LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

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European Commission
SANTE-B4-GL-ethics-minors
F101 08/058
B-1049 Brussels
Belgium

Comments from the Medical Products Agency to the public consultation on "Ethical Considerations for Clinical Trials on Medicinal products conducted with Minors"

1. General comments

1. We would recommend not to finalize this guidance document on " Ethical Considerations for Clinical Trials on Medicinal products conducted with Minors" until the addendum ICH GCP E11(R1) has been finalized, in order not to cause any conflicting wording between the two documents. Since this addendum is only in step 1, an alternative is to refer to the addendum process in the document.

2. Specific comments

Line number in original document	***Proposed change*** and *rational*
543	Insert after "some restrictions" "e.g. the need for a direct clinically relevant benefit for the subject resulting in a measurable health-related improvement alleviating the suffering and/or improving the health of the subject, or in the diagnosis of its condition" "Article 35 of the Regulation provides for derogation from prior informed consent requirement, including paediatric trials in emergency situations, with some restrictions, ***e.g. the need for scientific grounds to expect that participation of the subject in the clinical trial will have the potential to produce a direct clinically relevant benefit for the subject resulting in a measurable health-related improvement alleviating the suffering and/or improving the health of the subject, or in the diagnosis of its condition***". *The wording "some restrictions" does*

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	not explain the need for scientific grounds to expect that participation of the subject in the clinical trial will have the potential to produce a direct clinically relevant benefitfor the subject. This prerequisite must be fulfilled when allowing clinical trials in emergency situations without informed consent.
738	***Define*** "smart trial designs". *Essential from a regulatory perspective is the need of robust results of sufficient quality. A definition of smart design would be preferred.*
880-882	Delete reference to "Reflection paper on the need for active control in therapeutic areas where use of placebo is deemed ethical and one or more established medicines are available" *The reflection paper referred to is not finalized, why the reference should be removed.*
885-894 vs 915-917	The sections 9.2.2 and 10 appear inconsistent. *A conservative and critical view on non-inferiority design is expressed in section 9.2.2 whereas such trials appear to be potentially acceptable in a number of situations in section 10. We should strive for consistency. Furthermore, the Medical Products Agency believes that it is important to open up for well-designed non-inferiority trials also in minors, e.g. in situations where potential safety advantages are expected combined with non-inferior efficacy.*
Annex I, point 13	Among the listed issues, item 13 could be deleted. ~~**Design feasibility trial burden checked with children / patient and family representatives.**~~ *Although we agree that this is desirable, it is not obligatory. Today, such groups only exist in a few EU Member States.*