ORPHAN MEDICAL

0459 '03 JAN 30 A9:31

January 28, 2003

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

CITIZEN PETITION

The undersigned submits this petition under Subchapter C of Chapter VII of the Federal Food, Drug, and Cosmetic Act (FD&C Act), and in accordance with Section 10.30 of the FDA regulations, to request the Commissioner of Food and Drugs to take the following action:

First, we request that FDA revoke the Center for Drug Evaluation and Research (CDER) policy of determining that a company is "in arrears" with respect to payment of a user fee during the period that a waiver is under consideration by FDA. The result of this policy is that a small company -- particularly one that specializes in orphan drugs -- is required either to pay substantial fees before a waiver is determined or to wait for the waiver before submitting an application.

Second, we request that FDA establish a clear and fair waiver policy from the establishment and product fees for orphan drugs that have modest sales in order to avoid driving these drugs off the market. Current CDER administration of the user fee provisions has no policy regarding this problem.

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Third, because of the inherent conflict of interest in CDER determining user fees for financing its own operations, we request that you retransfer administration of the user fee program back to the Office of the Commissioner where it formerly resided.

A. Action Requested

We request that you take the specific action identified above.

B. Statement of Grounds

1. The Policy that a Company is in Arrears During the Time that a Waiver Request is Pending

Section 736(a) of the FD&C Act establishes user fees for applications, establishments, and products, and waives application fees for orphan drugs. Section 736(d) requires FDA to grant waivers from all three types of user fees under specified conditions. Section 736(e) provides that an application is considered incomplete, and shall not be accepted for filing by FDA, "until all fees owed by such person have been paid."

Nothing in these provisions states that, during the pendency of a waiver petition, the fees that are the subject of that petition are "owed" by the person involved. The statute contemplates that fees become owed once a waiver is denied. Subsection (d), which deals with waivers, comes before Subsection (e), which deals with refusal to file. It is clear that Congress intended that waivers take precedence over a determination of when fees are owed. If Congress had intended that fees be paid and then refunded after a waiver was granted, it would certainly have said so.

CDER's policy of requiring a company to pay the full fee while a waiver application is pending has an enormous impact on small companies, and particularly those involved (as we are) in orphan drugs. Small companies often do not have the cash available to pay FDA substantial fees and then later to obtain a refund. This is particularly true where orphan drugs are involved. The Orphan Drug Act of 1983 (as amended several times) has been one of the major success stories of the last two decades. By providing incentives for research and development of orphan drugs, this statute has encouraged major improvement in the field of orphan medicine. It is particularly anomalous that CDER would now initiate a user fee policy that discourages the development of orphan drugs.

The current CDER policy is set forth in FDA's Draft Interim Guidance for Waivers of and Reductions in User Fees[1] ("Draft Interim Guidance"), which CDER adopted without the benefit of notice-and-comment rulemaking. Rather than merely reflecting the agency's understanding of existing law, this policy imposes a requirement beyond those outlined in the FD&C Act. Under the four-factor test of American Mining Congress v. Mine Safety and Health Administration,[2] the policy is substantive, rather than administrative, and must comply with the requirements of the Administrative Procedure Act.[3] Because this legal requirement has been imposed without compliance with the Administrative Procedure Act, this policy is unlawful and cannot be enforced.

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1 Attachment G, FDA's Draft Interim Guidance for Waivers of and Reductions in User Fees (1993).

2 995 F.2d 1106, 1112 (D.C. Cir. 1993)

3 5 U.S.C. § 553(b).

FDA expects to grant waivers on only 55 product fees and 25 establishment fees, during fiscal year 2003.[4] It is therefore reasonable for FDA not to consider a small company in arrears while it is requesting a waiver of user fees.

A simple change in policy would be quite equitable and manageable. FDA could require that any waiver application for an establishment or product submitted on the same day as, or before, a product application would toll the payment until such time as FDA ruled on the waiver request. Once granted, a waiver would remain in place unless the economic facts justified a change. FDA could continue to require companies to certify that the conditions or circumstances described in the waiver request remain unchanged.

