19.12.2013

Submission of comments on 'Commission Guideline on the format and content of applications for paediatric investigation plans', Article 10 of Regulation (EC) No. 1901/2006

Comments from:

Name of organisation or individual
Pfizer Limited - EU Transparency Register # 4263301811-33

General Comments

Stakeholder number	General comment (if any)
	Pfizer supports the comments submitted by EFPIA on the proposed revisions to the Commission Guideline and offers in this document certain supplementary points of particular interest to the company. We welcome the opportunity to provide input on the Guideline. We consider the further clarification it provides to be useful, yet in places further clarity or context would be desirable. Generally, considering that this is a much-debated Guideline, it may be helpful to provide further detail in some areas as highlighted below. We note that the Consultation Paper does not propose substantial changes, which would be the preferred eventual solution, as the Paediatric legislation has significant potential for improvement.

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 number(s) of the relevant text	Comment and rationale; proposed changes
Covers Lines 48 - 541	
48	Comment: Part A form of Administrative and product information is difficult to use, particularly for injectables. Proposed change: Simplification of form, particularly as drop-down menus restricting choices are not particularly useful. The documentation should make it easy for the PIP Decision to be prepared at the end of the procedure - it should be very clear which sections are part of the Decision - perhaps the Part A could be reformatted to achieve this.
51	Comment: There should be the option for a "light" PIP application which acknowledges that paediatric work will be conducted, but later in development, so that a reduced PIP could be filed initially.
57	Comment: If the extensive PIP B-E template was broken down into individual sections, this may be easier. Proposed change: Break down PIP B-E template for ease of overview.
78	Comment: We note that it is stated on page 5 of the introduction to this Consultation Paper that the EMA "took the following approach: It mentioned specifically rather than implicitly the possibility of having multiple paediatric investigation plans for the same product." However, this does not appear to be mentioned expressly in the draft Commission guideline. We believe there should be a more explicit reference in the PIP guidance to the possibility of multiple PIPs. Proposed change: Include that for both article 7 and 8 submissions one PIP or multiple PIPs with links

Line number(s) of the relevant text	Comment and rationale; proposed changes
	between Decisions via a cross reference are permitted. Further, the full compliance opinion from the PDCO will be issued upon completion of the PIP relating to the condition which is the subject of the first MAA for the product.
88	Comment: The PIP Q & A page on the EMA web site is useful in PIP preparation.
91	Comment & Proposed change: The Part A form needs to be simplified/reformatted to make it clearer - as mentioned above the pdf drop down menus and filled fields are not helpful.
105	Comment & Proposed change: With regards to the application form it would be more useful for compounds in early development to use the company's compound number name rather than a scientific designation - which is not necessarily molecule / biologic specific - this company compound number could simply be updated with the INN when it becomes available; for example see PCSK9 compounds on EMA PIP website.
106	Comment: The term 'exact scientific designation' may be confusing – if this is eg. the IUPAC name or CAS name and number then this should be clarified. Proposed change: Refer explicitly to IUPAC / CAS nomenclature in the text.
167	Comment: This document could contain elements of the draft decision - see Part A comments; so that there is a specific use for this information instead of duplicating information. Proposed change: This document would benefit from being tabular in nature.
256	Comment: It would be better to have a reasonable set of adult data to facilitate therapeutic benefit discussions – instead of making assumptions.
332	Comment: Age ranges should reflect ICH classification in most instances.
332	Comment: The text states that "the application should outline the development of the medicinal product, including the pharmaceutical development." It remains unclear what level of detail is expected for this

Line number(s) of the relevant text	Comment and rationale; proposed changes
	development 'outline' and how this 'outline' relates to PIP commitments through the 'key elements' that will be considered in validation of the PIP on submission of the product's MAA. Proposed change: It should be clarified how this 'outline' is related to the 'key elements' for PIP validation.
335	Comment: This information would be much better presented in a tabular listing format than as a paragraph of text. Proposed change: We suggest a table is embedded in the PIP template – this could also include estimated completion dates for adult studies to support deferrals.
337	Comment: Rather than rewriting the summary of results etc. in the PIP, cross reference could be made to the investigator's brochure.
356	Comment: We do not think that an applicant can include consideration of cultural difference in palatability as part of a PIP. The PIP should consider only general palatability. Proposed change: The expectation of applicants to consider ethnic and cultural differences in palatability, route of administration and acceptable dosage forms should be reduced.
365	Comment: It is surprising to see 'precision of dose delivery' only focus on solid oral dosage forms. Other dosage forms are also subject to the requirement to show precision of dose delivery. Proposed change: Consider if this text should reflect on other dosage forms.
369	Comment: We welcome the text on industry-verified extemporaneous preparations.
375	Comment: This key elements information should only reside in the key elements pdf form and not be duplicated in the main body of the PIP. This also applies to the CMC, non clinical and clinical sections.
459	Comment: It is unclear if the use of the term 'recruitment capacity' is related to number of **patients** or number of **study centres**.
476	Comment: It is important that the key elements form is not restricted too much, so that some of the extra items as listed below can be added as appropriate.

Line number(s) of the relevant text	Comment and rationale; proposed changes
505	Comment: A summary table in the PIP template would help make this section clearer. Proposed change: Include a summary table in PIP template.
515	Comment: Full protocols of adult trials may be unnecessary – synopses would be sufficient in vast majority of cases.
532	Comment: It is presumed that the PIP commitments are the 'key elements' of the plan. Confirmation would be helpful.
540	Comment: By breaking down the B-E template to individual components for B,C,D,E the application could be facilitated, and thus submit the relevant section only.
542	Comment: Would a PIP modification be expected during development when the body of the PIP may change but the key elements remain the same?

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

Line number(s) of the relevant text	Comment and rationale; proposed changes
Covers lines 553-623	
573	Comment: It is not clear what elements of the PIP need to be maintained / modified – for example, only the 'key elements'? See also comment on line 532 above.
623	Consultation item 2, Comment: The annual report on deferrals and the interim compliance check seem to be somewhat duplicative - is there a way to streamline these further?

Line number(s) of the relevant text	Comment and rationale; proposed changes
	The compliance check process needs to be accelerated. Collectively the modification process followed by an interim compliance check can be a serious logistical challenge in preparing to file an MAA for a new formulation / indication etc.

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

Line number(s) of the relevant text	Comment and rationale; proposed changes

Consultation item No 4: Do you have any comments on the assessment criteria for significant studies?

Line number(s) of the relevant text	Comment and rationale; proposed changes

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.

Line number(s) of the relevant text	Comment and rationale; proposed changes
	We recommend further streamlining the modification procedure to allow for substantially faster completion. The procedure to link

Line number(s) of the relevant text	Comment and rationale; proposed changes
	or split PIPs could follow a 30 day process.