study assessing the progress, safety data and, if needed critical efficacy endpoints of a clinical study. In order to do so a DMC may review unblinded study information (on a patient level or treatment group level) during the conduct of the study. Based on its review the DMC provides the sponsor with recommendations regarding study modification, continuation or termination. Data Monitoring Committees also go under different names like Data Monitoring Board or Data Safety Monitoring Committee (Board).“

We think that the terms ‚independent' and ‚external' are extremely important to characterize a DMC, and thus these characteristics should allways be stressed.

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes
44-46		Comment: In Germany the law and ordinances provide explicitly the option for an ethical advice too, provided by the competent EC. In some EU MS (e.g. The Netherlands) basically the ECs authorize clinical trial applications. Thus this Q&A document should mention this option too. Proposed change (if any):Line 45: ….,the Sponsor may also wish to discuss the amendment with the competent regulatory authority **and/or ethics committee(EC)** during a scientific **and/or ethical advice** consultation before implementation.
48		Comment: The laws and regulations in many EU MS ask ECs to play a specified role while a trial is ongoing, e.g. re SUSARs, early stopping, risk/benefit monitoring. The Declaration of Helsinki states in 23. Too: "The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events." Thus we propose a change in the text as proposed. Proposed change (if any):…..between competent regulatory authorities, **ethics committees** and a DMC possible?
50 57 59 66 72-73		Comment: consequent to Comment line 48 Proposed change (if any):….competent regulatory authorities **and/or ethics committees** on all matters….. Proposed change: ….. competent regulatory authorities **and/or ethics committees** may consider……. Proposed change: ….. competent regulatory authorities **and/or ethics committees** but not to the DMC…. Proposed change: ….. competent regulatory authorities **and/or ethics committees** is needed….. Comment: The investigators should be informed without undue delay only about whether the trial can go on, or not.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		If the sponsor disagrees with this recommendation of the DMC, his position and rationale should accompany the recommendation of the DMC for the investigators. The rest, e.g. recommended modifications of the trial protocol etc. are in the sole responsibility of the sponsor. Finally, any additional information to the investigators beyond the go on/stop recommendation may introduce bias and endangers the validity and integrity of the trial.
75-81		Comments: The term safety review committee (SRC) is lacking a clear definition. Please specify the difference to a DMC. The headline uses the term DMC whereas the text uses the term safety review committee only. Please adjust accordingly.
76 77		In our experience most often safety and efficacy aspects have to be considered at the same time by a DMC. In many, not only in oncology, early trials, pharmacodynamic outcomes are measured too. In addition many laws, regulations and conventions ask that the risk/benefit balance has be continuously monitored.
82-95		**We are definitely in favour for having a DMC according to the definition mentioned above for all trial related advices and consultations. In case additional information that only the sponsor or a CRO knows, is needed, their representatives may report to the DMC, but all detailed deliberations and decisions by the DMC should be done only by the independent and external members of the DMC. We doubt that an internal SRC provides any added value re safety and wellbeing of the research subject compared to a true DMC. Therefore we suggest to delete lines 82-95 completely.**
		We are not convinced that it makes sense to prioritize the need for a SRC/DMC for early clinical trials vs. later ones. The risks of later trials regarding receiving an inferior treatment and to suffer from an irreversible endpoint does in our opinion not allow for any prioritisation due to being early or late.
76		Proposed change: ….intensive safety **and/or efficacy** monitoring in….
77		Proposed change:…. monitors **and/or efficacy and risk/benefit** aspects…..
78		Proposed change: ….is usually **high** in first in…..

Please add more rows if needed.