UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUN 10 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

PC-2396

David J. Hayes
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Re: FDA Exemption

Dear David:

The Environmental Protection Agency ("EPA" or "the Agency") takes this opportunity to respond to your October 18, 1993 inquiry in which you seek confirmation that process effluents and wastes from manufacturing of substances which are regulated pursuant to the Federal Food, Drug and Cosmetic Act ("FFDCA") are not regulated under the Toxic Substances Control Act ("TSCA").

In responding to your inquiry, the Agency would like to confirm its written history of the so-called "FDA exemption" as set forth in your letter. As you know, TSCA excludes from the term "chemical substance" any food, food additive, drug, cosmetic, or device when manufactured, processed, or distributed in commerce for use as a food, food additive, drug, cosmetic, or device. 15 U.S.C. §2602(1)(B)(vi).

EPA has consistently taken the position that if the chemical substance is being exclusively manufactured, processed, distributed in commerce, and used for uses falling within the Food and Drug Administration's (FDA's) jurisdiction, EPA would not assert jurisdiction under TSCA. H.R. No. 94-1341, 94th Cong., 2d Sess. 10, (1976). Further reference may be made to the Inventory Reporting Rule, 42 Federal Register 64585, Comment 41 (December 23, 1977) and the New Chemical Branch's prenotice communications 54, 57, 75, 83, 203, 261, 369, 416, 613, 621, 983, 1043, 1096, 1309, 1447, 1593, 1616, 1651, 1717, 1947, and 1970. Should the manufacturer develop an intent to use the chemical for a TSCA use, the activities associated with the substance would then be regulated under TSCA based on differentiated uses of the substance. This would be the case regardless of what percentage of production of an FDA regulated substance is intended to be

devoted to a TSCA use or uses (e.g; in the event only 1% of a batch chemical substance will be used for a TSCA use).

After receipt of your inquiry, we reviewed the issue of disposal of effluents and wastes from the manufacture of FDA substances with FDA and other EPA offices, and have concluded that there is no need to assert TSCA jurisdiction over these substances/activities. This is because other federal authorities convey adequate jurisdiction to regulate these substances/activities, and these authorities are currently being used to address these substances/activities. Specifically, wastes are addressed under FFDCA, the Resource Conservation and Recovery Act, and the Clean Water Act. Moreover, to the extent these substances have other uses, they may also be regulated under TSCA. This position is consistent with our past practices and section 9 of TSCA. If, at any future point, information becomes available to the Agency that indicates an area where TSCA review would be appropriate, we will reconsider this position. We would, of course, publicize any change in position.

Finally, in response to your inquiry regarding questions 2 and 3 in the 1984 Section 8(c) Question and Answer Document, we recognize that these passages may create some confusion. The cited responses in the 8(c) document were taken from an earlier document that was prepared prior to enactment and broad implementation of many of EPA's statutes. At that time, TSCA regulation of these substances may have seemed appropriate and justified. Since that time, EPA has considered the issue of medical/pharmaceutical effluents and wastes in the context of existing EPA statutes and regulations, as well as FDA jurisdiction. As indicated above, EPA now believes that these substances can be and are currently being addressed under other federal authorities, and need not be regulated under TSCA. We are in the process of amending the 8(c) guidance to reflect this position.

I trust that this letter serves to respond to your inquiry and will satisfy the interests of your client.

Sincerely,

Mark A. Greenwood, Director
Office of Pollution Prevention
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October 18, 1993

BY HAND DELIVERY

Mark A. Greenwood
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Re: FDA Exemption

Dear Mark:

I am writing on behalf of the Pharmaceutical Manufacturers Association ("PMA") to request that the Agency confirm the pharmaceutical industry's long-standing understanding of the scope of the FDA exemption under the Toxic Substances Control Act ("TSCA"), an understanding which has been drawn from the statute's legislative history and the Agency's previous guidance on the subject. PMA is requesting this confirmation now because the Agency is in the process of promulgating additional guidance on environmental reporting under Section 8(e). Due to the applicability of the FDA exemption, PMA is not intending to participate in the Section 8(e) process. If EPA disagrees with PMA's conclusion regarding the applicability of the exemption, we would appreciate immediate notice so that we can discuss the scope of the exemption further with you and, if necessary, file protective comments in the Section 8(e) docket.

