

# GlaxoWellcome

September 25, 1998

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Dockets Management Branch (HFA-305)  
Food and Drug Administration  
12420 Parklawn Drive, Room 1-23  
Rockville, MD 20857

Re: **Docket Number 98D-0265;**  
Comments on "Guidance for Industry -- Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug and Cosmetic Act"

Dear Sir or Madam:

Glaxo Wellcome Inc., a research-based pharmaceutical company, is engaged in the discovery, development, manufacture, and sale of prescription drug products and is the holder of numerous approved New Drug Applications. We are encouraged that FDA has begun implementing Section 505A with issuance of the above-referenced Guidance and the May 1998 "List of Approved Drugs for Which Additional Pediatric Information May Produce Health Benefits in the Pediatric Population." We welcome this opportunity to submit comments on the aspects of the Guidance of particular concern to us.

We are proud to say that, in our case, Section 505A does not require a new commitment to pediatric drug development, but rather it represents an opportunity to intensify our existing commitment. That being the case, our fundamental concerns with the Guidance are that (1) it sets up a review process that may delay or fail to effectively encourage submission of pediatric studies, and (2) it could serve inadvertently to penalize applicants who, prior to issuance of the guidance, did not delay submission of pediatric data, while rewarding applicants who withheld such data pending issuance of the Guidance and thus of Written Requests. Obviously, consequences such as these are not consistent with the intent of Congress when it enacted Section 111 of the Food and Drug Administration Modernization Act, nor do we believe these consequences are the intent of FDA. We describe our concerns below, in greater detail.

## **The Potential Consequences of Making "Written Requests" Unnecessarily Formalistic**

Under procedures outlined in the Guidance, the statutory requisite of a "Written Request" can be satisfied only if the applicable Office Director signs a "specific document" that is to set forth information in 15 specific categories. In our view, it would be preferable if discretion to issue a Written Request were vested in the Reviewing Divisions, with correspondingly less

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emphasis placed on the form of the communication. Centralized review at the Office level introduces the prospect of valuable pediatric clinical work being regrettably delayed pending the results of FDA's administrative process. Again, such an outcome could be counter to the goals of Congress in enacting Section 505A.

Collaborating as closely as they do with the Reviewing Divisions, sponsors know whether a pediatric drug development program is being encouraged and is well received within the Division. If, in a particular case, the Reviewing Division has been supportive, and assuming that discretion to issue a Written Request were vested at the Reviewing Division level, a sponsor could initiate pediatric clinical studies at the earliest possible opportunity, relatively unconcerned about the administrative details of extended exclusivity. The reason is that the sponsor could proceed with reasonable confidence that the Reviewing Division's past support would ultimately translate into a Written Request that conformed to the ongoing pediatric work. However, under the procedural framework established in FDA's Guidance, that is simply not the case. Notwithstanding a Reviewing Division's favorable disposition toward a particular program of pediatric drug development, a sponsor cannot routinely anticipate the position an Office Director or CDER's coordinating committee would take on the question of issuing a Written Request. If a sponsor is ready to begin meaningful pediatric work, but for the absence of a Written Request, it faces the dilemma of having either to delay the work until such time as an appropriate Request has been issued, or to assume the strategic risks of proceeding in the absence of a Written Request. There are at least two major aspects of this risk: (1) the possibility – admittedly remote -- of an Office Director being less likely to grant a Written Request at all, knowing that valuable pediatric clinical work is taking place in any event (and that the moral imperative would typically be to submit the results of that work so that appropriate labeling changes can be made); or (2) the possibility that a Written Request will be issued that does not conform to the ongoing work, such that additional (and possibly redundant) work would have to be done (at potentially considerable time and expense) to qualify for extended exclusivity. Obviously, if either of those unfortunate scenarios were to materialize, a sponsor that had elected not to delay valuable pediatric clinical work might later find itself considerably disadvantaged.

