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DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration

21 CFR Parts 201, 312, 314, 601, 610, 801, 807, 809, 812, and 814

[Docket No. 2006N-0466]

Exceptions or Alternatives to Labeling Requirements for Products Held by the Strategic National Stockpile

AGENCY: Food and Drug Administration, HHS.

ACTION: Interim final rule; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is issuing regulations to permit FDA Center Directors to grant exceptions or alternatives to certain regulatory labeling requirements applicable to human drugs, biological products, or medical devices that are or will be included in the Strategic National Stockpile (SNS). Under this rule, the appropriate FDA Center Director may grant an exception or alternative to such labeling requirements if he or she determines that compliance with the requirements could adversely affect the safety, effectiveness, or availability of specified lots, batches, or other units of human drugs, biological products, or medical devices that are or will be included in the SNS, including not only those that are approved, licensed, or cleared for marketing, but also those that are investigational. A grant of an exception or alternative under these regulations will include any safeguards or conditions deemed appropriate by the FDA Center Director to ensure that the labeling of such products includes information for the safe and effective use of the products given their anticipated circumstances of use. This rule will facilitate the safety, effectiveness, and availability of appropriate medical countermeasures in the event of a public health emergency.

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DATES: The interim final rule is effective on [insert date of publication in the FEDERAL REGISTER]. Submit written or electronic comments on the interim final rule by [insert date 90 days after date of publication in the FEDERAL REGISTER]. Submit written or electronic comments regarding the information collection by [insert date 30 days after date of publication in the FEDERAL REGISTER] to the Office of Management and Budget (OMB) (see ADDRESSES).

ADDRESSES: You may submit comments, identified by Docket No. 2006N-0466, by any of the following methods:

Electronic Submissions

Submit electronic comments in the following ways:

- Federal eRulemaking Portal: http://www.regulations.gov. Follow the instructions for submitting comments.
- Agency Web site: http://www.fda.gov/dockets/ecomments. Follow the instructions for submitting comments on the agency Web site.

Written Submissions

Submit written submissions in the following ways:

- FAX: 301-827-6870.
- Mail/Hand delivery/Courier [For paper, disk, or CD-ROM submissions]: Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

To ensure more timely processing of comments, FDA is no longer accepting comments submitted to the agency by e-mail. FDA encourages you to continue to submit electronic

comments by using the Federal eRulemaking Portal or the agency Web site, as described in the Electronic Submissions portion of this paragraph.

Instructions: All submissions received must include the agency name and docket number for this rulemaking. All comments received may be posted without change to http://www.fda.gov/ohrms/dockets/default.htm, including any personal information provided. For additional information on submitting comments, see the "Request for Comments" heading of the SUPPLEMENTARY INFORMATION section of this document.

Docket: For access to the docket to read background documents or comments received, go to http://www.fda.gov/ohrms/dockets/default.htm and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Information Collection Provisions: Submit written comments on the information collection provisions to the Office of Information and Regulatory Affairs, Office of Management and Budget (OMB). To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, FAX: 202– 395–6974.

FOR FURTHER INFORMATION CONTACT:

For information concerning human biological products:

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For information concerning medical devices:

Casper E. Uldriks,

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SUPPLEMENTARY INFORMATION:

I. Introduction

This interim final rule applies to human drugs, biological products, and medical devices (hereinafter referred to collectively as medical products) that are or will be held in the SNS, including those SNS assets that are held at the manufacturer's facility or elsewhere on behalf of the SNS (e.g., vendor managed inventory that is distributed, held, and managed by manufacturers

or commercial distributors for the SNS) and prepositioned locations (e.g., CHEMPACKs that are distributed, held, and managed by hospitals and other facilities for the SNS).

An act of terrorism or a natural disaster event may result in the need for rapid access to large quantities of medical products. Under the Public Health Service Act (PHS Act), the Department of Health and Human Services (HHS) stockpiles medical products that are essential to the health security of the Nation. (See PHS Act section 319F-2, 42 U.S.C. 247d-6b)). This collection of medical products , known as the SNS, is to "provide for the emergency health security of the United States, including the emergency health security of children and other vulnerable populations, in the event of a bioterrorist attack or other public health emergency." The SNS is maintained by the Assistant Secretary for Preparedness and Response (ASPR), exercising this responsibility and authority of the Secretary, in collaboration with the Director of the Centers for Disease Control and Prevention (CDC), and in coordination with the Department of Homeland Security. Examples of situations that may necessitate the deployment of such products from the SNS are:

- Acts of terrorism using chemical, biological, radiological, or nuclear agents;
- Mass trauma; or
- Natural disasters such as hurricanes, pandemics, or earthquakes.

The SNS is also designed to augment similar stockpiles of medical supplies held by State and local public health agencies for use in the event of a national emergency.

II. Background

It may be appropriate for certain medical products that are or will be held in the SNS to be labeled in a manner that would not comply with certain FDA labeling regulations, given their anticipated circumstances of use in an emergency. However, noncompliance with these labeling

requirements could render such products misbranded under section 502 of the Federal Food, Drug, and Cosmetic Act (the FFD&C Act or the act) (21 U.S.C. 352).

Under this rule, the appropriate FDA Center Director may grant an exception or alternative to certain FDA labeling requirements if compliance with the requirements could adversely affect the safety, effectiveness, or availability of products that are or will be in the SNS. An exception or alternative granted under this rule may include conditions or safeguards so that the labeling for such products includes appropriate information necessary for the safe and effective use of the product given the product's anticipated circumstances of use.

Issues relating to the labeling of products that are or will be in the SNS exist now and will likely continue to develop. Such labeling issues may arise as a result of many different factors, including the indicated use, the storage location, the necessary storage conditions for a particular product, or the unique distribution mechanisms that may be used in an emergency. The provisions of this rule apply only to medical products that are or will be included in the SNS.

The medical products that may be stockpiled in the SNS include not only those that are approved, licensed, or cleared for marketing, but also those that are investigational.[1] When HHS procures investigational medical products for the SNS (i.e., products for which investigational new drug (IND) applications or investigational device exemptions (IDE) are in effect), it anticipates that these products may eventually become licensed, approved, or cleared for marketing by FDA while the products remain stockpiled. Labels on investigational products, however, including those in the SNS, ordinarily would not contain all elements required on licensed, approved, or cleared product labels.

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[1] Medical products stockpiled in the SNS may also include products that will ultimately be used in an emergency under section 564 of the FFD&C act (21 U.S.C. 360bbb-3) (regarding Emergency Use Authorizations).

For example, certain information may not be available until after approval of the product. For licensed biological products, § 610.60 (21 CFR 610.60) requires the container label to include, among other things, the expiration date of the product and license number of the manufacturer. Similarly, § 201.17 (21 CFR 201.17), which applies to drugs, sets forth requirements regarding placement of an expiration date, when required, on the immediate container. This information may not be available for an investigational product and thus could not be placed on container labels if the investigational product was added to the SNS. (See section III.D of this document for a discussion of conditions or safeguards that may be imposed in connection with an alternative or exception granted under this rule to ensure that labeling includes information necessary for safe and effective use of the product.)

Similarly, for medical devices that are restricted to use by prescription, § 801.109 (21 CFR 801.109) requires that the device label, other than for surgical instruments, bear a statement restricting sale of the device by order of a healthcare practitioner licensed by the law of the State in which he practices (§ 801.109(b)(1)). Whether a particular investigational device will be limited to sale by prescription may not be known before approval or clearance and, thus, this statement could not be placed on the investigational device's label if the product was still investigational when the device was added to the SNS. Additionally, the label of approved or cleared in vitro diagnostic products (IVDs) must contain information, such as warnings for users and storage instructions, that may not be finalized until product approval or clearance and could not be placed on the label if the investigational products were added to the SNS (see § 809.10).