In order to assist EPA in responding to this request, PMA has set forth below its understanding of the scope of the FDA exemption, particularly as it applies to environmental emissions and releases from pharmaceutical operations.

Background: TSCA's FDA Exemption

TSCA's statutory obligations apply to "chemical substances." Chemical substances are defined in TSCA to exclude pharmaceutical-related substances. Specifically, the statute excludes:

> [A]ny food, food additive, drug, cosmetic or device (as such terms are defined in Section 201 of the Federal Food, Drug, and Cosmetic Act ["FFDCA"] [21 U.S.C. § 321]) when manufactured, processed, or distributed in commerce for use as a food, food additive, drug, cosmetic or device. [15 U.S.C. § 2602(1)(B)(vi).]

The FFDCA broadly defines the term "drugs" as ". . . articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; articles (other than food) intended to affect the structure or any function of the body; and . . . articles intended for use as a component of any article specified [above] . . ." 21 U.S.C. § 321(g)(1).

When enacting TSCA, Congress indicated that the exemption for FFDCA-related substances (the so-called "FDA exemption") was to be construed broadly to cover the full range of activities that could be regulated under the FFDCA. As the House Committee Report stated:

> By adopting the definition given the items by [the Federal Food, Drug and Cosmetic Act] the Committee has made the exclusion of these items from the bill coextensive with the authority to regulate them under [that] Act. [H.R. Rep. No. 1341 94th Cong., 2nd Sess. 10 (1976).]

EPA has remained true to this Congressional intent by interpreting the FDA exemption broadly and concluding that a substance is not subject to TSCA if it falls within the FDA's purview. In its original Inventory rulemaking, for example, the Agency acknowledged that all FDA-related activities are covered by the exemption:

> As soon as the FDA regulates a product, its manufacture, processing or distribution in commerce solely for a FDA regulated use will be excluded from the jurisdiction of TSCA. [Inventory Reporting

> Requirements, 42 Fed. Reg. at 64585-86 (Dec. 23, 1977).]

See also id., 42 Fed. Reg. at 65485 ("If the manufacturing, processing, distribution, or use of a substance is regulated under . . . FFDCA, the substance would not be subject to regulation under TSCA insofar as it is actually manufactured, processed or distributed in commerce for use as a pesticide, food, food additive, drug, cosmetic or device.")

Research and Development Activities

The broad coverage of the FDA exemption is illustrated by the approach that Congress and the Agency have taken in characterizing drug-related research and development activities. Both Congress and EPA have confirmed that all research that is dedicated to drug-related activity is subject to the FDA exemption.

The legislative history of TSCA is instructive on this point. Before the statute was enacted, the U.S. House of Representatives considered adopting an amendment to TSCA which would have specifically excluded research and development pharmaceuticals from coverage under TSCA. The House declined to do so, however, on grounds that the FDA exemption already was broad enough to exempt such activities. As explained in the House Report:

> The amendment was withdrawn with the understanding that the definition of the term "drug" in the Federal Food, Drug and Cosmetic Act included items described in the amendment . . . . The Federal Food, Drug, and Cosmetic Act clearly covers drugs during the "investigation" or research stage. Consequently, the definition of "drug" in the Act includes chemical substances used for drug research and development. [H.R. Rep. No. 1341, 94th Cong., 2d Sess. 10 (1976).]

In later guidance documents released by the Agency, EPA has confirmed its view that pharmaceutical research and development activities are fully covered by the FDA exemption:

> Question: Do the regulations under discussion affect the research laboratories of a drug company involved in the development (and sometimes limited production) of pharmaceuticals dosage forms?

> Answer: . . . . a drug research laboratory is not likely to be affected by this rule because such activities are considered covered by FDA. [Questions & Answers Concerning the TSCA Section 8(c) Rule p. 39, Question 6 (Nov. 10, 1983) (emphasis added).]