While FDA expressed concern in the Draft Interim Guidance that numerous unmeritorious waiver requests would be filed,[5] the small number of waivers actually requested shows that this effect is unlikely to materialize. Considering this, the major impact that tolling the payment would have on small companies, and the fact that FDA would have within its control the time that it takes to review and act on a waiver petition, the net impact on FDA would be negligible and the benefit to small companies and to the public health in general would be substantial.

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4 67 Fed. Reg. 50448, 50450 (August 2, 2002).

5 Draft Interim Guidance at 5.

2. Orphan Drug Waiver Rules

There are presently no regulations of any kind governing user establishment and product user fees for orphan drugs, or waivers of those fees, or even waivers of any fees. There is only the outdated Draft Interim Guidance made available by FDA in July 1993. The result is that policy is made by CDER on an ad hoc basis, without consideration of the substantial adverse impact that user fees can have upon research and development regarding orphan drugs.

The Draft Interim Guidance refers to orphan drugs only by mentioning that FDA will consider waivers or reductions of *application* fees for these drugs, but "does not expect to grant them often."[6] This statement directly conflicts with Congress' expectation that "the FDA will grant an exemption from user fees for orphan drugs (or for any product) where the fees would be a barrier to innovation."[7] It also conflicts with Dr. Kessler's statement to the Senate Committee on Labor and Human Resources that where developers are working on orphan drugs for a disease that affects only 60 children each year, "[t]here is no way we would expect them to pay these fees."[8]

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6 Draft Interim Guidance at 18.

7 H.R. Rep. No. 102-895, at 17 (1992).

8 Hearing of the Committee on Labor and Human Resources, United States Senate on Examining Proposed Legislation to Charge User Fees to Prescription Drug Manufacturers to Increase Resources to Improve the Review Time on Drug Applications, 102nd Cong. 19 (1992) (Statement of Dr. David Kessler, Commissioner, Food & Drug Administration). This comment echoes FDA testimony on prior versions of the bill, including Acting Deputy Commissioner Benson's statement that "Because orphan drugs, by statutory definition, are developed primarily for public health reasons and not for the benefit of the sponsor, the Agency believes it may be inappropriate to impose user charges for these products." Hearing Before the Committee on Small Business, United States Senate, to Assess the Impact of Proposed FDA User Fees on Small Business, 101st Cong. 30 (1989) (statement of James S. Benson, Acting Deputy Commissioner, Food & Drug Administration).

Congress' intent in passing PDUFA was to "give the FDA sufficient authority to waive fees for orphan drugs . . . unless such a waiver is not necessary to protect the public health or it is apparent that the fee will not be a disincentive to innovation because *the drug* will be profitable and would have been developed in any event."[9] Congress was interested in the profitability of the drug itself, not of the manufacturer overall. No matter how great a manufacturer's interest in the public health, it cannot as a sound economic strategy continue to develop drugs that lose money individually, even if the manufacturer is still profitable as an entity.

Examples below illustrate these problems. Orphan Medical obtained an approved NDA for the orphan drug, Elliotts B Solution, with an indication as an intrathecal diluent for anticancer intrathecal prophylaxis. It generates annual gross revenue of $30,000-$40,000. The product fee of $32,400 alone roughly equals the annual gross revenue of the product. For a small company like ours -- and probably even for a larger company -- this economic model is not sustainable. Either the product fee must be waived or we will take the product off the market. It makes no public health sense to remove orphan products from the market solely on the basis of an applicable user fee.

A second example is also applicable. Orphan Medical has an approved NDA for the orphan drug, Sucraid. The annual gross revenues are about $500,000 in the U.S. The combined product fee and establishment fee (since Sucraid is the only product in the establishment) result

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[9] H.R. Rep. No. 102-895, at 17 (1992) (emphasis added).

in a payment of $200,000, which is approximately 40 percent of the annual gross revenue. This is also not a sustainable economic model.