Prior to the implementation of this rule, when such investigational products were ultimately approved for marketing, the products would have been subject to relabeling, a potentially time-consuming, costly, and labor-intensive process given that the SNS can contain

large numbers of these products. The SNS does not have manufacturing facilities or equipment necessary to relabel products that the SNS stores. Therefore, it is not feasible for SNS personnel to relabel products that are physically located in SNS storage sites. Prior to the implementation of this rule, the products would have needed to be returned to the manufacturers or sent to relabelers in order to be relabeled. Requiring relabeling of such investigational medical products after approval, licensure, or clearance could adversely affect the safety, effectiveness, or availability of these medical products in a number of ways. For example, shipping certain products from the SNS storage sites to the manufacturer or a relabeler for relabeling could subject them to unacceptable temperature deviations and create opportunities for product mishandling, such as mixing of different batches of the same product. Relabeling is especially difficult for certain products that must be stored at extremely low temperatures. In some instances, relabeling could cause the product to be unavailable for dispensing, delay deployment of the product for use, or could result in reduced product quality (e.g., potency or stability) and the loss of critical products. Security issues may also affect availability, as there is the potential for sabotage and diversion if a product were shipped back to the manufacturer or to a relabeler.

For these reasons, as explained in the following section of this document, this rule allows FDA Center Directors to grant exceptions or alternatives to certain labeling requirements not explicitly required by statute for medical products that are or will be included in the SNS.

III. Provisions of the Interim Final Rule

A. Applicability of a Request for an Exception or Alternative

Under §§ 201.26, 610.68, 801.128, and 809.11 (21 CFR 201.26, 610.68, 801.128, and 809.11), the appropriate FDA Center Director may grant a request for an exception or alternative to certain regulatory provisions pertaining to the labeling of human drugs, biological products,

and medical devices that currently are or will be included in the SNS if certain criteria are met. Any grant of an exception or alternative will only apply to the specified lots, batches, or other units of medical products in the request. We request comments on whether the scope of the rule should be amended to extend to medical products in other Federal, State, and local stockpiles, and if so, to which stockpile(s) the rule should apply.

The appropriate FDA Center Director will only review requests for exceptions or alternatives to the labeling provisions specified in this rule. The rule is not intended to provide a mechanism for waiving applicable requirements of sections 502 and 503 (21 U.S.C. 353) of the FFD&C Act and/or section 351 of the PHS Act. For example, under this new rule, an SNS official (or a manufacturer with an SNS official's written concurrence) may submit to FDA a request for an exception or alternative to a regulatory provision identified in this rule, such as where an expiration date may be placed under § 201.17, but not to the requirements under the PHS Act that the package (not necessarily the container) of a biological product be plainly marked with the product's expiration date (section 351(a)(1)(B)(iii) of the PHS Act (42 U.S.C. 262(a)(1)(B)(iii))). To the extent that a request for an exception or alternative to labeling requirements under this rule implicates other regulations not specified in this rule (e.g., regulations in 21 CFR part 211, Current Good Manufacturing Practice for Finished Pharmaceuticals) or involves statutory requirements, FDA will limit its consideration of the exception or alternative request to the labeling provisions specified in this rule. The remaining portions of such a request or other requests (i.e., those that do not involve the labeling provisions specified in this rule) will be reviewed under other applicable waiver provisions, if any.

We note that FDA's authority to grant an exception or alternative to the regulatory provisions specified in the rule is distinct from the agency's authority to exercise enforcement

discretion (i.e., decide not to take or recommend enforcement action) with respect to statutory and regulatory requirements, including those involving product labeling (see Heckler v. Chaney, 470 U.S. 821 (1985)).

In granting an exception or alternative under this rule, the appropriate FDA Center Director will consider whether compliance with the labeling requirements specified in this rule could adversely affect the safety, effectiveness, or availability of medical products that are or will be included in the SNS. As previously explained in this document, relabeling these medical products in compliance with certain FDA labeling regulations could adversely affect the safety, effectiveness, or availability of the products in some circumstances. In those instances, the appropriate FDA Center Director may grant an exception or alternative to the labeling requirements specified in this rule. On the other hand, there may be some products for which full or partial relabeling in compliance with the labeling requirements specified by this rule will not adversely affect the safety, effectiveness, or availability of the products. In such cases, an exception or alternative to the labeling requirements specified in this rule would not be warranted.

On a case-by-case basis, the appropriate FDA Center Director may also determine when an exception or alternative is granted that certain safeguards and conditions are appropriate, such as additional labeling on the SNS products, so that the labeling of such products would include information needed for safe and effective use under the anticipated circumstances of use.

B. Who May Submit a Request

A request for an exception or alternative to the labeling requirements specified in this rule may be submitted by an SNS official, or by any entity that manufactures (including labeling, packing, repackaging, or relabeling), distributes, or stores the medical products subject to the

request. Requests from entities other than the SNS must be submitted with an SNS official's written concurrence. We believe that many of the requests under this rule will be submitted by manufacturers, with concurrence of SNS officials, prior to or at the time a specified lot, batch, or other unit of product is procured by the SNS, or when an investigational product held in the SNS has been approved, licensed, or cleared. We anticipate that SNS officials will also submit requests.

The appropriate FDA Center Director may also grant an exception or alternative to the labeling provisions specified in this rule at his or her own initiative.

C. Request Criteria

Except when initiated by an FDA Center Director, a request for an exception or alternative to the labeling requirements specified in this rule will be in writing and must contain:

- An identification of the specific lot, batch, or other unit of product, which are or will be in the SNS, that would be subject to the exception or alternative;
- An identification of the specific labeling provisions under this rule that are the subject of the request;
- An explanation of why compliance with the specified labeling provisions could adversely affect the safety, effectiveness, or availability of the product subject to the request;
- A description of any proposed safeguards or conditions to be implemented so that the labeling of the product includes appropriate information necessary for the safe and effective use of the product given the anticipated circumstances of use;
- Copies of the proposed labeling of the specified lots, batches, or other units of product that will be subject to the exception or alternative; and
- Any other information requested by the appropriate FDA Center Director.

D. Granting of the Request

When the appropriate FDA Center Director grants or denies a request for an exception or alternative to the labeling requirements specified in this rule, the FDA Center Director will convey this decision in writing. In the written decision, the FDA Center Director may also impose appropriate conditions or safeguards so that the labeling of the product includes appropriate information necessary for the safe and effective use of the product given the anticipated circumstances of use. Such safeguards or conditions need not be limited to those proposed in the request, nor do they need to include all conditions or safeguards proposed in the request. Conditions could include, for example, a requirement of additional labeling on the SNS product, such as including the statement "For Strategic National Stockpile Use Only" on the label or elsewhere within the product's labeling. Such conditions could also address how or where any packaging or labeling changes would be conducted, or with what personnel. For example, the manufacturer may be required to take additional steps to ensure that products licensed, approved, or cleared while in the SNS bear information in their outer package labeling that was not available when such products entered the SNS as investigational products.

After the request is granted, the manufacturer may need to report to FDA any resulting changes to the New Drug Application (NDA), Biologics License Application (BLA), Premarket Approval Application (PMA), or Premarket Notification (510(k)) in effect, if any. The submission and grant of a request for an exception or alternative to the labeling requirements specified in this rule may be used to satisfy certain reporting obligations relating to changes to product applications under § 314.70 (21 CFR 314.70) (human drugs), § 601.12 (21 CFR 601.12) (biological drugs), § 814.39 (21 CFR 814.39) (medical devices subject to premarket approval), or § 807.81 (21 CFR 807.81) (medical devices subject to premarket notification submission

(510(k) clearance) requirements). Specifically, because the information affecting the premarket application will already be reviewed and approved as part of the request for an exception or alternative, manufacturers of medical products to which annual or periodic reporting requirements apply must describe such changes in their annual (or periodic) reports but are not required to submit supplement(s) to an approved application describing this information. This will reduce regulatory burden on industry by reducing duplication of regulatory submissions. Supplements under 21 CFR 814.39 and periodic reports under § 814.84 are not required for medical devices with 510(k) clearance, however. For these devices, the Center Director may determine that the submission and grant of a written request for an exception or alternative under this rule satisfies the 510(k) submission requirements in § 807.81(a)(3).