Intermediates/Catalysts

EPA has been similarly expansive in its interpretation of the scope of the FDA exemption as applied to intermediates and catalysts which are used in the production of a drug. More specifically, EPA has confirmed that intermediates and catalysts intended solely for use in the production of a drug are excluded from TSCA:

> The Administrator considers that intermediates and catalysts intended solely for use in the production of a food, food additive, drug, cosmetic, or device are excluded from regulation under TSCA. The definitions of the FFDCA provide that chemical substances which are intended for use as a component of a food, food additive, drug, cosmetic, or device are encompassed within the meanings of such terms, respectively. The FDA considers intermediates and catalysts to be such components. Therefore, they are subject to regulation under the FFDCA. Any such substance is excluded from regulation under TSCA insofar as it is actually manufactured, processed, or distributed in commerce solely for use in the production of the food, food additive, drug, cosmetic, or device. [Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk, 43 Fed. Reg. at 11116 (March 16, 1978).]

EPA made the same point in a 1983 Question-and-Answer document:

> Question: If a chemical is manufactured solely for use as an intermediate in production of a drug, cosmetic or pesticide, but the intermediate is not regulated by FDA, is the chemical covered by TSCA and subject to 8(c)?
>
> Answer: Pesticide intermediates are subject to 8(c) recordkeeping unless the intermediate itself is a

pesticide. [1/] Intermediates in the production of drugs or cosmetics are not subject to 8(c) recordkeeping. [Questions & Answers Concerning the TSCA Section 8(c) Rule pp. 38-39, Questions 4, 7 (Nov. 10, 1983)(emphasis added).]

Emissions/Releases

EPA has addressed the application of the FDA exemption to releases and emissions from pharmaceutical facilities in connection with the filing of "FYI" and Section 8(e) reports. The Agency has issued a number of "status reports" under Section 8(e), for example, which indicate that the FDA exemption extends to emissions and releases from pharmaceutical plants which might otherwise qualify for reporting under Section 8(e).

In commenting on a 1985 report filed by a pharmaceutical company, for example, EPA stated that "the information . . . did not need to be reported to EPA under Section 8(e) of TSCA unless the submitting company is or has engaged in the manufacture, importation, processing, or distribution [of chemical substances] . . . for uses covered by TSCA." See 8EHQ-0485-0051, May 14, 1985. Likewise, in response to a 1979 status report, the Agency indicated that an environmental release of an FDA/FIFRA substance is not subject to Section 8(e). See 8EQ-0779-0299, Aug. 6, 1979 (p. 23). In that case, FMC Corp. had submitted a report which addressed the release of a pesticide (Furadon). EPA stated that because Furadon is a FIFRA-registered pesticide, it is not a "chemical substance" as defined by TSCA.

Similarly, in response to a report on the characteristics of waste effluent for an FDA-regulated product (ampicillin trihydrate), EPA stated that the report was inappropriate for Section 8(e) consideration, presumably due to application of the FDA exemption. See 8EHQ-0278-0045 (Mar. 17, 1978).

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1. PMA recognizes that EPA has taken the view that intermediates and catalysts used in the production of pesticides generally are not excluded from TSCA. EPA traditionally has interpreted the FIFRA exemption in TSCA much more narrowly than the FDA exemption.

PMA always has agreed with EPA's conclusion that information about emissions and releases from pharmaceutical plants qualify for coverage under the FDA exemption. Emissions and releases are a necessary part of the pharmaceutical manufacturing process. They are not unlike intermediates and catalysts, which do not become part of a finished pharmaceutical product, but which are a necessary element in the manufacturing process. Similarly, even though many research and development activities do not lead to the manufacture or distribution of drug products, they are considered to be so closely tied to the drug manufacturing process so as to be included within the scope of the FDA exemption.

