DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Office of Policy, Planning, and
Legislation HF-11
5600 Fishers Lane
Rockville, MD 20857

9541 '02 MAY 8 P1:33

MAY 7 2002

Thomas J. Donegan, Jr.
Vice-President - Legal & General Counsel
The Cosmetic, Toiletry, and Fragrance Association
1101 17th Street, NW, Suite 300
Washington, DC 20036-4702

Re: Docket No. 98N-0583/PSA

Dear Mr. Donegan,

In your recent petition for stay of action, dated March 12, 2002, regarding the final export notification and recordkeeping rule (66 Fed. Reg. 65429 (December 19, 2001)), you stated that, "[i]t is unclear what products may be subject to the rule in addition to commercially marketed or marketable products," and referred specifically to "product combinations that mix product categories, e.g., devices and drugs or for shipments that mix categories of products such as devices, drugs, and cosmetics."

On March 18, 2002, we notified you that the agency intended to grant a 90-day stay of the rule's effective date. We now take this opportunity to respond to your question regarding the rule's applicability to certain products.

The final rule implements the export notification and recordkeeping requirements contained in section 802 of the Federal Food, Drug, and Cosmetic Act (the Act), and also describes the types of records that would be satisfactory to show compliance with the export requirements in section 801(e)(1) of the Act. Sections 802 and 801(e)(1) of the Act provide exemptions to otherwise applicable provisions of the Act. If the product is not subject to the Act, sections 802 and 801(e)(1) do not apply. But if the product is subject to the Act and does not comply with the relevant requirements of the Act for commercial distribution and sale in the United States, it may not be exported unless it meets the requirements of section 802 or 801(e)(1) of the Act, as applicable. 98N-0583 LET 4

The final rule did not attempt to describe the types of products that are subject to the

statutory export requirements because the Act itself describes which products fall within sections 802 and 801(e)(1) of the Act. For example, section 802(a) of the Act clearly states that:

> (a) A drug or device–
> (1) which, in the case of a drug–
> (A)(i) requires approval by the Secretary under section 505 before such drug may be introduced or delivered for introduction into interstate commerce; or
> (ii) requires licensing by the Secretary under section 351 of the Public Health Service Act or by the Secretary of Agriculture under the Act of March 4, 1913 (known as the Virus-Serum Toxin Act) before it may be introduced or delivered for introduction into interstate commerce;
> (B) does not have such approval or license; and
> (C) is not exempt from such sections of Act; and
> (2) which, in the case of a device–
> (A) does not comply with an applicable requirement under section 514 or 515;
> (B) under section 520(g) is exempt form either such section; or
> (C) is a banned device under section 516, is adulterated, misbranded, and in violation of such sections or Act unless the export of the drug or device is, except at provided in subsection (f), authorized under subsection (b), (c), (d), or (e) or section 801(e)(2). . . .

Thus, section 802 of the Act applies to exports of *unapproved* drugs and devices. It does *not* establish requirements for exports of approved drugs or devices. If a drug or device has marketing approval in the United States and otherwise complies with all applicable requirements under the Act, the product may be introduced or delivered for introduction into interstate commerce, including exportation (see, e.g., sections 201(b), 301(d), 505(a), and 515(a) of the Act). Therefore, to the extent that your petition's reference to "commercially marketed products" was meant to be synonymous with approved drugs and devices, the export requirements at section 802 of the Act do *not* apply.[1]

As for section 801(e)(1) of the Act, the statutory requirements have remained essentially

---

[1] As for "commercially marketable products," we do not know whether you mean products that deviate from the FDA-approved product in some fashion, products that could be marketed in the United States if the manufacturer took the necessary steps to obtain marketing approval, or products that are approved in the United States but might not be sold domestically. In general, if a product deviates from the approved product in some manner, such as a drug with a different indication for use or different ingredient, the product would be a "new" product and require its own approval. If a manufacturer could obtain FDA approval for a product, but has declined or failed to obtain such approval, the product is still unapproved. However, if a product has FDA approval, it remains "approved" even if the sponsor elects to discontinue sales in the United States.

unchanged since 1938.[2] Section 801(e)(1) of the Act applies to the export of food, drugs, devices, and cosmetics that would otherwise be considered to be "adulterated or misbranded under this Act." Section 201(f) of the Act defines "food," section 201(g) of the Act defines "drug," section 201(h) of the Act defines "device," and section 201(i) of the Act defines "cosmetic." The statutory definitions at section 201 of the Act apply to section 801(e)(1) of the Act. Accordingly, as in the case of section 802 of the Act, a food, drug, device, or cosmetic that is legally commercially marketed in the United States is not subject to the export requirements at section 801(e)(1) of the Act.[3]

With respect to combination or "mixed" products – i.e., products that constitute a combination of two or more different FDA-regulated products – we must disagree with the suggestion that the final rule is ambiguous. There have been numerous opportunities since the enactment of the FDA Export Reform and Enhancement Act in 1996 to submit comment seeking clarification of how section 801(e)(1) and 802 of the Act apply to combination products. The agency did not receive comments following the enactment of the 1996 Export Act's enactment, or in response to the draft guidance document in 1998 (see 63 Fed. Reg. 32219 (June 12, 1998)), or the proposed export notification and recordkeeping rule in 1999 (see 64 Fed. Reg. 15944 (April 2, 1999)) that asked the agency to address combination products. Moreover, the statute adequately defines which products are subject to sections 801(e)(1) and 802 of the Act.

