

DEPARTMENT OF HEALTH SERVICES

Infant Botulism Treatment & Prevention Program
850 Marina Bay Parkway, Room E361
Richmond CA, 94804
Phone: (510) 231-7600
Fax: (510) 231-7609
E-mail: ibttp@infantbotulism.org



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By electronic transmission
(<http://fda.gov/dockets/ecomments>)

Division of Dockets Management
U.S. Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 2006N-0061; RIN 0910-AF13: "Charging for Investigational Drugs"

To Whom It May Concern:

Please find accompanying this letter a four-page comment from the California Department of Health Services (CDHS) regarding the proposed revised regulations.

Also included as part of this submission are two electronic pdf files of articles relating to development of CDHS' orphan drug BabyBIG® and approved cost-recovery for it.

Sincerely yours,

/s/ Stephen S. Arnon

Stephen S. Arnon, M.D.
Chief, Infant Botulism Treatment
and Prevention Program

Attachments: Comments

Pdf of NEJM 2006;354:462-71

Pdf of Pediatrics 2007;119:785-89

Charging for Investigational Drugs: Proposed Regulations at 21CFR312.8

Docket No. 2006N-0061; RIN 0910-AF13

Comments from the California Department of Health Services, The Sponsor of a Licensed Orphan Drug

There are three fundamental assumptions implicit in these proposed regulations, all of which are incorrect. The first incorrect assumption is that all drug development is done by commercial entities with access to capital markets and driven by a profit motive. The second incorrect assumption is that in regulations, “one size fits all.” The third incorrect assumption is that the patient, rather than his or her insurance company, will personally pay the charge for authorized cost-recovery.

Based on its 19-year experience as the sponsor of a highly cost-effective, public service orphan drug that would not have achieved licensure without meaningful cost-recovery (see accompanying articles), CDHS believes that the proposed cost-recovery regulations at 21CFR312.8 will significantly impede the development and licensure of other orphan drugs. For this reason the proposed regulations should not be adopted in their present form.

There are approximately 6000 orphan diseases, yet less than 300 licensed orphan drugs and devices. Patients with orphan diseases need any medicine that can benefit their condition. For most of the especially small orphan disease populations (the true “orphan orphan” diseases), even the financial incentives in the Orphan Drug Act are insufficient to stimulate the development of therapeutics. As that law envisioned, there is a place and role for governmental, academic and other not-for-profit entities in orphan drug development. These entities by their very nature cannot raise funds from the capital markets for drug development. For these not-for-profit entities, it is essential to be able to recoup developmental costs while advancing their orphan candidates to licensure.

1. Not all drug development is done by commercial, for-profit entities.

Academic, governmental and other not-for-profit entities often have substantial difficulty in obtaining the funding needed to traverse the “valley of death” between the end of the phase III clinical trial or trials (when FDA OOPD funding ends) and the completion of the remaining requirements for licensure.

More true “orphan orphan” drugs could be developed if these not-for-profit entities were permitted meaningful cost-recovery during or after their phase III trial. Such cost-recovery would occur only if safety and efficacy had been shown (the “*Evidence*” criteria contained in proposed CFR 312.320(a)(3)). “Meaningful cost recovery” should be defined in regulation to include the costs of the clinical trials, all related research and developmental costs, as well as administrative, labor and other costs. An inclusive definition of allowable recoverable costs is needed because not-for-profit sponsors have to pay these costs and cannot raise funding in the capital markets to do so.

2. One size [of regulations] does not fit all

The needs and circumstances of orphan disease populations and the medications needed to treat them are quite different from those of non-orphan, widely prevalent diseases. The adoption of the Orphan Drug Act in 1982 was an acknowledgement of this truth. The obstacles and disincentives to development of orphan drugs are substantial and are different from those facing new products that have large markets ahead of them. The Agency needs to recognize these differences in regulations for cost-recovery that have separate provisions to aid and advance the development of orphan drugs. The Agency should not adopt regulations that impede the development of orphan drugs, especially by not-for-profit sponsors.

Many at the Agency may remember in the late 1980s the abuses of the then newly-promulgated cost-recovery regulations perpetrated by a prominent surgeon at the University of Minnesota. The preamble to those regulations (which are the subject of the proposed revision) made clear that they were intended in part to advance orphan drug development.

The Agency's distasteful experience with the Minnesota surgeon's disregard of fiscal, safety and data requirements should not be used as justification to "poison the well" for those who follow in orphan drug development, especially with regard to not-for-profit sponsors of orphan drugs. The mistake made with the Minnesota surgeon was failure to enforce early on the requirements for requesting approval for cost recovery, for annual reporting, for human subjects protections and for pursuing a marketing license with due diligence. These enforcement failures should not obscure the need for legitimate cost-recovery.

It is reasonable to allow "meaningful cost recovery" under a Treatment IND or even earlier while the sponsor is pursuing licensure with due diligence because recovery of these costs can enable the sponsor to complete licensure requirements. Without meaningful cost recovery, it may not be possible for some orphan drug sponsors, especially not-for-profit ones, to survive the "valley of death." More importantly, without certainty that meaningful cost recovery is possible under a Treatment IND, potential not-for-profit sponsors of orphan drugs may not ever try to begin new product development.

3. Insurance companies can and will pay for cost-recovery under Treatment IND status.

The burden of meaningful cost recovery does not have to fall on the patients and their families.

For example, licensure of BabyBIG® in October 2003 occurred more than six years after completion of the pivotal clinical trial. Yet, during this time insurance companies willingly paid the fee for the product under an approved Treatment IND cost-recovery plan because the insurers were persuaded of the medicine's benefits by the safety and efficacy data of the pivotal clinical trial (see Table 4 in the NEJM article). Having authorized cost-recovery during these six years, even as limited as it was by the Agency, was essential to accomplishing the eventual licensure of BabyBIG® (see Pediatrics article). A paradigm for meaningful cost-recovery before licensure needs to be established in regulation for other not-for-profit sponsors, especially those who sponsor orphan drugs.

4. Other Needed Improvements to the Proposed Regulations

Proposed 312.8(a)(3) states that “A sponsor must obtain prior written authorization from FDA to charge for an investigational drug.” In whatever numbering this clause may eventually have, the words, “Such authorization shall not be unreasonably withheld,” need to be added.

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