The involvement of Office Directors is likely to introduce not only the delay associated with the sponsor's uncertainty, but also delay associated with a centralized process itself. Office Directors and a centralized coordinating committee can be expected to take longer than Reviewing Divisions to issue Written Requests. One obvious reason is that the number of cases presented for review will be some multiple of the number, which would come before a single Reviewing Division. Another is that Office Directors and members of a centralized coordinating committee are typically more distant than personnel in the Reviewing Division from the detailed knowledge of a drug's development and its regulatory history. Perhaps this accounts for the elaboration in the Guidance of 15 "issues" which are generally to be addressed in a Written Request, and which sponsors are "strongly encouraged" to address in a "proposed pediatric study request" meant to facilitate FDA's issuance of a Written Request. Since Reviewing Divisions would often already be well acquainted with the details

subsumed within these 15 categories, giving the Divisions authority to issue a Written Request could serve to expedite and simplify the administrative process, and certainly reduce the need for reiteration of information already documented in a drug's regulatory history.

FDA's formation of a centralized coordinating committee and FDA's policy of requiring Office Director sign-off may reflect a concern to assure uniform application of standards across the reviewing divisions. That concern can, however, be met by clear managerial guidance and supervision. We believe that, just as Directors of Reviewing Divisions are authorized to approve the Supplemental Applications that may result from the completion of pediatric studies, they should appropriately be given authority to issue the Written Requests necessary to permit extended exclusivity to be granted based on such studies.

#### **Adverse Effects of Requiring that a "Written Request" Precede the Submission of Data**

Inequitable consequences could flow from the Guidance's injunction that "[s]tudies submitted before FDA issued a Written Request should *not* be used to request pediatric exclusivity." One practical effect of this prohibition could be the denial of exclusivity to any sponsor that submitted otherwise potentially eligible data before June 29, 1998 (the publication date of the Guidance). Similarly, this condition will, in some cases, necessitate delay in submission of an NDA or Supplemental Application until a Written Request is obtained. The unfairness of these results are manifest: withholding or delaying recognition for otherwise meritorious pediatric drug development programs that sponsors were willing to undertake even in the absence of any concrete prospect of being rewarded with extended exclusivity. These are arguably the initiatives that most deserve to be recognized under Section 505A. The inequity is particularly pronounced in the case of sponsors who chose not to delay submitting data even though an exclusivity-extension provision had already been enacted into law or was foreseeable. Although narrow self-interest might have called for a delay, some sponsors put self-interest aside and proceeded apace. That they might now effectively be penalized for having acted in good faith would be unfortunate.

Although the Guidance partially gives effect to the intent of Congress that Section 505A serve a dual purpose of incentivizing AND rewarding valuable pediatric work, it does not go far enough. As the agency is aware, the Joint Explanatory Statement of the FDAMA Conference Committee expressed the intent of Congress that "data collected prior to a request . . . may be used . . . in satisfying the provisions of this section [111, codified as Section 505A]." Given this statement of intent, Congress clearly meant for the new provision to serve in appropriate cases as a reward for pediatric clinical work that went forward even before there was the promise of extension of market exclusivity to compensate for the cost and effort associated with that work. For that reason, it is inappropriate that the Guidance insists that submission of data (in pursuit of pediatric exclusivity) be preceded by issuance of a Written Request. If Section 505A can serve to reward meaningful pediatric work that it could not have triggered in the sense of "stimulus and response," why should it matter

whether the Written Request comes before or after the data is submitted? We respectfully suggest, from a policy standpoint, that it should not matter any more than the order of the Written Request and the collection of data. In this latter respect, the Guidance takes a position that is fully faithful to congressional intent: “[d]ata collected prior to or after FDA issues a Written Request may be used to respond to the request.” Given the agency’s interpretive discretion, we respectfully request that similar latitude be shown toward data submitted prior to issuance of a Written Request.

Although we have expressed concern about certain aspects of the Guidance, we do look forward to enhanced opportunities to collaborate with the agency on pediatric drug development. We appreciate the opportunity to comment, and commend the agency for its continued commitment to improving the treatment of our nation’s children. Thank you for your consideration.

Sincerely,

A handwritten signature in cursive script that reads "David M. Cocchetto".

David M. Cocchetto, Ph.D.  
Group Director, Regulatory Affairs