E. Labeling Provisions Subject to Exception or Alternative

We are listing in §§ 201.26(f) (human drug products), 610.68(f) (biological products), 801.128(f) (medical devices), and 809.11(f) (in vitro diagnostic products) those labeling provisions for which the appropriate FDA Center Director may grant an exception or alternative. As indicated in section III.A of this document, requests for exceptions or alternatives to other requirements of FDA's labeling regulations (such as bar code label requirements), or to other general regulations or statutory provisions, will be handled under any waiver provisions that may be applicable to those statutory or regulatory requirements. Additionally, FDA may exercise enforcement discretion with respect to the labeling requirements specified in this rule or other regulatory and statutory requirements.

1. Human Drug Products (§ 201.26(f))

For human drug products, including biological drugs, the following requirements pertaining to labeling in part 201, subpart A (21 CFR part 201, subpart A) and § 312.6 (21 CFR

312.6) may be the subject of an exception or alternative under this rule, except to the extent that they are explicitly required by statute:

- Identification of persons other than the manufacturer, packer, or distributor (§ 201.1(h)(1));
- Appearance of a person's name without qualification on the label (§ 201.1(h)(2));
- Appropriate qualifying phrases for the identity of the distributor or packer (§ 201.1(h)(5) and (h)(6));
- Criteria for the statement of the place of business (§ 201.1(i));
- Placement of the ingredient information required by section 502(e) of the FFD&C Act (§ 201.10(a));
- Criteria for the statement of the percentage of an ingredient in a drug (§ 201.10(d)(2));
- Declaration that an ingredient is a derivative or a preparation of a substance specifically named in section 502(e) of the FFD&C Act when the established name does not indicate such (§ 201.10(f));
- Criteria for the frequency of use and use in the running text of the established name in association with the proprietary name or designation for the drug or any ingredient thereof in the label or labeling of a prescription drug (§ 201.10(g)(1));
- The placement of the quantitative ingredient information when the established name does not correspond to the proprietary name or designation and the prescription drug contains two or more active ingredients (§ 201.10(h)(1));
- The location of the expiration date (§ 201.17);
- The information provided by the lot number (§ 201.18);
- Use of the term "infant" (§ 201.19);

- Declaration of the presence of FD&C Yellow No. 5 and FD&C Yellow No. 6 in certain drugs for human use (§ 201.20);
- Declaration of the presence of phenylalanine as a component of aspartame in over-the-counter and prescription drugs for human use (§ 201.21);
- Required warning statements for prescription drugs containing sulfites (§ 201.22);
- Labeling statements for systemic antibacterial drug products (§ 201.24); and
- The prescribed statement for investigational new drugs limiting them to investigational use (§ 312.6(a)).

2. Biological Drug Products (§ 610.68(f))

In addition to the labeling requirements for investigational new drugs in § 312.6, certain labeling requirements for biological products in 21 CFR part 610 subpart G, except to the extent that they are explicitly required by statute, may also be the subject of an exception or alternative under this rule:

- The information required on the product's container label (§ 610.60);[2]
- Certain information on the package label, specifically: Lot number, information on the preservative, number of containers, recommended storage temperature, certain instructions for use, recommended individual dose, route of administration, known sensitizing substances, type and amount of added antibiotics, inactive ingredients, adjuvant, source of product, identity of microorganisms used in manufacture, and minimum potency (§ 610.61(c) and (e) through (r));
- Requirements relating to the position and prominence of the proper name on the package label as well as requirements relating to size and type of characters (21 CFR 610.62);

[2] This is distinct from the requirements for a product's package label under § 610.61 (21 CFR 610.61).

- The placement on the container and package label of the name, address, and license information of each manufacturer participating in the manufacture of a biological product, if two or more manufacturers participate in manufacturing (21 CFR 610.63);
- The name and address of the distributor, and the required identifying phrases on the label (21 CFR 610.64); and
- Label requirements relating to products for export (21 CFR 610.65)

3. Medical Devices (§ 801.128(f))

For medical devices, the appropriate FDA Center Director may grant a request for an exception or alternative to certain labeling requirements in parts 801 and 812 (21 CFR parts 801 and 812), except to the extent that they are explicitly required by statute:

- Criteria for the statement of the place of business (§ 801.1(d));
- Labeling information on the principal display panel of over-the-counter devices in package form, i.e., the part of a label that is most likely to be displayed, presented, shown, or examined under customary conditions of display for retail sale (§ 801.60);
- Requirements related to an accurate statement of principal intended action and format of a statement of identity for an over-the-counter device in package form (§ 801.61);
- Requirements related to the declaration of net quantity of contents on the label of an over-the-counter device in package form (§ 801.62);
- Warning statement for over-the-counter devices containing or manufactured with chlorofluorocarbons and other class I ozone-depleting substances (§ 801.63);
- Labeling requirements for prescription devices (§ 801.109);
- Labeling requirements for specific devices including dentures and hearing aids (part 801, subpart H);

- The prescribed statement for investigational devices limiting the device to investigational use (§ 812.5(a)); and
- The prescribed statement for investigational devices used solely on research animals limiting the device to investigational use in laboratory animals (§ 812.5(c)).

4. In Vitro Diagnostic Products (§ 809.11(f))

The appropriate FDA Center Director may grant a request for an exception or alternative to the following requirements pertaining to IVDs in parts 809 (21 CFR part 809) and 812, except to the extent that they are explicitly required by statute.

- Certain label information for IVDs, i.e., the proprietary name; the intended use or uses of the product; for a reagent, the declaration of the established name, if any, the quantity, proportion, and concentration of each reactive ingredient, and the source and activity if derived from a biological material; statement of warnings or precautions; for a reagent, appropriate storage instructions adequate to protect the stability of the product; for a reagent, a means by which the user may be ensured that the product meets appropriate standards of identity, strength, quality and purity at the time of use; and a lot or control number (§ 809.10(a)(1) through (a)(6) and (a)(9));
- Labeling accompanying each IVD, including reagents and instruments, i.e., such information as proprietary name, intended use or uses, summary and explanation of the test, a statement of warnings or precautions for users, information regarding specimen collection and preparation for analysis, outline of recommended procedures, information regarding results, limitation of the procedure, expected values, specific performance characteristics, and bibliography (§ 809.10(b));

- The prescribed statements for investigational IVDs that are not subject to part 812 (§ 809.10(c)(2));
- The label of general purpose laboratory reagents, i.e., the proprietary name; the quantity, proportion, or concentration of the reagent ingredient; and for a reagent derived from biological material, the source and measure of activity; statement of purity and quality of the reagent; statement of warnings or precautions; appropriate storage instructions adequate to protect the stability of the product; and a lot or control number (§ 809.10(d)(1)(i) through (d)(1)(v) and (d)(1)(viii));
- Labeling of general purpose laboratory equipment, i.e., description of the product, its composition, and physical characteristics if necessary for use (§ 809.10(d)(2)); and
- Labeling for analyte specific reagents, i.e., the proprietary name; the quantity, proportion, or concentration of the reagent ingredient; and for a reagent derived from biological material, the source and measure of activity; statement of purity and quality of the reagent; statement of warnings or precautions for users; date of manufacture and appropriate storage instructions adequate to protect the stability of the product; a lot or control number; prescribed statements regarding analytical and performance characteristics specific to class I, II, and III analyte specific reagents (§ 809.10(e)(1)(i) through (e)(1)(vi) and (e)(1)(ix) through (e)(1)(xi)).

IV. Legal Authority

In this interim final rule, FDA is amending regulations pertaining to the content and format of medical product labeling. The provisions of this rule will allow FDA to grant exceptions or alternatives to certain of those labeling requirements. The labeling regulations to which exceptions or alternatives will be permitted were issued by FDA under authority of the

FFD&C Act and the PHS Act to mandate particular ways that firms must satisfy the broad requirements and prohibitions in those statutes, such as the prohibition on false and misleading drug and device labeling. As described in section II of this document, FDA has determined that circumstances may arise in which compliance with those regulatory mandates could adversely affect the safety, effectiveness, or availability of certain medical products that are or will be included in the SNS. Moreover, due to the unique nature of the SNS, those products could deviate from particular mandates of existing labeling regulations without violating the broad statutory requirements and prohibitions in the FFD&C Act and the PHS Act. For those reasons, FDA is exercising its authority to regulate labeling by modifying the existing regulations in a way that will allow exceptions or alternatives for medical products that are or will be included in the SNS.

