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April 16, 1998

VIA FACSIMILE & U.S. MAIL

Ms. Khyati N. Roberts
Executive Operations Staff (HFD-6)
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Ms. Roberts:

On behalf of our client, Arnall Golden & Gregory, LLP (AG&G) is writing to you in your capacity as the Project Manager of the Food and Drug Administration's Pediatric Subcommittee, established to establish regulations and procedures to implement the FDA Modernization Act's (FDAMA's) pediatric exclusivity provisions. As you suggested to us informally, we are submitting our recommendations on the type of pediatric studies that FDA should accept to you, rather than the public docket created to receive comments on the recently-issued "Draft List of Drugs for Which Additional Pediatric Information May Produce Health Benefits in the Pediatric Population" (Docket No. 98N-0056). When FDA creates a separate public docket for comments on this issue, we might also submit a copy of this letter to that docket.

As you are aware, Section 111 of FDAMA added new section 505A to the Federal Food, Drug, and Cosmetic Act (FDC Act) and extends market exclusivity by six months for clinical studies conducted in pediatric populations. FDAMA defines "pediatric studies" to mean "at least one clinical investigation (that, at the Secretary's discretion, may include pharmacokinetic studies)" in the intended pediatric age groups. However, FDAMA does not elaborate on the type of studies that FDA might accept, which is necessary for FDA to grant an additional six months of exclusivity.

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In light of the ambiguity in FDAMA, we wish to offer our suggestions on how FDA might implement the pediatric exclusivity provisions. Specifically, AG&G recommends that FDA define "pediatric studies" to include both short- and long-term safety and efficacy studies. The data results from these studies will provide additional pediatric information that may "produce health benefits in the pediatric population," as FDAMA requires. We also suggest that FDA adopt pharmacokinetic (PK) studies in the "pediatric studies" definition. We agree with PhRMA's recommendation to include PK, PK/PD, safety (from post-market through controlled safety trials) and efficacy (for difficult to extrapolate indications or novel pediatric indications). PK study data can provide a better understanding of the drug product's metabolism in children and adolescents, which might be particularly useful in comparison to existing adult data, if any. In addition, PK data can offer invaluable information to guide clinical practice and assist health care practitioners to determine a rational dosing regimen for drug indications other than those approved by FDA.

AG&G advises FDA to incorporate in the "pediatric studies" definition postapproval commitment studies or FDA-requested studies, even if the NDA holder began the studies prior to FDAMA's enactment date. In the FDAMA Conference Report (at p. 60), Congress stated:

With respect to any requested studies under this provision, the conferees intend that data collected prior to a request or requirement by the Secretary may be used, in addition to data collected after such request or requirement in satisfying the provisions of this section.

The legislative history makes clear that Congress was less concerned with when or how the NDA holder obtained the pediatric data and more with the issue that the NDA holder indeed obtain the data; Congress recognized the importance of having the pediatric data, regardless of when the NDA holder might have begun the data collection process.

We contend that the adoption of postapproval commitment studies and any FDA-requested studies (even those not required as a condition of NDA approval) in the "pediatric studies" definition furthers the Congressional intent that pediatric data be obtained to determine possible health benefits in the pediatric population. If these studies are excluded from the definition of "pediatric studies," FDA will ignore potential valuable pediatric data, thereby defeating the purpose of Section 111 of FDAMA. Furthermore, by excluding these studies, the Agency will effectively punish those NDA holders that might have already begun generating the type of pediatric data sought by Congress and FDA but, because of the mere timing of FDAMA's enactment date, will fail to receive the additional six-month exclusivity afforded to

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those companies that started the data collection process afterwards. This outcome would be unfair and contrary to the laudable goals of FDAMA.

In conclusion, AG&G recommends that FDA include in the definition of "pediatric studies" the following types of studies: (1) short- and long-term safety and efficacy studies, (2) PK studies, (3) postapproval commitment studies, and (4) any studies requested by FDA of the NDA holder, even if the request occurred before the enactment date of FDAMA. We believe that an NDA holder that conducts these studies to obtain pediatric data and provides the results to FDA has complied with FDAMA, according to the letter and intent of the law.

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We appreciate FDA's consideration of our comments. Please feel free to call us if you would like to discuss these issues further.

Sincerely yours,

ARNALL GOLDEN & GREGORY, LLP



Alan G. Minsk

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