# Class II Special Controls Guidance Document: Pharmacy Compounding Systems; Final Guidance for Industry and FDA

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**U.S. Department Of Health and Human Services**
**Food and Drug Administration**
**Center for Devices and Radiological Health**

**General Hospital Devices Branch**
**Division of Dental, Infection Control, and General Hospital Devices**
**Office of Device Evaluation**

# Preface

## Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. When submitting comments, please refer to the exact title of this guidance document. Comments may not be acted upon by the Agency until the document is next revised or updated.

For questions regarding the use or interpretation of this guidance contact John W. Levchuk, Ph.D., at (301) 443-8913 x133 or by email JWL@cdrh.fda.gov.

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***This document is intended to provide guidance. It represents the Agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind the Food and Drug Administration (FDA) or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations.***

## Background

On March 21, 2001, FDA classified Pharmacy Compounding Devices/Systems (PCDs) from Class II designation to Class II with exemption from the premarket notification requirements of the Federal Food, Drug, and Cosmetic Act (the Act). This guidance document describes a means by which PCDs may comply with the requirement of Class II Special Controls. Designation of this guidance document as a special control means that manufacturers of PCDs who follow the recommendations listed in this document before introducing their device into commercial distribution in the United States will be able to market their device. Manufacturers must maintain their device master records and be able to demonstrate that their specific device complies with either the recommendations of this guidance or some alternate means that provides equivalent assurance of safety and effectiveness. If the manufacturer cannot comply with these recommendations or equivalent measures, they will not be exempt from the requirements of premarket notification and will need to submit a premarket notification and receive clearance prior to marketing.

## The Least Burdensome Approach

The issues identified in this guidance document represent those that we believe need to be addressed before your device can be marketed. In developing the guidance, we carefully considered the relevant statutory criteria for Agency decision-making. We also considered the burden that may be incurred in your attempt to comply with the guidance and address the issues we have identified. We believe that we have considered the least burdensome approach to resolving the issues presented in the guidance document. If, however, you believe that there is a less burdensome way to address the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least

Burdensome Issues" document. It is available on our Center web page at http://www.fda.gov/cdrh/modact/leastburdensome.html

## Scope

FDA identifies a PCD as an apparatus, often controlled by software, that is intended to deliver a specified quantity of one or more injections through a designated fluid pathway to achieve in a receiving vessel an injection having a specified concentration or proportion of ingredients different from the initial injections. PCDs are for use within the practice of pharmacy to compound injections in accordance with approved drug product labeling. This generic type of device is an I.V. Fluid Transfer Set classified under 21 CFR 880.5440, product code NEP.

The exemption from premarket notification for PCDs does not encompass the ancillary devices that make up the delivery and container system. Examples of ancillary devices include fluid transfer sets, metering chambers, I.V. bags, connectors, or other components that provide a fluid contact surface. The ancillary devices are classified separately from PCDs, i.e., they are not accessories to the PCDs and may require premarket notification. CDRH guidance documents for these devices include:

- Guidance on Premarket Notifications for Intravascular Administration Sets, http://www.fda.gov/cdrh/ode/guidance/1189.html
- Guidance on the Content of Premarket Notification [510(K)] Submissions for Piston Syringes, http://www.fda.gov/cdrh/ode/odegr821.html
- Guidance on the Content of Premarket Notification [510(K)] Submissions for Hypodermic Single Lumen Needles, http://www.fda.gov/cdrh/ode/odegr450.html

## Risks to Health

FDA has identified the following risks to health associated with PCDs:

- Incorrect use or faulty device design or software that could lead to inaccurate concentrations or volumes, non-sterility, or incompatibilities resulting in therapeutic failures, overdoses, fluid or electrolyte imbalances, sepsis, or other adverse events
- Incorrect use or faulty device design or software that could cause or contribute to the cross-contamination or adulteration of drug products
- Faulty electrical design or shielding that could lead to unsafe current leakage and/or electromagnetic interference, resulting in operational failure, electric shock, burns, or death.

# Special Controls Guidance

FDA believes that conformance with this guidance document, when combined with the general controls of the Act, will provide reasonable assurance of the safety and effectiveness of PCDs:

1. Labeling that includes the following:

    - Validated performance specifications including, for example, minimum and maximum operating speeds, accuracy, and sensitivity
    - User instructions for installation, operational, and performance checks on set-up to verify correct performance status and functionality
    - User instructions for periodic maintenance and calibration to ensure continuous accuracy, sensitivity, and reliability
    - The identification by name, manufacturer, and model number of all ancillary devices such as fluid transfer sets, metering chambers, I.V. bags, and connectors necessary for the intended use of the PCD
    - Pilot tested detailed operating instructions, including the proper handling and use of all ancillary devices identified in the labeling as necessary for the intended use of the PCD
    - Instructions for recognizing and responding to performance failure alerts
    - Warnings or precautions to avoid practices that might compromise the accuracy, sensitivity, reliability, or functionality of the PCD
    - Instructions, warnings, or precautions necessary to avoid the non-sterility, cross-contamination or adulteration of drug products or incompatibilities
    - Warnings and instructions for the general prevention of cross-contamination
    - Warnings and instructions specific to the prevention of cross-contamination from penicillin and related agents, mutagenic agents, drugs with narrow therapeutic indexes, and high potency drugs, addressing, for example, the seriousness of the associated clinical hazards and the importance of changing fluid pathways.

