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2 June 2000

Dockets Management Branch
HFA-305
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: **Docket No. 00D-1223**
International Conference on Harmonisation; E11: Clinical Investigation of Medicinal Products in the Pediatric Population

Dear Sir or Madam:

Reference is made to the Draft Guidance entitled International Conference on Harmonisation; E11: Clinical Investigation of Medicinal Products in the Pediatric Population. Procter & Gamble Pharmaceuticals acknowledges the need and commends FDA for the efforts taken to address the very important issues associated with clinical investigations in the pediatric population. Submitted herewith, are comments from Procter & Gamble Pharmaceuticals regarding the draft guidance. We appreciate the opportunity to respond to the Agency's request for comments.

Section 1.4 General Principles

Paragraph 1. Delete the sentence "Major advances in formulation chemistry and in pediatric study design ensure that this goal can be achieved." This statement seems to imply that there has been some breakthrough that ensures that all of the goals in this guidance can be achieved. In fact, developing products and clinical data to support indications in the pediatric population is likely to be difficult, costly, and require many compromises. The guidance should not imply that all of our problems have been solved. In fact, Section 2.3 Timing of Studies confirms that "development of pediatric formulations can be difficult and time consuming."

Paragraph 2. It should be clear that sponsors are not required or expected to study indications other than those being sought in the adult populations. Therefore, please revise the first sentence to read: "Drug development programs should include the pediatric patient population when a product is being developed for a disease/condition in adults and it is anticipated the product will be used in the pediatric population for the same indication."

Section 2.2 Pediatric Formulations

Paragraph 1. This paragraph seems to be encouraging diversification rather than harmonisation. The goal should be to meet the patients' needs in an efficient manner; and that availability is more important than multiple formulations. It should be stated that developing a spectrum of formulations that address local custom, regional differences, and clinician preferences should not slow or prevent a medication from reaching children. P&GP suggests revising the first paragraph to read: "There is a need for pediatric formulations that permit accurate dosing and enhanced patient compliance. Formulations should be developed to meet the needs of all of the geographic regions in which they will be marketed. Formulation

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type and concentration should also meet the needs of potential differing ages and routes of administration in the intended patient populations.”

Paragraph 2. If there are known excipients that should be avoided in certain age groups, it would be helpful to provide these in a list.

Delete the last sentence in this paragraph. ICH Q-1-3 does not address harmonisation of excipients, and method validation is a universal requirement that does not need mention in a guidance specific to pediatric clinical investigations.

Section 2.3 Timing of Studies

Sub-section 2.3.3 Medicinal Products Intended to Treat Other Diseases and Conditions

In addition to the considerations stated in the draft guidance for determining the best time to initiate clinical investigations in pediatric populations, it should be noted that many adverse drug effects do not show up until the larger Phase III trials or sometimes even later (post-market experience). Therefore, consideration should be given to initiating pediatric trials later rather than sooner in poorly characterized or uncharacterized drug classes.

Sub-section 2.4.4 Post-marketing experience

It should be noted that not all diseases/conditions require long-term medication therapy and thus long-term follow-up studies may be overly burdensome and not required. Therefore, P&GP suggests revising the paragraph to read: “Normally the pediatric database is limited at the time of approval. Therefore, postmarketing surveillance is particularly important. In some cases, long-term follow-up studies may be important to determine effects of chronic medications on growth and development of pediatric patients. The data from postmarketing surveillance and/or long-term follow-up studies may provide safety and/or efficacy information for subgroups within the pediatric population or additional information for the entire pediatric population.”

Section 2.5 Age Classification of Pediatric Patients

The suggested age categorization in this section seems to be encouraging diversification rather than harmonisation. The age classification for adolescents should be defined as 12 to 18 years of age, to ensure that the population between the ages 16 to 18 years are indeed studied internationally. Currently, recruitment into adult clinical trials do not allow for persons under 18 years of age to be included. The risk is that the population between 16 to 18 years of age will not be studied in either adult or pediatric clinical trials; and health care professionals will still be faced with making dosage and administration decisions based on little to no knowledge for this age group. Therefore, for the Adolescents age classification, please delete the phrase in braces ‘dependent on region’ and revise it to read: “Adolescents (12 to 18 years).”

Sub-section 2.5.4 Children (2-11 years)

Paragraph 3, last sentence. The draft guidance notes that in some cases “it may be appropriate to record Tanner stages of pubertal development.” It would be beneficial to the users of this guidance to provide definitions of the Tanner Stages, thereby avoiding confusion from using multiple references on this topic. In addition, it may be appropriate to define the age classification by a combination of age in years and/or Tanner Stage. For instance, it may be appropriate to stratify adolescents as (≥ 12 years or $>$ Tanner Stage 3 to 18 years of age).

Similarly, for the age categorization of Children (2-11 years) which encompasses a broad age range and several Tanner stages, it may be appropriate to stratify by age in years and/or by Tanner Stage of pubertal development.

Sub-section 2.5.5 Adolescents

Please refer to the comments under Section 2.5 regarding the upper age limit for this age classification.

Section 2.6 Ethical Issues in Pediatric Studies

Paragraph 2, last sentence. A minor typographical error is noted; the sentence should read: "In addition, participants in clinical studies are expected to obtain some direct or indirect benefit from the clinical study except under very special circumstances as discussed in ICH E-6 (GCP; section 4.8.14)."

Thank you again for the opportunity to provide comments. If you have any questions regarding the above, please contact the undersigned by telephone at 513.622.5278, or by facsimile at 513.622.5363.

Sincerely,



Wendy M. Sauber, RN, BSN
Section Head, U.S. Regulatory Affairs

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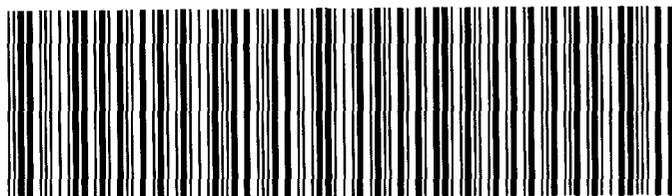
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