Children's Research Industry Group (CRIG) response to Commission guideline on the format and content of applications for Paediatric Investigation Plans (Article 10 of Regulation (EC) No 1901/2006) - concept paper submitted for public consultation

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Please note this response was prepared by CRIG members, but does not necessarily reflect the views of the companies that CRIG members work for or the NIHR Medicines for Children Research Network (MCRN) that has convened CRIG.

Consultation item No 1: Do you have any comments on the format and content of applications for agreement on or modification of a paediatric investigation plan and requests for waivers or deferrals?

Line 14 – 22: CRIG members were concerned that the definition of condition can be interpreted broadly, and this could lead to companies being required to undertake studies in several paediatric indications.

Line 14 – 40: Can a definition of the product be included in section 1 to complement definitions of condition, paediatric investigation plan indication, proposed indication etc?

Line 148 - 151: CRIG members wonder whether it essential to ask for details of any decisions, opinions or advice given by competent authorities on the paediatric development of a product?

Line 163 – 166: CRIG members would like to inquire whether submission of PIPs shortly after completion of adult pharmacokinetic studies reflects actual practice, or have most PIPs been submitted later in development? CRIG members would like to further inquire whether there is an opportunity to harmonize with the US requirement for submission shortly after adult Phase 2, when more information is available to inform the development of a PIP? CRIG members recognize this may require revision of Article 16 of the Paediatric Regulation (EC 1901/2006), but believe that the submission of a PIP after Phase 2 would increase the soundness of the submission, thereby decreasing the number of modifications requested after initial approval. Alternatively, an outline PIP could be prepared in the early stages of product development, with a full PIP developed at the end of phase 2 studies.

Line 189 – 190: For vaccines or products being developed only for children, could consideration be given for PIP development/additional PDCO processes to not be required? Similarly, as EMA has a regulatory process for orphan/rare diseases products, is it necessary for the PDCO to also assess products? Additional processes risk delaying product approval.

Line 216 – 217: In this section on current methods of diagnosis, prevention or treatment in paediatric populations, it is stated that, "Information on generic medicinal products need not be provided." CRIG members recommend adding the qualifying statement, "provided the innovator product is identified" because it can be that the innovator product is no longer marketed.

Line 413: Could points be included within section 2.5.4.1 to encourage applicants to consult with Enpr-EMA or members of national/specific research networks when developing PIPs?

Lines 421 – 422 requests an extrapolation protocol. CRIG members recommend an expanded description of what would be contained in an extrapolation protocol. In addition, some of the rows in the table in the PIP template for an extrapolation study are not easily completed (e.g. do study population, number of participants apply to the original study that is being extrapolated from?)

Lines 468 – 470: Regarding timelines, the concept paper appears to allow for timelines to be expressed relative to the completion of adult studies, which would be a welcome revision that would be expected to significantly decrease the number of requests for PIP modifications. Provided this is the intent, CRIG members recommend to revise the sentence for clarity to state, "Alternatively, timelines for initiation may be linked to the completion of a study in adults ('x months after completion of study y) or a measure in the paediatric investigation plan, provided a duration is also specified for the measure."

Lines 502 – 504: As an extension of the previous comment, for clarity revise to read, “For timelines, specific months and years should be given, or timelines may be expressed in relation to the development in adults.”

Line 515: Because the Investigators’ Brochure (IB) and protocols serve two different purposes and contain different types of information, they should be listed separately. The IB provides information on CMC, non-clinical and clinical studies already performed, whereas the protocol describes studies yet to be completed.

Consultation item No 2: Do you have any comments on the operation of the compliance check and/or the compliance statement?

No comments

Consultation item No 3: Do you have any comments on the assessment criteria for significant studies?

No comments

Consultation item No 4: Do you have any comments on the key elements of a paediatric investigation plan? Is it appropriate to list key elements in this guideline or should key elements only be specified in the individual decision of the Agency agreeing a specific paediatric investigation plan?

No comments

Consultation item No 5: Please feel free to raise any other issues or make any comments which have not been addressed in the consultation items above.

No further comments