

information for certain premarket application reviews. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations. This guidance document is issued as a level 1 guidance consistent with GGP's.

This guidance, when used in conjunction with the QS regulation, illustrates an approach for complying with the content requirements for premarket submissions found in section 515(c) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360e(c)) and 21 CFR part 814. A manufacturer who chooses to meet application requirements for the QS information in an alternative way may wish to consult with the appropriate office prior to the submission. The FDA staff can help identify areas that might raise particular concerns for CDRH and CBER reviewers or investigators.

### III. Comments from the Draft Guidance

In the *Federal Register* of August 3, 1999 (64 FR 42137), "Medical Devices, Draft Guidance on Quality System Regulation Information for Various Premarket Submissions; Availability" was published as a draft level 1 guidance document for comment under GGP's. Six individuals or organizations filed comments on the draft guidance.

Most of the comments requested a better understanding of how FDA used the information previously submitted under the GMP manufacturing section and how the information requested in this guidance would be used. The introduction of the final guidance document explains that CDRH's Office of Compliance (OC) will review the QS information submitted in the premarket application at the same time the Office of Device Evaluation (ODE) reviews the other portions of the application. The appropriate offices in CBER will review the QS information submitted in CBER-regulated premarket submissions. Applicants who use this guidance should be able to focus their submissions on the information CDRH/CBER will need for review. Based on their review, CDRH/CBER will provide inspectional guidance to FDA field staff. Submission of this information can help focus the preapproval inspection process and limit the amount of time field staff will need to spend in the facility.

A few comments questioned the recommendation that manufacturers have design control information available, upon request, for devices subject to 510(k) clearance because it

suggested that such documentation could be requested as part of the determination of substantial equivalence. FDA agrees with the comments and, therefore, has limited the applicability of this guidance document to exclude 510(k) submissions.

A few comments questioned whether the draft guidance document exceeded requirements in the QS regulation. The introduction to the final guidance document explains that the guidance document requests copies of written procedures or lists of items related to the QS regulation. In most cases, these procedures or lists are explicitly required under provisions of the QS regulation. In a few cases, the explanations or lists will facilitate FDA's review of your QS information. In the cases where the information is not explicitly required under statute or regulation (e.g., production flow diagram, list of any standards used, process validation master plan), FDA believes the information is the type you are likely to create and maintain as part of your QS. FDA believes submission of such information as part of your application will reduce or eliminate the need for us to request additional information during our review and preapproval inspection. However, because this is a guidance document, compliance with the recommendation is not required.

The final guidance also incorporates many editorial comments and wording suggestions that were submitted by comments.

### IV. Electronic Access

In order to receive the guidance document "Quality System Information for Certain Premarket Application Reviews" via your fax machine, call the CDRH Facts-On-Demand (FOD) system at 800-899-0381 or 301-827-0111 from a touch-tone telephone. At the first voice prompt press 1 to access DSMA Facts, at the second voice prompt press 2, and then enter the document number (1140) followed by the pound sign (#). Then follow the remaining voice prompts to complete your request.

Persons interested in obtaining a copy of the document may also do so by using the Internet. CDRH maintains an entry on the Internet for easy access to information including text, graphics, and files that may be downloaded to a personal computer with access to the Internet. Updated on a regular basis, the CDRH home page includes the "Quality System Information for Certain Premarket Application Reviews," device safety alerts, *Federal Register* reprints, information on premarket submissions

(including lists of approved applications and manufacturers' addresses), small manufacturers' assistance, information on video conferencing and electronic submissions, mammography matters, and other device-oriented information. The CDRH home page may be accessed at <http://www.fda.gov/cdrh>. The guidance entitled "Quality System Information for Certain Premarket Application Reviews" will be available at <http://www.fda.gov/cdrh/comp/guidance/1140.pdf>.

### V. Paperwork Reduction Act of 1995

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (the PRA) (44 U.S.C. 3501-3520). The collections of information addressed in the guidance document have been approved by OMB in accordance with the PRA under the regulations governing premarket approval applications (21 CFR part 814, OMB control number 0910-0231) and the regulations governing quality systems (21 CFR part 820, OMB control number 0910-0073).

### VI. Comments

Interested parties may submit to Dockets Management Branch (see **ADDRESSES**) written or electronic comments regarding this guidance. Submit two copies of any mailed comments, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The guidance document and received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: January 10, 2003.

**Linda S. Kahan,**

*Deputy Director, Center for Devices and Radiological Health.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. 98N-1109]

#### **Mercury Compounds in Drugs and Food; List**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice; request for information.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing a

request for information to update a list of drug and biologic products that contain intentionally introduced mercury compounds, e.g., phenylmercuric acetate, phenylmercuric nitrate, and thimerosal. This request is part of the implementation of the Food and Drug Administration Modernization Act of 1997 (FDAMA).