2. Design controls that satisfactorily include or address the following:

    - Operational and performance qualification encompassing "worst-case" operational conditions, parameters, or stresses on functionality, accuracy, sensitivity, and reliability
    - Validation of all performance claims pertaining to ensuring product potency, quantity, quality, and purity, for example, software compatibility checks and prevention of in-line incompatibilities

- Prevention of the cross-contamination of the source fluids
- The sensitivity and reproducibility of the alerting response to sensing failures such as illogical weight, volume, or commands; and dry lines, empty source containers, line blockages, and deviations between intended and actual quantities transferred caused by mechanical failures or power interruptions
- The sensitivity and reliability of the "go/no-go" indicator to properly/improperly positioned, arrayed, or attached ancillary devices such as the source fluid containers, transfer sets, and receiving container

3. Software controls that:

- Evaluate the accuracy of conversions between weight and volume that are calculated on the basis of product and concentration-specific specific gravity data
- Ensure the accuracy of the specific gravity data included in a software file for such conversions that have been determined experimentally
- Ensure that conversions between weight and volume will be impossible in the absence of product and concentration-specific specific gravity
- Ensure that product and concentration-specific specific gravity data that are entered and stored by the user are identifiable as user-defined entries
- Ensure the effectiveness of sensors, detectors, etc., that alert the user of safety and performance failure of the device
- Ensure the effectiveness of valvular operation that is responsible for mixing accurate amounts of admixtures in order to obtain the intended, resultant compound

The FDA provides a guidance document entitled “Guidance for FDA Reviewers and Industry: Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices,” http://www.fda.gov/cdrh/ode/57.html which may be used to verify and validate the effectiveness of software design controls. In addition, FDA recognizes several software consensus standards. A declaration of conformity to these standards, in part or whole, may be used to show the manufacturer has verified and validated pertinent specifications of the design controls. The consensus standards are:

- ISO/IEC 12207:1995 Information Technology - Software Life Cycle Processes
- IEEE/EIA 12207.O-1996 Industry Implementation of International Standard ISO/IEC12207:1995 (ISO/IEC 12207) Standard for Information Technology - Software Life Cycle Processes

- ANSI/UL:1998 Software in Programmable Components IE 1074:1997 Standard for Developing Software Life Cycle Processes

- IE 1012:1998 Standard for Software Verification and Validation

4. Electrical/Electronic controls that ensure:

   - Proper electrical isolation between the user and the power source of the device

   - Device leakage current does not exceed a safe limit

   - Electromagnetic compatibility between use of the device and its environment

   FDA recognizes several electrical consensus standards. A declaration of conformity to these standards, in part or whole, may be used to show the manufacturer has verified and validated pertinent specifications of the design controls. The consensus standards are:

   - IEC 60601-1 Medical Electrical Equipment - Part 1: General Requirements for Safety, 1988; Amendment 1, 1991-11, Amendment 2, 1995-03

   - IEC 60601-1-1 Medical Electrical Equipment - Part 1: General Requirements for Safety; Safety Requirements for Medical Electrical Systems, 1992-06 Amendment 1, 1995-11

   - IEC 60601-1-2 (First Edition, 1993-04), Medical Electrical Equipment - Part 1: General Requirements for Safety; Electromagnetic Compatibility - Requirements and Tests

   - IEC 60601-1-4:1996 Medical Electrical Equipment - Part 1: General Requirements for Safety; 4. Collateral Standard: Programmable electrical medical systems

5. Cleared 510(k)s or evidence of legal market status (e.g., premarket, exempt from 510(k) review) for all ancillary devices identified in the labeling as necessary for the intended use of the PCD, including, for example, the validation of the sterilization process and the biocompatibility testing of all fluid contact materials as required for External Communicating Devices, Blood Path, Indirect in ISO and USP standards.

# Premarket Notification Requirements

Section 510(m) of the act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the act if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. FDA has determined premarket notification is not

necessary to provide reasonable assurance of the safety and effectiveness of this generic type of device if the manufacturer follows the recommendations in this special controls guidance or equivalent measures to address the risks identified in this guidance. Thus, persons who intend to market a device of this type do not need to submit a premarket notification to FDA and receive agency clearance prior to marketing the device, but must comply with the general and special controls.

# Limitations of Exemption from Premarket Notification

FDA's decision to exempt a Class II device from the requirement of premarket notification is based on the existing and reasonably foreseeable characteristics of devices within that generic type that currently are, or have been, in commercial distribution. The regulation 21 CFR 880.9 specifies certain circumstances when the exemption does not apply. If any of these circumstances apply to your device, your device is not exempt and you must submit a premarket notification.

**Product Code and title changes were made to this document on 03-23-2001**