FDA has various sources of authority to issue labeling regulations. For example, under section 502(a) of the FFD&C Act, a drug (including biological products) or device is misbranded if its labeling is false or misleading in any particular. In determining whether a product's labeling is misleading, FDA may consider not only representations or suggestions made in the labeling, but also whether the labeling fails to reveal material facts in light of those representations or suggestions or with respect to consequences which may result from the use of the product under customary or usual conditions of use (section 201(n) of the FFD&C Act (21 U.S.C. 321(n))). By authority delegated under section 701(a) of the FFD&C Act (21 U.S.C. 371(a)), FDA is authorized to issue regulations for the efficient enforcement of the FFD&C Act. Existing FDA regulations mandating specific labeling content and format for drugs and devices satisfy those general statutory standards. For example, many labeling regulations are designed to ensure that nothing in the labeling is false or misleading in any particular, to ensure that the

labeling reveals all material facts in light of the representations or suggestions in the labeling, and to ensure that FDA may efficiently enforce those statutory requirements as well as other requirements of the FFD&C Act and the PHS Act.

Because biological products are also drugs as defined within the FFD&C Act, the authority discussed previously extends to regulations prescribing content and format requirements for biological product labeling. There is, however, additional legal authority in the PHS Act for this rule's requirements with respect to biological products generally. For example, section 351(a)(1)(A) of the PHS Act provides that no person may introduce or deliver for introduction into interstate commerce any biological product unless a biologics license is in effect for the product. By authority delegated under section 351(a)(2)(A) of the PHS Act, FDA is required to establish, by regulation, requirements for the approval, suspension, and revocation of biologics licenses.

Because the SNS is intended "to provide for the emergency health security of the United States * * * in the event of a bioterrorist attack or other public health emergency,"[3] the SNS may contain products that would otherwise not be available for widespread distribution. For example, the ASPR (exercising the Secretary's authority), in collaboration with the Director of the CDC and in coordination with the Department of Homeland Security, may determine that it is appropriate to include certain investigational medical products in the SNS. As described in section II of this document, some of these products require storage at extremely low temperatures and cannot be temporarily removed from storage for relabeling without compromising their integrity. Moreover, shipping products from SNS storage sites to relabelers

[3] Section 3 of the Project BioShield Act of 2004 (section 319F-2 of the PHS Act (42 U.S.C. 247d-6b)).

or back to manufacturers for relabeling could increase the potential for sabotage and diversion, as well as increase exposure to conditions affecting product quality, such as temperature deviations. As a result, removing these investigational products from storage for relabeling at the time of approval and then returning them to storage could undermine their safety, effectiveness, or availability and, in some cases, would be impracticable. Compliance with the FDA regulations that would require such relabeling could discourage SNS procurement of these products and thereby limit available countermeasures in the event of a bioterrorist attack or other public health emergency.

To address this concern, FDA is creating a mechanism to allow exceptions or alternatives to the labeling regulations specified in this rule to help ensure the safety, effectiveness, and availability of medical products that are or will be included in the SNS. FDA has concluded that exceptions or alternatives granted under this rule will not render products misbranded due to the additional safeguards and conditions that may be required when an exception or alternative is granted, as well as the unique storage, deployment, and distribution considerations essential to the SNS. As explained in section III.D of this document, a grant of an exception or alternative under this rule may include additional safeguards or conditions so that the labeling of products subject to the exception or alternative includes information needed for safe and effective use under the anticipated circumstances of use. Moreover, products intended for use in certain public health emergencies are likely to be administered to large numbers of people within confined geographic areas, such as in the case of a natural disaster. These SNS products may therefore be packaged in large quantities to facilitate rapid distribution on extremely short notice. Consequently, their packaging and distribution may differ from that of non-SNS products.

Moreover, HHS may establish special mechanisms to provide product information, collect adverse event information, and track the product's distribution.

This rule does not create exemptions from express statutory requirements or prohibitions regarding medical product labeling. The FFD&C Act and the PHS Act set forth certain types of information that must appear in the labeling for medical products. For example, section 351(a)(1)(B) of the PHS Act provides that each package of a biological product must be marked with the proper name of the biological product; the name, address, and applicable license number of the manufacturer of the biological product; and the expiration date of the biological product. Drugs (including biological products) and medical devices in package form must bear labels containing the name and place of business of the manufacturer, packer, or distributor (section 502(b)(1) of the FFD&C Act). This interim final rule does not permit exceptions or alternatives to any of those requirements. In addition, the FFD&C Act and the PHS Act both prohibit false labeling (section 502(a) of the FFD&C Act); section 351(b) of the PHS Act). This interim final rule does not allow false information to appear in medical product labeling.

As noted previously, this rule does not limit FDA's ability to exercise enforcement discretion with respect to statutory and regulatory requirements, including those involving medical product labeling (see Heckler v. Chaney, 470 U.S. 821 (1985)).

To the extent that a State requires labeling that directly conflicts with, is different from, or is in addition, to any exceptions or alternatives granted under this rule, the State-required labeling would be subject to implied conflict preemption and, in some cases, express preemption. FDA restated its longstanding views on preemption in the preamble to the recently promulgated final rule entitled "Requirements on Content and Format of Labeling for Human Prescription

Drug and Biological Products" (see 71 FR 3922 at 3933 through 3936 and 3967 through 3969; January 24, 2006), and that discussion reflects the agency's current position on this issue.

Under the principles of implied conflict preemption, courts have found State law preempted where it is impossible to comply with both Federal and State law or where the State law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." See English v. General Electric Co., 496 U.S. 72, 79 (1990); Florida Lime & Avocado Growers, Inc., 373 U.S. 132, 142-143 (1963); Hines v. Davidowitz, 312 U.S. 52, 67 (1941). Consistent with this case law, section 4(a) of Executive Order 13132 states that "[a]gencies shall construe * * * a Federal statute to preempt State law only where the statute contains an express preemption provision or there is some other clear evidence that the Congress intended preemption of State law, or where the exercise of State authority conflicts with the exercise of Federal authority under the Federal statute."

As explained previously, this interim final rule will facilitate the safety, effectiveness, and availability of appropriate medical countermeasures in the event of a public health emergency. Because Congress authorized the SNS to "provide for the emergency health security of the United States * * * in the event of a bioterrorist attack or other public health emergency," products held in the SNS should be ready for deployment at all times. In an emergency, it is critical that State requirements regarding the content and format of labeling do not interfere with the safety, effectiveness, or availability of SNS products. FDA believes that State-required labeling requirements different from or in addition to FDA requirements would "stand as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." See Hines, 312 U.S. at 67. Moreover, these State requirements would "conflict with the exercise

of Federal authority under [PHS Act section 319F-2, 42 U.S.C. 247d-6b]." See Executive Order 13132.

Additionally, under section 751 of the FFD&C Act (21 U.S.C. 379r), State or local requirements that are different from or in addition to exceptions or alternatives granted under this rule, and relate to the regulation of nonprescription drugs, are expressly preempted. Similarly, in accordance with section 521 of the FFD&C Act (21 U.S.C. 360k), State or local requirements that are different from, or in addition to, exceptions or alternatives granted under this rule with respect to approved medical devices are expressly preempted. See the Federalism section in this document for additional discussion of preemption in the context of this interim final rule.

V. Issuance of an Interim Final Rule, Immediate Effective Date, and Opportunity for Public Comment

FDA is issuing this rule as an interim final rule, effective immediately, with an opportunity for public comment. Section 553(b)(3)(B) of the Administrative Procedure Act (5 U.S.C. 553(b)(3)(B)) provides that, when an agency for good cause finds that notice and public procedure are impracticable, unnecessary, or contrary to public interest, the agency may issue a rule without providing notice and public comment. FDA has determined that there is good cause under 5 U.S.C. 553(b)(3)(B) and 21 CFR 10.40(d) to publish this regulation as an interim final rule. An emergency requiring deployment of medical products in the SNS could happen at any time. Without this rule, the safety, effectiveness, or availability of medical products held in the SNS could be adversely affected because of relabeling requirements. An interim final rule ensures that a legal mechanism is immediately available for addressing labeling issues associated with medical products in the SNS without compromising their safety, effectiveness, or

availability for use in an emergency. Products held in the SNS should be ready for deployment at all times.

