LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

2016-08-31

Dnr: 3.4-2016-064613

European Commission
SANTE-B4-GL-risk-proportionate-approach
F101 08/058
B-1049 Brussels
Belgium

Comments from the Medical Products Agency to the public consultation on "Risk proportionate approaches in clinical trials"

1. General comments

1. We would recommend not to finalize this guidance document on "Risk proportionate approaches in clinical trials" until the ICH GCP E6(R2) addendum has been finalized, in order not to cause any conflicting wording between the two documents, especially in regard to section 4.4. This addendum is now in step 3, why it should be possible to wait with this guideline from the European Commission.

2. As requirements may differ and an overall study design may be affected by a risk based approach assessment, sponsors are recommended to seek prior national or central scientific advice.

2. Specific comments

Line number in original document	**Proposed change** and *rational*
223	Insert "low-intervention" in the sentence explaining Table 1. Table 1 below highlights the specific areas where the Regulation sets out possibilities to apply risk adaptations ("less stringent rules") in the design and conduct of ***low-intervention*** clinical trials. " *Articles mentioned in the Table (e.g. Articles 48, 51,57 refer to simplifications explicit in the legal text for the category of trials defined as "low-intervention clinical trials)*
251-252	Delete "**as being potentially related to the IMP, and therefore representing**

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.lakemedelsverket.se E-mail: registrator@mpa.se

	adverse reactions". *Regulation 536/2014 Article 41.2 states that "The investigator shall record and document all adverse events, unless the protocol provides differently". The sentence on line number 251 starts with "As a general rule, ... " and should therefore reflect Article 41.2. Thus, the issue if an adverse event is potentially related to the investigational medicinal products or not is not correct in this sentence. Such limitations in reporting is rather part of a possible risk adaptation, as described on line 257 and onwards.*
386	Insert, "as described in ICH Guideline E6 for Good Clinical practice" in first sentence: Centralised monitoring process, ***as described in ICH Guideline E6 for Good Clinical practice.*** *This reference to ICH GCP is important as the term centralised monitoring could be (and is) interpreted very differently by different parties.*
388-390	Delete sentence starting "On-site monitoring…" and replace with: **"Some extent of on-site monitoring remains a general requirement in the majority of clinical trials, as it is instrumental for the verification of several critical aspects at the trial site, for e.g. the informed consent process, source data verification and IMP handling on site."** *This change is needed to be in to be in line with ICH GCP 5.18.3*
392-394	Delete sentence starting "The level of onsite…." and replace with: **"The level of on-site monitoring activities may vary from frequent and extensive monitoring to low frequency of visits with only targeted monitoring activity, or targeted visits to certain sites only or there may be no on-site visits in certain trials."**
399-400	Delete sentence starting "Centralised

	and/or on-site monitoring" and replace with: **"Centralised and/or on-site monitoring can be used with flexibility to adapt to the requirements and observed quality of reported data throughout the life cycle of a trial."**
411-412	Delete nine words in sentence after "…reported data". **"Centralised monitoring enables the review of reported data ~~/ information, remote contact, communication and training where relevant and~~"** *The deleted part is not relevant in this sentence. Do not mix with the term centralised monitoring.*