In addition to the inexorable linkage between emissions and releases and the drug manufacturing process, it also is noteworthy that the FDA's jurisdiction extends to environmental impacts associated with the manufacturing process. To illustrate, FDA's environmental impact regulations at 21 C.F.R. Part 25 require applicants seeking approval of drugs and other FDA-regulated products to prepare an environmental assessment which includes information regarding expected emissions into the environment from product sites, environmental concentration and fate of emitted substances, and environmental effects of the releases on animals, plants, humans and other organisms. See generally 21 C.F.R. § 25.31(a). No other industry evaluates the fate and effects impacts of its products.

Although the statutory and regulatory history of the FDA exemption leads to the clear conclusion that drug-related emissions and releases fall within the scope of the exemption, PMA is aware of a single 1983 document which does not square with this long-standing understanding of the FDA exemption. Specifically, in a 1983 "Question & Answer" document, EPA indicated that process wastes from pharmaceutical manufacturing operations are subject to Section 8(c)'s recordkeeping requirements. As the Agency stated:

> Question: Are allegations related to intermediates, process discharges, and emissions from plant manufacturing and processing pesticides or pharmaceuticals required to be recorded under 8(c)?
>
> Answer: . . . . In the manufacturing and processing of pharmaceuticals, only the wastes are considered chemical substances covered by TSCA. . . . .

> Question: Are treated process effluents for fully FDA or FIFRA regulated processes exempt from recordkeeping?
>
> Answer: No. Effluents (treated or not) from . . . FDA regulated processes are covered by TSCA and therefore subject to 8(c) recordkeeping. [Questions & Answers Concerning the TSCA Section 8(c) Rule pp. 38-39, Questions 2, 3, 5 (Nov. 10, 1983)(emphasis added).]

Elsewhere in the Q-and-A document, EPA stated that "[o]nly those portions of the manufacturing process that are regulated by FDA are exempt from TSCA." See Questions & Answers Concerning the TSCA Section 8(c) Rule p. 39, Question 7 (Nov. 10, 1983)(emphasis added).

These statements are inconsistent with the language and history of the FDA exemption. In particular, the statements are inconsistent with the Agency's own interpretation of the exemption as applied to other operations that are related to the pharmaceutical manufacturing process, and which EPA has confirmed to be covered by the FDA exemption, including R&D activities and the use of intermediates and catalysts. The statements also are inconsistent with the direct guidance provided by the Agency under Section 8(e). Finally, the statements likely were made without an appreciation for FDA's jurisdiction over environmental aspects of pharmaceutical operations.

Given the heavy weight of authority which indicates that emissions and release information from pharmaceutical operations falls within the scope of the FDA exemption, PMA has continued to follow that line of authority.

Limits to the FDA Exemption

Any discussion of the scope of the FDA exemption would not be complete without mention of limitations on the application of the exemption. In particular, PMA recognizes that the exemption does not cover "dual use" situations. That is, PMA members who utilize chemicals both for exempt FDA purposes, and for non-exempt purposes, must comply with TSCA. The following excerpts from interpretations published in the Federal Register make this important point:

> If a substance has multiple uses only some of which are regulated under FIFRA or FFDCA, the manufacture, processing and distribution, and use

> of the substance for the remaining uses would come within the jurisdiction of TSCA. [Inventory Reporting Requirements, 42 Fed. Reg. at 64585, (Dec. 23, 1977)]
>
> Many chemicals subject to regulation under . . . FFDCA, however, are also used as chemical substances which may be regulated under TSCA. Part of the company's production or use many be subject to TSCA and part subject to regulation under other authorities. [45 Fed. Reg. at 13653 (Feb. 29, 1980).]

In accordance with this limitation, the FDA exemption covering release and emissions information applies only to pharmaceutical manufacturing activities, and not to non-exempt manufacturing activities. This important limitation ensures that the exemption applies only to those activities that clearly fall within the FDA's traditional jurisdiction -- drug manufacturing activities.

* * * *

PMA appreciates your attention to this issue. We look forward to receiving your early response to our request for confirmation that the pharmaceutical manufacturing operations of PMA's members continue to be covered by the FDA exemption, and that EPA's new Section 8(e) guidance will not purport to apply to pharmaceutical manufacturing activities.

With best regards,

Sincerely,

David J. Hayes
of LATHAM & WATKINS