FDA invites public comment on this interim final rule. The comment period on this interim final rule will be 90 days. The agency will consider modifications to this interim final rule based on comments made during the comment period. Interested persons may submit to the Division of Dockets Management (see ADDRESSES) written or electronic comments regarding this interim final rule. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

FDA will address comments received and confirm or amend this interim final rule in a final rule.

VI. Analysis of Impacts

FDA has examined the impacts of the interim final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104-4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this interim final rule is not a significant regulatory action under the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because of the deregulatory nature

of this rule and the minimal costs associated with applying for an exception or alternative under this rule, the agency certifies that the interim final rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is $127 million, using the most current (2006) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this interim final rule to result in any 1-year expenditure that would meet or exceed this amount.

A. Need for the Interim Final Rule

FDA is issuing this interim final rule to allow for exceptions or alternatives to specified labeling requirements for certain medical products that are or will be in the SNS. As explained in other sections of this preamble, compliance with these labeling requirements in some circumstances could adversely affect or compromise the safety, effectiveness or availability of these products. Exceptions or alternatives to certain labeling requirements will provide the flexibility needed to help ensure that FDA-regulated medical products that are or will be in the SNS are not deemed misbranded and are available in an emergency situation.

B. Scope of the Interim Final Rule

This interim final rule applies to medical products that are or will be stockpiled by the SNS. It allows entities that manufacture (including labeling, packing, relabeling, or repackaging), distribute, or store affected SNS products to request an exception or alternative to

specified regulatory labeling requirements for human drugs, biological products, and medical devices to prevent misbranding of those products in the SNS. Any grant of such a request by an FDA Center Director would apply to specified lots, batches, or other units of medical product identified in the request. When reviewing requests, the FDA Center Director will consider whether complying with the specified labeling regulations could adversely affect the safety, effectiveness, or availability of stockpiled products and may impose appropriate safeguards and conditions so that the labeling of products subject to the request would include information needed for safe and effective use under the anticipated circumstances of use. Alternatively, at his or her own initiative, an FDA Center Director may grant an exception or alternative to the specified labeling provisions without receiving a written request. Allowing the agency the ability to act on its own initiative could help avoid misbranding of products that are or will be in the SNS.

C. Costs of the Interim Final Rule

This rule would allow SNS officials and entities that manufacture (including labeling, packing, relabeling, or repackaging), distribute, or store medical products in the SNS to request exceptions from certain labeling requirements in FDA regulations. An exception or alternative from specified labeling requirements for FDA-regulated medical products can also be initiated by the appropriate FDA Center Director. The interim final rule would impose compliance costs on industry when entities prepare and submit requests for exceptions or alternatives to labeling requirements to avoid misbranding of their products that are or will be in the SNS. However, granting exceptions or alternatives to labeling requirements would provide the government with the flexibility needed to more efficiently manage medical products in the SNS without risking

the availability of medical products for emergency use (see section VI.D of this document, Benefits of the Interim Final Rule).

FDA estimates that requests for exceptions would cost from $380 to $1,130 for each request. Regulatory Affairs personnel may spend from 8 to 24 hours per request preparing the information that would be required in an application for an exception or alternative under this rule. According to Bureau of Labor Statistics data, the fully loaded hourly wage for management and professional employees working in goods-producing industries was $47.25 in 2004 (U.S. Department of Labor, Bureau of Labor Statistics, "Employer Cost Employee Compensation--December 2004," Bureau of Labor Statistics News, USDL 05-432, March 16, 2005).

D. Benefits of the Interim Final Rule

Although the agency has no data to quantify the benefits, this interim final rule provides flexibility in labeling requirements for FDA-regulated medical products in the SNS. If an exception or alternative is granted, affected medical products in the SNS would not be misbranded and would not be rendered unavailable for emergency use due to relabeling operations. Exceptions or alternatives may be granted on a case-by-case basis at the initiative of the appropriate FDA Center Director or after receipt of a written request from an entity that manufactures, distributes, or stores products in the SNS. To illustrate the potential benefits of this rule we describe costs that could be avoided by granting an exception or alternative to certain labeling requirements upon written request of a manufacturer.

In some cases, granting an exception to labeling requirements may save direct relabeling costs. For example, to change information on a carton or container label, a firm might spend $300 in material costs for new artwork, $600 to $1,000 in labor costs to prepare the new artwork and about 10 cents to print each new carton or container label. Besides the costs to prepare a

new carton, there would be additional labor costs to remove the product from the old carton and insert it in the new carton. With a container label, it is likely that the new label could be affixed directly on top of the existing label, reducing the amount of effort needed to make this change. Because packaging is normally automated, the agency has no information about how much time it would take to manually replace a container label or exchange a carton, but believes this could cost about 5 to 10 cents per unit.

Before the implementation of this rule, when an investigational product in the SNS was subsequently approved, the product labeling would have needed to be immediately changed to add approved labeling information that was unavailable prior to approval. An exception or alternative to these labeling requirements might allow entities to ship investigational products with labeling that can be manually modified or supplemented at the SNS location once the drug is approved. Without an exception or alternative, it would be necessary to remove the investigational products from the SNS for relabeling or, in some cases, to replace the product.

This rule would avoid other potential costs. Without an exception or alternative, the SNS might be required to purchase costly replacement units. In other cases, some products may be appropriate for exceptions or alternatives because their availability for use in an emergency could be compromised if they had to be shipped out of the SNS to be relabeled. Removing such products from the stockpile, even temporarily, could jeopardize or adversely affect product safety or effectiveness (due to conditions of relabeling or related shipping, storage, and handling), requiring additional product testing or product replacement. Because replacement costs would vary widely and depend on the nature of the product, the number of units affected, and current market price, the amount of these avoided costs is unknown.

Although we only describe the potential benefits of this interim final rule in qualitative terms, we believe it is reasonable to assume that the benefits of providing flexibility in labeling requirements for SNS products justify the potential compliance costs of the rule. Moreover, the rule will allow FDA the flexibility to manage the products in the SNS without risking the safety, effectiveness, or availability of these products for use in an emergency.

E. Small Business Impacts

FDA has examined the economic implications of this proposed rule as required by the Regulatory Flexibility Act (5 U.S.C. 601-612). If a rule has a significant economic impact on a substantial number of small entities, the Regulatory Flexibility Act requires agencies to analyze regulatory options that would lessen the economic effect of the rule on small entities. This rule is not expected to have a significant impact on a substantial number of small entities. It is estimated that this interim final rule will cost small entities no more than $1,130 when they submit a request. For affected small entities (e.g., medical product manufacturers, relabelers, or packers) we expect that this would represent a negligible proportion of annual receipts. Therefore, the agency certifies that the interim final rule will not have a significant economic impact on a substantial number of small entities.

F. Regulatory Options Considered

No new regulatory action. The agency considered and rejected this option. The Agency recognized that certain medical products in the SNS, due to their anticipated circumstances of use in an emergency, might need to be labeled in a manner that did not comply with certain FDA labeling regulations. Without the ability to grant an exception to labeling requirements, existing FDA labeling regulations would have rendered such medical products misbranded. Moreover, the relabeling of these products to comply with FDA labeling regulations could have adversely

affected their safety, effectiveness, or availability. As a result, FDA would have needed to exercise enforcement discretion to allow labeling to deviate from FDA requirements. To the extent possible, FDA believes that amending its labeling regulations is preferable to reliance on enforcement discretion to ensure the continued availability of medical products that are or will be in the SNS.

VII. The Paperwork Reduction Act of 1995

This interim final rule 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 title, description, and respondent description of the information collection provisions are shown as follows with an estimate of the annual reporting burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

FDA invites comments on the following topics: (1) Whether the collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Title: Exceptions or Alternatives to Labeling Requirements for Products Held by the Strategic National Stockpile.

Description: FDA is issuing regulations to permit FDA Center Directors to grant a request submitted under §§ 201.26(c)(1)(i) (human drug products), 610.68(c)(1)(i) (biological products), 801.128(c)(1)(i) (medical devices), and 809.11(c)(1)(i) (in vitro diagnostic products for human use) for an exception or alternative to certain applicable regulatory labeling provisions when these products are or will be included in the SNS. The request must:

- Identify the specified lots, batches, or other units of the affected product;
- Identify the labeling provisions under this rule that are the subject of the request;
- Explain why compliance with the specified labeling provisions could adversely affect the safety, effectiveness, or availability of the product subject to the request;
- Describe any proposed safeguards or conditions that will be implemented so that the labeling of the product includes appropriate information necessary for the safe and effective use of the product given the anticipated circumstances of use of the product;
- Provide a draft of the proposed labeling; and
- Provide any other information requested by the FDA Center Director in support of the request.

The FDA Center Director will grant the request if he or she determines that compliance with the identified labeling provisions could adversely affect the safety, effectiveness, or availability of specified lots, batches, or other units of human drugs, biological products, or medical devices that are or will be included in the SNS.

Description of Respondents: Entities that manufacture (including labeling, packing, relabeling, or repackaging), distribute, or store affected products.

FDA estimates the information collection burden as follows:

Table 1.--Estimated Annual Reporting Burden[1]

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
201.26(c)(1)(i)	18	1	18	24	432
610.68(c)(1)(i)	10	1	10	24	240
801.128(c)(1)(i) and 809.11(c)(1)(i)	2	1	2	24	48
Total					720

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

Although FDA cannot predict the number of future requests, based on limited information within FDA, we estimate that approximately 30 respondents will request annually one exception or alternative to labeling provisions to avoid misbranding of their products in the SNS. The estimate of one request per respondent is based on the anticipated occasional occurrence of a product being misbranded while in the SNS. We are estimating that each respondent will spend from 8 to 24 hours preparing each request. The hours per response are based on estimated time that it takes to prepare a supplement to an application, which may be considered similar to a request for an exception or alternative.

The information collection provisions in §§ 314.70, 601.12, 807.81 and 814.39 have been approved under OMB control numbers 0910-0001 (expires May 31, 2008), 0910-0338 (expires September 30, 2008), 0910-0120 (expires August 31, 2010), and 0910-0231 (expires September 30, 2007), respectively.

The information collection provisions for this interim final rule have been approved under the emergency processing provisions of the PRA. The assigned OMB approval number of this collection of information is 0910-0614. This approval expires on June 30, 2008. Interested persons are requested to fax comments regarding the information collection by (see DATES) to the Office of Information and Regulatory Affairs, OMB (see ADDRESSES).

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

VIII. Environmental Impact

The agency has determined under 21 CFR 25.30(k) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

IX. Federalism

As stated in the preamble, FDA has analyzed this interim final rule in accordance with the principles set forth in Executive Order 13132. Section 4(a) of this Executive Order requires agencies to "construe * * * a Federal statute to preempt State law only where the statute contains an express preemption provision or there is some other clear evidence that the Congress intended preemption of State law, or where the exercise of State authority conflicts with the exercise of Federal authority under the Federal statute." In this rule, FDA is revising certain requirements concerning the format and content of labeling for human drugs, biological products, and medical devices that are or will be included in the SNS to provide for exceptions or alternatives to these requirements under specified circumstances. To the extent that a State requires labeling that directly conflicts with, is different from, or is in addition, to any exceptions or alternatives granted under this rule, the State-required labeling would be subject to implied conflict preemption. Moreover, certain State requirements regarding the format and content of nonprescription drug labeling and/or labeling of approved medical devices may be subject to the express preemption provisions in section 751 of the FFD&C Act (21 U.S.C. 360k) (nonprescription drugs) and section 521 of the FFD&C Act (approved medical devices).

FDA is aware that State requirements on medical product labeling, often as a result of product liability lawsuits, may conflict with Federal requirements. FDA restated its longstanding views on preemption in the preamble to the recently promulgated final rule entitled "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products" (*see* 71 FR 3922 at 3933 through 3936 and 3967 through 3969). That discussion is applicable to this interim final rule as well, and reflects the agency's current position on this issue.

Section 4(c) of Executive Order 13132 instructs us to restrict any Federal preemption of State law to the "minimum level necessary to achieve the objectives of the statute pursuant to which the regulations are promulgated." This interim final rule meets the preceding requirement because, as discussed previously, it would preempt only State laws that directly conflict with, are different from, or are in addition to any Federal requirements. Section 4(d) of Executive Order 13132 states that when an agency foresees the possibility of a conflict between State law and federally protected interests within the agency's area of regulatory responsibility, the agency "shall consult, to the extent practicable, with appropriate State and local officials in an effort to avoid such a conflict." In this case, FDA foresees the possibility of a conflict between State law and federally protected interests within the agency's area of regulatory responsibility.

Section 4(e) of Executive Order 13132 adds that "when an agency proposes to act through adjudication or rulemaking to preempt State law, the agency "shall provide all affected State and local officials notice and an opportunity for appropriate participation in the proceedings." FDA is seeking input from all stakeholders on the provisions of this interim final rule through publication of the rule in the FEDERAL REGISTER, and will consult with State

and local officials in an effort to avoid conflicts between State law and Federal protected interests in accordance with Executive Order 13132.

In conclusion, the agency believes that it has complied with all of the applicable requirements under Executive Order 13132 and has determined that this interim final rule is consistent with the Executive order.

X. Request for Comments

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

List of Subjects

21 CFR Part 201

Drugs, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 312

Drugs, Exports, Imports, Investigations, Labeling, Medical research, Reporting and recordkeeping requirements, Safety.

21 CFR Part 314

Administrative practice and procedure, Confidential business information, Drugs, Reporting and recordkeeping requirements.

21 CFR Part 601

Administrative practice and procedure, Biologics, Confidential business information.

21 CFR Part 610

Biologics, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 801

Labeling, Medical devices, Reporting and recordkeeping requirements.

21 CFR Part 807

Confidential business information, Imports, Medical devices, Reporting and recordkeeping requirements.

21 CFR Part 809

Labeling, Medical devices.

21 CFR Part 812

Health records, Medical devices, Medical research, Reporting and recordkeeping requirements.

21 CFR Part 814

Administrative practice and procedure, Confidential business information, Medical devices, Medical research, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR chapter I is amended as follows:

PART 201--LABELING

1. The authority citation for 21 CFR part 201 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 358, 360, 360b, 360gg-360ss, 371, 374, 379e; 42 U.S.C. 216, 241, 262, 264.

2. Add § 201.26 to subpart A to read as follows:

§ 201.26 Exceptions or alternatives to labeling requirements for human drug products held by the Strategic National Stockpile.

(a) The appropriate FDA Center Director may grant an exception or alternative to any provision listed in paragraph (f) of this section and not explicitly required by statute, for specified lots, batches, or other units of a human drug product, if the Center Director determines that compliance with such labeling requirement could adversely affect the safety, effectiveness, or availability of such product that is or will be included in the Strategic National Stockpile.

(b)(1)(i) A Strategic National Stockpile official or any entity that manufactures (including labeling, packing, relabeling, or repackaging), distributes, or stores a human drug product that is or will be included in the Strategic National Stockpile may submit, with written concurrence from a Strategic National Stockpile official, a written request for an exception or alternative described in paragraph (a) of this section to the Center Director.

(ii) The Center Director may grant an exception or alternative described in paragraph (a) of this section on his or her own initiative.

(2) A written request for an exception or alternative described in paragraph (a) of this section must:

(i) Identify the specified lots, batches, or other units of the human drug product that would be subject to the exception or alternative;

(ii) Identify the labeling provision(s) listed in paragraph (f) of this section that are the subject of the exception or alternative request;

(iii) Explain why compliance with such labeling provision(s) could adversely affect the safety, effectiveness, or availability of the specified lots, batches, or other units of a human drug product that are or will be held in the Strategic National Stockpile;

(iv) Describe any proposed safeguards or conditions that will be implemented so that the labeling of the product includes appropriate information necessary for the safe and effective use of the product, given the anticipated circumstances of use of the product;

(v) Provide a draft of the proposed labeling of the specified lots, batches, or other units of the human drug product subject to the exception or alternative; and

(vi) Provide any other information requested by the Center Director in support of the request.