**DATES:** Submit written and electronic comments and information by April 4, 2003.

**ADDRESSES:** Submit written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>.

**FOR FURTHER INFORMATION CONTACT:** Gerald M. Rachanow, Center for Drug Evaluation and Research (HFD-560), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-2222.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

FDAMA (Public Law 105-115) was enacted on November 21, 1997. Section 413 of FDAMA entitled "Food and Drug Administration Study of Mercury Compounds in Drugs and Food" required FDA to: (1) Compile a list of drugs and foods that contain intentionally introduced mercury compounds, and (2) provide a quantitative and qualitative analysis of the mercury compounds in this list. The statute did not differentiate whether the mercury compound was present in the products as an active or an inactive ingredient and required FDA to compile the list and provide the analysis within 2 years after the date of its enactment. FDA prepared this list and announced its availability in the **Federal Register** of November 19, 1999 (64 FR 63323).

**II. Request for Information**

The agency is aware that some manufacturers or distributors with products on the list have reformulated their products since 1999. Accordingly, the agency would like to update the list to delete any products that no longer contain mercury ingredients. The agency is requesting any affected manufacturer or distributor with a product(s) on the list that no longer contains mercury to send an acknowledgement to the agency [to Docket No. 98N-1109] stating that the product(s) has been reformulated to no longer contain mercury. The agency will compile this information and announce the availability of an updated list in a future issue of the **Federal Register**.

The agency wishes to assure that it has a copy of the revised labeling for any product that has been reformulated. Part 207 (21 CFR part 207) entitled "Registration of Producers of Drugs and Listing of Drugs in Commercial Distribution" provides that owners or operators of drug establishments that engage in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs register and submit a list of every drug in commercial distribution (§ 207.20(a)). Owners or operators of establishments that distribute under their own label or trade name a drug manufactured or processed by a registered establishment may submit listing information directly to FDA and obtain a labeler code (§ 207.20(b)). Registrants are required to provide a copy of all current labeling for each new drug (§ 207.25(b)(2)) and human prescription drug that is not a new drug (§ 207.25(b)(4)), and a copy of the label for each human over-the-counter drug listed that is not a new drug (§ 207.25(b)(5)). Information about inactive ingredients in the product is requested but not required (§ 207.31(b)).

Owners and operators of all registered establishments are required to update their drug listing information every June and December (§ 207.21(b)). The updated information includes listing each drug for which commercial distribution has been discontinued or for which any material change has occurred in any information previously submitted (e.g., reformulation) (§ 207.30(a)(2) and (a)(4), respectively). The agency is requesting that any manufacturers or distributors who have reformulated their products to remove the mercury ingredients update their labeling in accordance with part 207. These submissions should be highlighted with the words "Mercury List" on the envelope. The submission of information to FDA under part 207 is an approved collection of information under the Office of Management and Budget (OMB) control number 0910-0045 entitled "Registration of Producers of Drugs and Listing of Drugs in Commercial Distribution," which expires July 31, 2004.

Affected manufacturers or distributors should submit the acknowledgement information to the Dockets Management Branch (see **ADDRESSES**). Two copies of all written information are to be submitted. Anyone submitting information electronically may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. A copy of the list and received comments may be seen in the Dockets Management Branch between 9

a.m. and 4 p.m., Monday through Friday.

**III. Electronic Access**

The list is entitled "Mercury in Drug and Biologic Products" and is available on the Internet at <http://www.fda.gov/cder/fdama/mercury300.htm>.

Dated: January 15, 2003.

**Margaret M. Dotzel,**

*Assistant Commissioner for Policy.*

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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

[Docket No. 98D-0834]

**Draft Guidance for Industry on Labeling for Noncontraceptive Estrogen Drug Products for the Treatment of Vasomotor Symptoms and Vulvar and Vaginal Atrophy Symptoms—Prescribing Information for Health Care Providers and Patient Labeling; Availability**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "Labeling Guidance for Noncontraceptive Estrogen Drug Products for the Treatment of Vasomotor Symptoms and Vulvar and Vaginal Atrophy Symptoms—Prescribing Information for Health Care Providers and Patient Labeling." The draft guidance is intended to assist applicants in developing labeling for new drug applications for such drug products. This is the second draft of the guidance, which initially issued in September 1999.

**DATES:** Submit written or electronic comments on the draft guidance by April 4, 2003. General comments on agency guidance documents are welcome at any time.

**ADDRESSES:** Submit written requests for single copies of the draft guidance to the Division of Drug Information (HFD-240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the draft guidance to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm.