

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2008-N-0523]

DDM

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Certifier A. Corbin

**FDA-Regulated Products that Contain Bisphenol-A; Request for Information**

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

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

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**SUMMARY:** The Food and Drug Administration (FDA) is requesting assistance in the identification of types of FDA-regulated products that contain Bisphenol A (BPA), whether as a component of the product or its packaging, and any information relating to the leaching of BPA from the packaging to the product and/or from the product from the product following human administration.

**DATES:** Submit written or electronic comments and information by [*insert date 75 days after date of publication in the Federal Register*].

**ADDRESSES:** Submit written comments and information to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments and information to <http://www.regulations.gov>. Information submitted will be reviewed by the FDA BPA Task Force.

**FOR FURTHER INFORMATION CONTACT:** Norris Alderson, Office of Science and Health Coordination (HF-32), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-3340, FAX 301-827-3042, e-mail: [norris.alderon@fda.hhs.gov](mailto:norris.alderon@fda.hhs.gov).

**SUPPLEMENTARY INFORMATION:**

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## I. Background

BPA is a chemical commodity used primarily in the production of polycarbonate plastics and epoxy resins. Such plastics and resins have many applications including as components of packaging for food and drink, and as components of certain medical products and their packaging. Consequently, low levels of residual BPA may be present in such products. On April 14, 2008, the National Toxicology Program (NTP) released a draft brief on BPA for public comment and peer review. The NTP draft brief raises concerns that exposure to BPA could be linked to developmental problems of the endocrine system in infants and young children. The NTP draft brief also contains an exposure estimate to BPA for infants and young children due to leaching of BPA to food from plastic baby bottles and the linings of certain baby food containers. NTP has subsequently released a final report on BPA on September 3, 2008.

In response to the NTP draft brief, Commissioner von Eschenbach has convened an agency-wide task force to facilitate cross-agency review of current research and new information on BPA for all FDA-regulated products. The review will include the NTP brief and all other available information on the exposure of US consumers to BPA from FDA-regulated products.

During the course of this process the task force has been making an inventory of all FDA-regulated products that are known to contain BPA. The task force has already completed a thorough assessment of the potential exposure to BPA due to leaching from food-contact materials and is now interested in additional information on other types of products, specifically medical devices, biological products (including blood, blood products, vaccines, and cell and gene therapies, and drugs.

To ensure that we have current information to support our review of issues related to BPA risks, we are requesting information on the presence and levels of BPA for products with either direct or indirect patient contact. This would include situations where the BPA is a component of the product or its packaging. Information relating to the leaching of BPA from the packaging to the product and/or from the product to patients is also of interest.

At this time, exposure to BPA from the use of the following BPA-related materials provides an initial basis for the agency's query:

- Polycarbonate.
- Polyether sulfone.
- Polycarbonate/siloxane co-polymer.
- Biostable polyurethanes.
- Epoxy resin.

The agency's query also extends to products that contain certain bisphenol acrylic oligomers, such as the following:

- Bisphenol A diglycidylether methacrylate (BIS-GMA).
- Bisphenol A diglycidylether (BADGE).
- Bisphenol A dimethacrylate (BIS-DMA).
- Ethoxylated bisphenol A diacrylates.

## **II. Information Requested for FDA-Regulated Products**

### *A. Medical Devices and Articles Used in Product Manufacturing*

Direct contact devices would include, but not be limited to, those with direct contact with tissue, blood, other fluids, such as cerebrospinal fluid, and skin. Implants, catheters, and most dental devices are additional examples of devices with direct patient contact.

Indirect patient contact or external communicating devices would include, but are not limited to the following:

- Components of blood pathway circuits, (e.g., hemodialysis, apheresis, and cardiopulmonary bypass).
- Respiratory tubing circuits.
- Blood and parenteral solution administration sets.
- Apheresis instrument harnesses including separation bowls and break away closures.
- Hard casing for leukocyte reduction filters.
- Platelet rich plasma preparation devices including tubes for centrifugation of blood.
- Tops for vials or other container closures.
- Large volume containers used in preparation of raw materials for biological products production when lined with epoxy material that contains BPA.
- Materials used for preparation of cell/tissue/gene therapies, including: T-flasks, roller bottles, cell factories, cell culture beads, hard conical tubes, and disposable plastic pipettes.

In submitting your comments, we ask you to provide information with respect to any Class I, Class II, and Class III medical device that has direct or indirect patient contact. Whenever possible, include a description of the analytical method used to develop the submitted data and information.

If the device contains polycarbonate or BPA, we request the submission of data concerning the following:

- The rate and extent of BPA release from devices under clinically relevant extraction conditions.
- What conditions affect the release and leaching of BPA?
- Estimates of patient exposure to BPA from use of the device.

FDA is interested in possible alternatives to BPA.

- Are you aware of available alternatives to the use of BPA in certain medical devices? Provide information concerning the alternative material and any associated risks.

FDA is interested in receiving information concerning devices that have been shown to release BPA, including cardiopulmonary bypass circuits, hemodialysis circuits and certain dental devices. For these devices provide the following information:

- Describe the device type and intended use.
- Describe how the device directly or indirectly contacts a patient.
- Describe whether, and how, the device is used in pediatric patients, and describe the pediatric population by age and gender.
- Identify and attach any study reports related to BPA release from this device type.

*B. Human-Use Biological Products and Drugs (Including Protein Drugs)*

For products that are: (1) Formulated with BPA-containing components or (2) liquid-based dosage forms [including solutions, suspensions, semisolids (cream, lotion, ointment, foam, gel etc.)] and packaged in plastic containers or in metal canisters with plastic lining or coating (e.g., epoxy) if either the container or the coating have been made by using BPA, please provide the following information:

- NDA/ANDA/BLA number.
- Drug product name, dosage form and route of administration.
- Components and composition of the formulation.
- Container closure system (CCS) and components in direct contact with the formulation.
- Drug Master File number(s) for the CCS, if applicable.

- Levels of BPA found either as an extractable (in model solvents from the CCS) or a leachable (in the formulation) through expiry, if known.
- Identify the analytical method(s) for quantitation of BPA.
- Acceptance criteria either as an extractable or leachable, if established.

Please also provide summary reports from any studies that you may have performed to evaluate the toxicity and to justify the safety of BPA in these products.

### *C. Other FDA-Regulated Products*

We are also soliciting any relevant information on the use of, and potential exposure to, BPA from any other FDA-regulated products, including cosmetics, that have not been discussed in the above paragraphs.

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments and information. Submit a single copy of electronic comments and information or two paper copies of any mailed comments and information, except that individuals may submit one paper copy. Comments and information are to be identified with the name of the technology and the docket number found in brackets in the heading of this document. A copy of this notice and received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Dated: 10/3/08  
October 3, 2008.

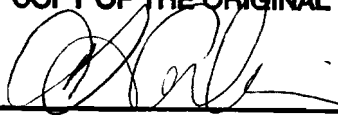
  
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Jeffrey Shuren,  
Associate Commissioner for Policy and Planning.

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