(c) The Center Director must respond in writing to all requests under this section.

(d) A grant of an exception or alternative under this section will include any safeguards or conditions deemed appropriate by the Center Director so that the labeling of product subject to the exception or alternative includes the information necessary for the safe and effective use of the product, given the anticipated circumstances of use.

(e) If you are a sponsor receiving a grant of a request for an exception or alternative to the labeling requirements under this section:

(1) You need not submit a supplement under § 314.70(a) through (c) or § 601.12(f)(1) through (f)(2) of this chapter; however,

(2) You must report any grant of a request for an exception or alternative under this section as part of your annual report under §§ 314.70(d) or 601.12(f)(3) of this chapter.

(f) The Center Director may grant an exception or alternative under this section to the following provisions of this chapter, to the extent that the requirements in these provisions are not explicitly required by statute:

(1) § 201.1(h)(1) through (h)(2), (h)(5) through (h)(6), and (i);

(2) § 201.10(a), (d)(2), (f), (g)(1), and (h)(1);

(3) § 201.17;

(4) § 201.18;

(5) § 201.19;

(6) § 201.20;

(7) § 201.21;

(8) § 201.22;

(9) § 201.24; and

(10) § 312.6.

PART 312--INVESTIGATIONAL NEW DRUG APPLICATION

3. The authority citation for 21 CFR part 312 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 371, 381, 382, 383, 393; 42 U.S.C. 262.

4. Section 312.6 is amended by adding paragraph (c) to read as follows:

§ 312.6 Labeling of an investigational new drug.

* * * * *

(c) The appropriate FDA Center Director, according to the procedures set forth in §§ 201.26 or 610.68 of this chapter, may grant an exception or alternative to the provision in paragraph (a) of this section, to the extent that this provision is not explicitly required by statute,

for specified lots, batches, or other units of a human drug product that is or will be included in the Strategic National Stockpile.

PART 314--APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG

5. The authority citation for 21 CFR part 314 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 355a, 356, 356a, 356b, 356c, 371, 374, 379e.

6. Section 314.70 is amended by revising paragraph (a)(1) to read as follows:

§ 314.70 Supplements and other changes to an approved application.

(a) * * *

(1)(i) Except as provided in paragraph (a)(1)(ii) of this section, the applicant must notify FDA about each change in each condition established in an approved application beyond the variations already provided for in the application. The notice is required to describe the change fully. Depending on the type of change, the applicant must notify FDA about the change in a supplement under paragraph (b) or (c) of this section or by inclusion of the information in the annual report to the application under paragraph (d) of this section.

(ii) The submission and grant of a written request for an exception or alternative under § 201.26 of this chapter satisfies the applicable requirements in paragraphs (a) through (c) of this section. However, any grant of a request for an exception or alternative under § 201.26 of this chapter must be reported as part of the annual report to the application under paragraph (d) of this section.

* * * * *

PART 601--LICENSING

7. The authority citation for 21 CFR part 601 continues to read as follows:

Authority: 15 U.S.C. 1451-1561; 21 U.S.C. 321, 351, 352, 353, 355, 356b, 360, 360c-360f, 360h-360j, 371, 374, 379e, 381; 42 U.S.C. 216, 241, 262, 263, 264; sec 122, Pub. L. 105-115, 111 Stat. 2322 (21 U.S.C. 355 note).

8. Section 601.12 is amended by revising paragraph (f)(3)(i)(D) and by adding paragraph (f)(5) to read as follows:

§ 601.12 Changes to an approved application.

* * * * *

(f) * * *

(3)(i) * * *

(D) A change made pursuant to an exception or alternative granted under § 201.26 or § 610.68 of this chapter.

* * * * *

(5) The submission and grant of a written request for an exception or alternative under § 201.26 or § 610.68 of this chapter satisfies the requirements in paragraphs (f)(1) through (f)(2) of this section.

* * * * *

PART 610--GENERAL BIOLOGICAL PRODUCTS STANDARDS

9. The authority citation for 21 CFR part 610 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 360, 360c, 360d, 360h, 360i, 371, 372, 374, 381; 42 U.S.C. 216, 262, 263, 263a, 264.

10. Add § 610.68 to subpart G to read as follows:

§ 610.68 Exceptions or alternatives to labeling requirements for biological products held by the Strategic National Stockpile.

(a) The appropriate FDA Center Director may grant an exception or alternative to any provision listed in paragraph (f) of this section and not explicitly required by statute, for specified lots, batches, or other units of a biological product, if the Center Director determines that compliance with such labeling requirement could adversely affect the safety, effectiveness, or availability of such product that is or will be included in the Strategic National Stockpile.

(b)(1)(i) A Strategic National Stockpile official or any entity that manufactures (including labeling, packing, relabeling, or repackaging), distributes, or stores a biological product that is or will be included in the Strategic National Stockpile may submit, with written concurrence from a Strategic National Stockpile official, a written request for an exception or alternative described in paragraph (a) of this section to the Center Director.

(ii) The Center Director may grant an exception or alternative described in paragraph (a) of this section on his or her own initiative.

(2) A written request for an exception or alternative described in paragraph (a) of this section must:

(i) Identify the specified lots, batches, or other units of the biological product that would be subject to the exception or alternative;

(ii) Identify the labeling provision(s) listed in paragraph (f) of this section that are the subject of the exception or alternative request;

(iii) Explain why compliance with such labeling provision(s) could adversely affect the safety, effectiveness, or availability of the specified lots, batches, or other units of the biological product that are or will be included in the Strategic National Stockpile;

(iv) Describe any proposed safeguards or conditions that will be implemented so that the labeling of the product includes appropriate information necessary for the safe and effective use of the product, given the anticipated circumstances of use of the product;

(v) Provide a draft of the proposed labeling of the specified lots, batches, or other units of the biological product subject to the exception or alternative; and

(vi) Provide any other information requested by the Center Director in support of the request.

(c) The Center Director must respond in writing to all requests under this section.

(d) A grant of an exception or alternative under this section will include any safeguards or conditions deemed appropriate by the Center Director so that the labeling of product subject to the exception or alternative includes the information necessary for the safe and effective use of the product, given the anticipated circumstances of use.

(e) If you are a sponsor receiving a grant of a request for an exception or alternative to the labeling requirements under this section:

(1) You need not submit a supplement under § 601.12(f)(1) through (f)(2) of this chapter; however,

(2) You must report any grant of a request for an exception or alternative under this section as part of your annual report under § 601.12(f)(3) of this chapter.

(f) The Center Director may grant an exception or alternative under this section to the following provisions of this chapter, to the extent that the requirements in these provisions are not explicitly required by statute:

(1) § 610.60;

(2) § 610.61(c) and (e) through (r);

(3) § 610.62;

(4) § 610.63;

(5) § 610.64;

(6) § 610.65; and

(7) § 312.6.

PART 801--LABELING

11. The authority citation for 21 CFR part 801 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 360i, 360j, 371, 374.

12. Add § 801.128 to subpart D to read as follows:

§ 801.128 Exceptions or alternatives to labeling requirements for medical devices held by the Strategic National Stockpile.

(a) The appropriate FDA Center Director may grant an exception or alternative to any provision listed in paragraph (f) of this section and not explicitly required by statute, for specified lots, batches, or other units of a medical device, if the Center Director determines that compliance with such labeling requirement could adversely affect the safety, effectiveness, or availability of such devices that are or will be included in the Strategic National Stockpile.

(b)(1)(i) A Strategic National Stockpile official or any entity that manufactures (including labeling, packing, relabeling, or repackaging), distributes, or stores devices that are or will be included in the Strategic National Stockpile may submit, with written concurrence from a Strategic National Stockpile official, a written request for an exception or alternative described in paragraph (a) of this section to the Center Director.

(ii) The Center Director may grant an exception or alternative described in paragraph (a) of this section on his or her own initiative.