Furthermore, FDA's responses to these situations reflect an ill-considered public policy that is in direct odds with the purposes of the law. In circumstances similar to those just described, FDA has suggested that entities consolidate manufacturing in another establishment and close an existing establishment in order to avoid the establishment fee. This suggestion is counterproductive and would require a tremendous waste of company and agency resources. PDUFA's purpose was to speed the review process to allow products to come to market faster while maintaining a high level of review. Among other things, transferring manufacturing between establishments only adds to the regulatory burden, increases manufacturing cost, and slows the process, as the consolidated establishment will require new FDA inspections. Waiving or reducing the fee for the orphan drug would be a more straightforward and effective solution to the problem.

Current CDER policy precludes waivers where an entity's annual worldwide gross sales for any firm exceed $10 million.[10] As the above two examples show, this is not an economically workable policy. This policy also encumbers total world wide sales, where such revenues outside the U.S. may already be encumbered in local foreign markets (i.e., Canada). This policy has not been adopted in compliance with the Administrative Procedure Act. The policy creates new legal norms by essentially requiring an additional showing by profitable entities. Beyond

[10] Draft Interim Guidance at 16.

showing that the fee is a barrier to developing orphan products, the entity must also show that it is unable to pay the fee because of limited resources. Because FDA is modifying the requirements of the FD&C Act, the policy is substantive and must meet the requirements of the Administrative Procedure Act.[11] FDA has not used notice and comment rulemaking to create the Interim Draft Guidance, so it cannot lawfully use this policy.

These two examples demonstrate that FDA is badly in need of clear and unequivocal rules regarding waiver of product and establishment fees for orphan drugs. As already noted, CDER should not be in the position of imposing fees that discourage the very types of drugs that the Orphan Drug Act is intended to encourage.

3. Retransfer of Administration of the User Fee Program

When PDUFA I was established in 1992, the administration of the program was located in the Office of the Commissioner. In 1999, it was relocated to CDER.[12] We believe that the current location results in an inherent and unavoidable conflict of interest. The very organization that uses the money determines whether waivers are to be granted. Obviously, CDER is deeply biased against waivers. As the examples given above show and the additional one provided below, CDER policies emphasize wringing every penny out of the user fee program, to the detriment of drug research and development by small companies in general, and orphan drugs in particular.

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[11] American Mining Congress v. Mine Safety and Health Admin., 995 F.2d 1106, 1112 (D.C. Cir. 1993).
[12] 21 C.F.R. § 5.108.

With the advent of user fees within other centers at FDA, the only logical place to administer such programs correctly is in the Commissioner's office.

Orphan Medical submitted a manufacturing supplement to our Cystadane NDA 20-576 last November 2002. This supplement was not accepted by CDER due to Orphan Medical being placed into arrears. We discussed this verbally with the FDA officer who made this determination and he was unwilling to accept the supplement until either the waiver was granted or we paid our user fee bill. By not accepting this supplement for review, which was for a change in manufacturing site, it is possible that our firm may not be able to meet market demand for the product due to shortage of the manufactured drug product. This supplement must be accepted and reviewed prior to our utilization of drug product manufactured at a new firm. This example further illustrates the need for even handed central administration of the user fee programs among the various centers at FDA.

We strongly urge that the user fee program be returned to its origin in the Office of the Commissioner. This will allow an independent analysis of the policy impact of all aspects of any user fee program, without the current taint of the overwhelming CDER desire to maximize user fees. It will provide the proper focus for development of an orphan drug policy regarding product and establishment fees, and it will allow a neutral forum where any issues can be resolved independent of the organization that actually uses the fees.

C. Environmental Impact

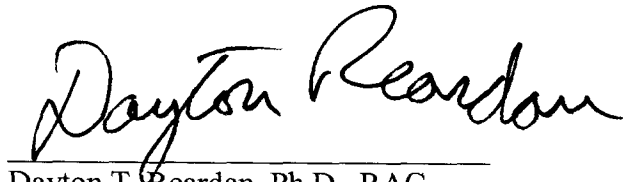
This Citizen Petition is subject to a categorical exclusion under Section 25.30 of the FDA Regulations.

D. Economic Impact

Implementation of this Citizen Petition will not have a significant economic impact. As noted in the Federal Register (Vol. 67, No. 149, August 2, 2002, page 50450) the Agency has already estimated granting waivers for establishments and product fees into the user fee budget amount.

E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that there are no data or information known to the petitioner which are unfavorable to the petition.



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