Nevertheless, we note that the agency has provided guidance to the public regarding certain issues of primary center jurisdiction regarding combination products. For example, intercenter agreements exist to describe the allocation of administrative responsibility for categories of products or specific products (see, e.g., 21 CFR 3.5).[4] We also note that the preamble to the final rule indicated that we would determine the applicability of sections 801(e)(1) or 802 of the Act to a product according to the product's classification or type in the United States (see 66 Fed. Reg. at 65433 (comment 12)). While the regulation of combination products does present some complex issues, those complexities are not attributable to the final

---

[2] See Public Law 75-717. In 1938, the provision was codified at 21 U.S.C. 381(d). Congress renumbered the provision as 21 U.S.C. 381(e)(1) as a result of the Drug Export Amendments Act of 1986 (Public Law 99-960).

[3] As in footnote 1 regarding "commercially marketable products," we are unsure as to your interpretation of "commercially marketable." In any event, if the product to be exported is adulterated or misbranded, then a person wishing to export that product would have to comply with section 801(e)(1) of the Act.

[4] While this regulation is part of a "product jurisdiction" program for FDA review of premarket applications, the principles expressed in the intercenter agreements are equally applicable to a determination as to the center with lead administrative responsibility for a combination product intended for export.

rule.

Furthermore, with respect to most exports of combination products, the issue of which center has primary jurisdiction issue may be largely irrelevant. For example, if a person sought to export a drug/device combination product, and both components were unapproved, the drug would be subject to the export requirements at section 802 of the Act,[5] whereas the device could be exported under section 801(e)(2) or 802 of the Act. If the export complied with section 802 of the Act, the product could be exported. As a further example, if a person sought to export a product consisting of a combination of an unapproved drug and misbranded device, the drug would be subject to the export requirements at section 802 of the Act and the device could be exported if it complied with section 801(e)(1) of the Act. Again, if the export complied with section 802 of the Act, the product could be exported because exports under section 802 of the Act must also comply with section 801(e)(1) of the Act.

Although the export of a combination or "mixed" product may present questions as to which FDA component should receive the required notification, several options exist. For example, in the case of a combination product consisting of two components in which both components could, if they were exported individually, be exported under section 802 of the Act, the exporter could contact FDA to determine which center should be sent the notification. Alternatively, the exporter could decide to submit notifications to both centers, even though the final rule would not require such a result. Consistent with the rule, the exporter could also could send the notification to one center, and that center could pass the notification to another center if appropriate. Moreover, this notification issue only exists if the "mixed" product consists of a drug, device and/or biologic combination, and both components are subject to section 802(b)(1) of the Act and section 802's notification requirement. If the exported product is a drug-cosmetic combination product, for example, and the product is being exported under section 802(b)(1) of the Act, the notification would go to the Center for Drug Evaluation and Research (CDER). Section 801(e)(1) of the Act does not require a notification for cosmetic exports.

Please note, however, that if a shipment contains different FDA-regulated products being exported pursuant to section 802 or 801(e)(1) of the Act, each product must comply with the relevant export requirements and, if any products are being exported under section 802(b)(1) of the Act, the notification requirements must also be met for those products. For example, an exporter ships in a single shipping container 20 boxes of an unapproved drug, 10 boxes of an unapproved device, 30 boxes of a misbranded cometic, and 15 boxes of a second unapproved device. The drugs and the device are being exported pursuant to section 802(b)(1) of the Act. No notification is required for the cosmetic, but a notification for the device should be sent to the Center for Devices and Radiological Health (CDRH), and notification for the two drug products

---

[5] Most drugs subject to the Act's export requirements would be exported under section 802 of the Act because at least one court has held that section 801(e) of the Act does not apply to exports of "new drugs" (see 63 Fed. Reg. 32219, at 32221, col. 1).

should be sent to CDER. Because the drugs and the devices are separate products, separate notifications should be sent to the appropriate centers. With respect to the CDER notifications, the exporter could send the required information for both drugs in a single document.

Should you have any additional questions, please feel free to contact us.

Sincerely,

Margaret M. Dotzel
Associate Commissioner for Policy