(2) A written request for an exception or alternative described in paragraph (a) of this section must:

(i) Identify the specified lots, batches, or other units of the medical device that would be subject to the exception or alternative;

(ii) Identify the labeling provision(s) listed in paragraph (f) of this section that are the subject of the exception or alternative request;

(iii) Explain why compliance with the labeling provision(s) could adversely affect the safety, effectiveness, or availability of the specified lots, batches, or other units of a medical device that are or will be held in the Strategic National Stockpile;

(iv) Describe any proposed safeguards or conditions that will be implemented so that the labeling of the device includes appropriate information necessary for the safe and effective use of the device, given the anticipated circumstances of use of the device;

(v) Provide a draft of the proposed labeling of the specified lots, batches, or other units of the medical device subject to the exception or alternative; and

(vi) Provide any other information requested by the Center Director in support of the request.

(c) The Center Director must respond in writing to all requests under this section. The Center Director may impose appropriate conditions when granting such an exception or alternative under this section.

(d) A grant of an exception or alternative under this section will include any safeguards or conditions deemed appropriate by the Center Director so that the labeling of devices subject to the exception or alternative includes the information necessary for the safe and effective use of the device, given the anticipated circumstances of use.

(e) If the Center Director grants a request for an exception or alternative to the labeling requirements under this section:

(1) The Center Director may determine that the submission and grant of a written request under this section satisfies the provisions relating to premarket notification submissions under § 807.81(a)(3) of this chapter.

(2)(i) For a Premarket Approval Application (PMA)-approved device, the submission and grant of a written request under this section satisfies the provisions relating to submission of PMA supplements under § 814.39 of this chapter; however,

(ii) The grant of the request must be identified in a periodic report under § 814.84 of this chapter.

(f) The Center Director may grant an exception or alternative under this section to the following provisions of this chapter, to the extent that the requirements in these provisions are not explicitly required by statute:

(1) § 801.1(d);

(2) § 801.60;

(3) § 801.61;

(4) § 801.62;

(5) § 801.63;

(6) § 801.109; and

(7) Part 801, subpart H.

PART 807--ESTABLISHMENT REGISTRATION AND DEVICE LISTING FOR MANUFACTURERS AND INITIAL IMPORTERS OF DEVICES

13. The authority citation for 21 CFR part 807 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 360, 360c, 360e, 360i, 360j, 371, 374, 381, 393; 42 U.S.C. 264, 271.

14. Section 807.81 is amended by revising paragraph (b) to read as follows:

§ 807.81 When a premarket notification submission is required.

* * * * *

(b)(1) A premarket notification under this subpart is not required for a device for which a premarket approval application under section 515 of the act, or for which a petition to reclassify under section 513(f)(2) of the act, is pending before the Food and Drug Administration.

(2) The appropriate FDA Center Director may determine that the submission and grant of a written request for an exception or alternative under § 801.128 or § 809.11 of this chapter satisfies the requirement in paragraph (a)(3) of this section.

* * * * *

PART 809--IN VITRO DIAGNOSTIC PRODUCTS FOR HUMAN USE

15. The authority citation for 21 CFR part 809 continues to read as follows:

Authority: 21 U.S.C. 331, 351, 352, 355, 360b, 360c, 360d, 360h, 360i, 360j, 371, 372, 374, 381.

16. Add § 809.11 to subpart B to read as follows:

§ 809.11 Exceptions or alternatives to labeling requirements for in vitro diagnostic products for human use held by the Strategic National Stockpile.

(a) The appropriate FDA Center Director may grant an exception or alternative to any provision listed in paragraph (f) of this section and not explicitly required by statute, for specified lots, batches, or other units of an in vitro diagnostic product for human use, if the Center Director determines that compliance with such labeling requirement could adversely

affect the safety, effectiveness, or availability of such products that are or will be included in the Strategic National Stockpile.

(b)(1)(i) A Strategic National Stockpile official or any entity that manufactures (including labeling, packing, relabeling, or repackaging), distributes, or stores an in vitro diagnostic product for human use that is or will be included in the Strategic National Stockpile may submit, with written concurrence from a Strategic National Stockpile official, a written request for an exception or alternative described in paragraph (a) of this section to the Center Director.

(ii) The Center Director may grant an exception or alternative described in paragraph (a) of this section on his or her own initiative.

(2) A written request for an exception or alternative described in paragraph (a) of this section must:

(i) Identify the specified lots, batches, or other units of an in vitro diagnostic product for human use that would be subject to the exception or alternative;

(ii) Identify the labeling provision(s) listed in paragraph (f) of this section that are the subject of the exception or alternative request;

(iii) Explain why compliance with such labeling provision(s) could adversely affect the safety, effectiveness, or availability of the specified lots, batches, or other units of the in vitro diagnostic product for human use that are or will be held in the Strategic National Stockpile;

(iv) Describe any proposed safeguards or conditions that will be implemented so that the labeling of the product includes appropriate information necessary for the safe and effective use of the product, given the anticipated circumstances of use of the product;

(v) Provide a draft of the proposed labeling of the specified lots, batches, or other units of the in vitro diagnostic products for human use subject to the exception or alternative; and

(vi) Provide any other information requested by the Center Director in support of the request.

(c) The Center Director must respond in writing to all requests under this section. The Center Director may impose appropriate conditions or safeguards when granting such an exception or alternative under this section.

(d) A grant of an exception or alternative under this section will include any safeguards or conditions deemed appropriate by the Center Director to ensure that the labeling of the product subject to the exception or alternative includes the information necessary for the safe and effective use of the product, given the anticipated circumstances of use.

(e) If the Center Director grants a request for an exception or alternative to the labeling requirements under this section:

(1) The Center Director may determine that the submission and grant of a written request under this section satisfies the provisions relating to premarket notification submissions under § 807.81(a)(3) of this chapter.

(2)(i) For a Premarket Approval Application (PMA)-approved in vitro diagnostic product for human use, the submission and grant of a written request under this section satisfies the provisions relating to submission of PMA supplements under § 814.39 of this chapter; however,

(ii) The grant of the request must be identified in a periodic report under § 814.84 of this chapter.

(f) The Center Director may grant an exception or alternative under this section to the following provisions of this part, to the extent that the requirements in these provisions are not explicitly required by statute:

(1) § 809.10(a)(1) through (a)(6) and (a)(9);

(2) § 809.10(b);

(3) § 809.10(c)(2);

(4) § 809.10(d)(1)(i) through (d)(1)(v), (d)(1)(viii), and (d)(2); and

(5) § 809.10(e)(1)(i) through (e)(1)(vi) and (e)(1)(ix) through (e)(1)(xi).

PART 812--INVESTIGATIONAL DEVICE EXEMPTIONS

17. The authority citation for 21 CFR part 812 continues to read as follows:

Authority: 21 U.S.C. 331, 351, 352, 353, 355, 360, 360c-360f, 360h-360j, 371, 372, 374, 379e, 381, 382, 383; 42 U.S.C. 216, 241, 262, 263b-263n.

18. Section 812.5 is amended by adding paragraph (d) to read as follows:

§ 812.5 Labeling of investigational devices.

* * * * *

(d) The appropriate FDA Center Director, according to the procedures set forth in § 801.128 or § 809.11 of this chapter, may grant an exception or alternative to the provisions in paragraphs (a) and (c) of this section, to the extent that these provisions are not explicitly required by statute, for specified lots, batches, or other units of a device that are or will be included in the Strategic National Stockpile.

PART 814--PREMARKET APPROVAL OF MEDICAL DEVICES

19. The authority citation for 21 CFR part 814 continues to read as follows:

Authority: 21 U.S.C. 351, 352, 353, 360, 360c-360j, 371, 372, 373, 374, 375, 379, 379e, 381.

20. Section 814.39 is amended by adding paragraph (g) to read as follows:

§ 814.39 PMA Supplements.

* * * * *

(g) The submission and grant of a written request for an exception or alternative under § 801.128 or § 809.11 of this chapter satisfies the requirement in paragraph (a) of this section.

21. Section 814.84 is amended by adding paragraph (b)(3) to read as follows:

§ 814.84 Reports.

* * * * *

(b) * * *

(3) Identify changes made pursuant to an exception or alternative granted under § 801.128 or § 809.11 of this chapter.

Date: DEC 20 2007
December 20, 2007.

Jeffrey Shuren

Jeffrey Shuren,
Assistant Commissioner for Policy.

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