Guidance for Industry

Guidance for the Submission of Premarket Notifications For Radionuclide Dose Calibrators

Document Issued on: November 20, 1998

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

Radiological Devices Branch
Division of Reproductive; Abdominal; Ear, Nose, and Throat;
and Radiological Devices
Office of Device Evaluation

Preface

Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to Robert Phillips, Ph.D., Radiological Devices Branch, Division of Reproductive; Abdominal; Ear, Nose, and Throat; and Radiological Devices, 9200 Corporate Blvd, Rockville, MD 20874. 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 Robert Phillips, Ph.D., at (301) 594-1212.

Additional Copies

World Wide Web CDRH page at http://www.fda.gov/cdrh/ode/radcalibrators.pdf or CDRH Facts on Demand at 1-800-899-0381 or 301-827-0111, specify number 2238 when prompted for the document shelf number.

Table of Contents

I. Purpose

The purpose of this document is to provide a detailed description of the information which should be included in a premarket (510(k)) notification for a radionuclide dose calibrator (RDC) submitted to the Center for Devices and Radiological Health (CDRH). This information is an elaboration of the general requirements contained in 21 CFR 807.87.

II. Scope

This document is applicable to Radionuclide Dose Calibrators as defined in 21 CFR 892.1360:

"A radionuclide dose calibrator is a radiation detection device intended to assay radionuclides before their administration to patients."

RDCs are currently in Class II and require premarket notification and an agency determination of substantial equivalence prior to marketing. The product code currently used to identify this device is KPT. This guidance covers calibrators used to calibrate doses of radionuclides used in nuclear medicine and radionuclide sources used in brachytherapy.

The principal components of current RDCs are a measurement chamber (such as a vented or sealed gas ionization chamber or scintillation detector) and readout (such as an electrometer).

This guidance is applicable to premarket notifications for new RDCs, new components, and modifications to RDCs and components that have a significant influence on safety or effectiveness.

III. Background

In the last few years, a number of legislative changes relating to the authority of the agency have occurred. These changes have resulted in the adoption of new regulations and administrative procedures by CDRH, which affect the 510(k) process. The Safe Medical Devices Act of 1990 (SMDA) has resulted in new Good Manufacturing Practice (GMP) regulations requiring pre-production design controls, and several administrative requirements (Truthful and Accurate statements, Summaries of Safety and Effectiveness, and Statements of Indications for Use) have been added. The Food and Drug Administration Modernization Act (FDAMA) of 1997 and a re-engineering effort have resulted in the development of a new 510(k) paradigm that incorporates alternative approaches to demonstrating substantial equivalence in premarket notifications. These approaches are intended to facilitate the marketing clearance of devices for which recognized standards exist, and for cases in which the new device is a modification of a previously cleared product.

A. The New 510(k) Paradigm

On March 20, 1998 CDRH issued a document entitled "The New 510(k) Paradigm - Alternative Approaches to Demonstrating Substantial Equivalence in Premarket Notifications". This document is available on the CDRH web site (http://www.fda.gov/cdrh/ode/parad510.html). In addition to the traditional 510(k), this document describes two alternatives, the "Special 510(k): Device Modification" and the "Abbreviated 510(k)".

1. Special 510(k)

The Special 510(k) is based on the requirement that manufacturers establish design controls in accordance with the SMDA and 21 CFR 820.30. A manufacturer uses the FDA guidance document entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" to decide if a device modification could be implemented without submission of a new 510(k). If a new 510(k) is needed, and if the modification does not affect the intended use of the device or the basic fundamental scientific technology, conformance with design controls may form the basis for clearing the application. Under this option, a manufacturer who is intending to modify a legally marketed Class II device would conduct the necessary verification and validation activities to demonstrate that the design output of the modified device meets the design requirements. Once the company has ensured the satisfactory completion of this process through a design review, a Special 510(k) may be submitted. While the basic content requirements for the submission are the same, this type of submission should also reference the cleared 510(k) and contain a "Declaration of Conformity" with design control requirements. In the Special 510(k) the manufacturer has the option of using a third party to assess conformance with design controls (refer to the paradigm document for details). Special 510(k)s are to be processed by the Office of Device Evaluation within 30 days of receipt by the Document Mail Center.

