



Date: NOV 03 2005

Dockets Management Branch
(HFA-305)
Food and Drug Administration
Central Document Room
5901-B Ammendale Road
Beltsville MD 20705-1266

Re: Docket Number 2005D-0334

Response to FDA Call for Comments
Draft guidance for Industry: How to Comply with the Pediatric Research Equity Act

Dear Sir or Madam:

Reference is made to the September 7, 2005 (Volume 70, Number 172) Federal Register notice announcing the request for comments on the Draft guidance for Industry: How to Comply with the Pediatric Research Equity Act.

AstraZeneca has reviewed the document and is offering the attached comments in an effort to further increase the usefulness of the Agency guidance.

Please direct any questions or requests for additional information to me, or in my absence, to Laura E. Garcia-Davenport, Associate Director, at (302) 886-7533.

Sincerely,

A handwritten signature in black ink, appearing to read "Gary Cooper", with a long horizontal flourish extending to the right.

Gary Cooper,
Sr. Director
Regulatory Affairs
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lgd

Enclosure

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AstraZeneca Response to FDA Call for Comments on Draft Guidance for Industry: How to Comply with the Pediatric Research Equity Act

Docket Number 2005D-0334

General Comments

AstraZeneca appreciate the opportunity to provide comments on the FDA Draft Guidance for Industry: How to Comply with the Pediatric Research Equity Act (PREA). AstraZeneca supports the Agency’s initiative to provide preliminary assistance to individuals and industry sponsors with the development of this guidance. The draft guidance effectively outlines the recommended process for fulfilling the regulatory requirements under PREA.

AstraZeneca comments and recommendations described below are intended to provide the Agency with the end user’s point of view with regard to areas within the draft guidance that might benefit from the inclusion of language further clarifying the Agency’s expectations.

As the guidance would be anticipated to be the first source of information an applicant may use when planning work toward the fulfillment of the pediatric requirements under PREA, whenever possible we suggest the addition of examples to further illustrate the important point(s) being communicated by the Agency.

Specific Comments to the Draft Guidance for Industry: How to Comply with the Pediatric Research Equity Act		
Section	Page or Line Number	Comment or proposed replacement text
IV. The Pediatric Assessment C. What Types of Data Are Submitted as Part of the Pediatric Assessment?	Page 6, first full paragraph	<p>“If extrapolation from adult effectiveness data is inappropriate, adequate and well-controlled efficacy studies in the pediatric population may nevertheless be required. Additional information, such as dosing and safety data, could also be important to support pediatric labeling decisions.”</p> <p>Comment: AstraZeneca anticipates that when age extrapolation is not possible and additional information from pediatric studies is required, specialty societies and other pediatric experts will contribute to the sponsor's evaluation and development of proposals for designing pediatric clinical studies. These proposals are usually submitted and discussed with the Agency prior to the initiation of the pediatric studies.</p> <p>When the Agency rejects proposals that have been carefully developed in collaboration with pediatric experts, the sponsor may question the Agency’s view of the value of such expert input.</p> <p>Consequently, it would be helpful to include in the final guidance the Agency's current thinking regarding the value of such collaborations</p>

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		and suggestions on the timing for seeking expert consultation and input when developing pediatric study protocol proposals that address the pediatric assessment requirements under PREA.
V. The Pediatric plan and submissions A. When to develop a Pediatric plan	Page 7, first paragraph	<p>“For products that are not intended for treatment of life-threatening or severely debilitating illnesses, applicants are encouraged to submit and discuss the pediatric plan no later than the end-of phase 2 meeting. Information to support any planned request for a waiver or deferral of pediatric studies also should be submitted as part of the background package for this meeting.”</p> <p>Comment: It is suggested that the Agency include clarification regarding what a sponsor should expect if a Pediatric Plan is submitted for Agency review outside of the end-of Phase 2 meeting or the formal meeting request process.</p>
V. The Pediatric plan and submissions C. Must the Sponsor develop a Pediatric Formulation?	Page 8, first paragraph	<p>“PREA requires pediatric assessments to be gathered “using appropriate formulations for each age group for which the assessment is required” (section 505B(a)(2)(A) of the Act).”</p> <p>Comment: The practical utility of this guidance would be enhanced if additional clarification on the issue of when and in what age group a pediatric formulation will be required. The younger pediatric population (i.e., neonates and infants) is recognized as generally requiring a pediatric oral formulation independently of a disease area and/or the type of product being developed. Below a certain age, no child will ever be able to take a medication that is not in liquid form or crushed and added to a suitable vehicle.</p> <p>In the Guidance for Industry, <i>Content and Format for Pediatric Use Supplements</i>, the Agency defined the term “children” to include the age range between 2 years and 12 years. Further, in the past the Agency had used age sub-categories within the children age strata (for example < 6 years) to determine that a pediatric formulation is required.</p> <p>Therefore, to add clarity and increase the practical usefulness of the guidance, we encourage the inclusion of general recommendations on the age group(s) that would generally be considered by the Agency as an acceptable age cut-off for the purpose of determining when crushing of tablets (if possible) is acceptable and also when a true</p>

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		<p>liquid formulation is required. This would help set a general standard that extends to every drug being considered under PREA.</p> <p>Alternatively, the Agency could include cross-references to existing Agency guidances or to relevant scientific literature to illustrate the children sub-categories that have been used in the past and/or that are likely to be used as cut-off age group(s) for requiring a pediatric formulation.</p>
	Page 8, second paragraph, third sentence	<p>AstraZeneca suggests amending the sentence as follows: “FDA believes that this partial waiver provision will generally apply to situations where the applicant can demonstrate <u>that reasonable attempts have been made to produce a pediatric formulation but</u> that unusually difficult technological problems prevented the development of the pediatric formulation.”</p> <p>Additional comment: The practical utility of this guidance might be enhanced by the addition of general examples of the types of information (perhaps by reference to existing guidances) that the Agency has considered or might consider as sufficient evidence to demonstrate that a sponsor has encountered “unusually difficult technological problems” that prevent the development of a pediatric formulation.</p>
<p>VI. Waivers and Deferrals</p> <p>B. How to Apply for a Waiver</p> <p>3. Information in a Waiver Request</p> <p>Also, in Attachment A</p>	<p>Page 11, last bullet</p> <p>Point 4</p>	<p>“Applicant certification”</p> <p>Comment: For clarity, please add a footnote indicating whether the requirement for “certification” should be interpreted in the same context used within 21 CFR 314.50 or whether a notary public certification would be required.</p>