2. Abbreviated 510(k)s

The Abbreviated 510(k) is based on the use of conformance to voluntary standards in place of data review as the means by which the safety and effectiveness of Class II devices can be assured. Manufacturers may submit an Abbreviated 510(k) when FDA has recognized an individual or several voluntary standards that cover aspects of the new device. In addition to the required elements of a 510(k) as described in 21 CFR 808.87, Abbreviated 510(k) submissions should include information that describes how conformance to one or several voluntary standards, recognized by CDRH, have been used to address risks associated with the device, and a "Declaration of Conformity" to those standards. The "Declaration of Conformity" should provide the information listed in the paradigm. A third party may be used to assess conformance with these standards (refer to the paradigm document for details). The review of abbreviated 510(k)s is intended to be more efficient since they are not required to contain the experimental data from which conformance is determined.

B. Standards for Radionuclide Dose Calibrators

The Food and Drug Administration Modernization Act of 1997 authorizes CDRH to recognize consensus standards established by national and international standards development organizations that may be used to satisfy identified portions of device review requirements. On February 19, 1998 CDRH issued a "Guidance on the Recognition and Use of Consensus Standards" which is intended to provide information relating to the recognition and use of national and international consensus standards. It is available on the CDRH web site (hhtp://www.fda.gov/cdrh/modact/k982.html), and describes how the agency will use information on conformance with recognized standards to satisfy premarket review requirements. It also describes the content of a declaration of conformity. In the case of 510(k)s, information on conformance with recognized standards might help establish the substantial equivalence of a new device to a legally marketed predicate in the areas covered by the standards. If a premarket notification contains declarations of conformity, this will in most cases eliminate the need to review the actual test data for those aspects of the device addressed by the standards. However, the results of testing are expected when the standard specifies a test method without the associated performance limits. There are currently no consensus standards related to RDCs that are recognized by CDRH, however, several bodies have published standards and requirements. Several of these are listed for convenience.

1. 10 CFR 35.50 Possession, use, calibration and check of dose calibrators

The Nuclear Regulatory Commission (NRC) requires a licensee to possess and use a dose calibrator to measure the activity of dosages of photon-emitting radionuclides prior to administration to each patient or human research subject. This requirement specifies when a RDC will be used and the timing of required quality control checks (constancy, accuracy, linearity, and geometrical dependence.

2. IEC 61303(1994-10) Medical Electrical Equipment: Radionuclide calibrators –Particular methods for describing performance.

This standard covers radionuclide calibrators of the well type, with a gas-filled ionization chamber as used in the practice of nuclear medicine. The object of this standard is to identify the most important characteristics of radionuclide calibrators and lay down associated test methods to enable manufacturers to declare the characteristics of their devices in a standardized way and facilitate comparisons between devices.

3. IEC 61145(1992-05) Calibration and usage of ionization chamber systems for assay of radionuclides.

This standard covers the techniques for the quantification of the activity of identified radionuclides using any of a variety of ionization chambers currently available for this purpose.

4. ANSI N42.13-1986 Calibration and usage of "dose Calibrator" ionization chambers for the assay of radionuclides

This standard covers the techniques for the quantification of the activity of identified radionuclides using any of a variety of ionization chambers currently available for this purpose. Application of the standard is limited to instruments that incorporate well-type ionization chambers as detectors.

IV. Information Required in a Premarket Notification

Information required under 21 CFR 807.87 for RDC devices is listed and discussed in detail below.

A. General Information

1. Name and address of manufacturer.
2. Establishment registration number (if not available, registration application should be submitted).
3. Name, title, phone number, fax number and E-mail of contact.
4. Trade name and common name of device.
5. Type of submission (special, abbreviated or traditional)
6. Classification and class of device (21 CFR 892.1360, class II), and product code (KPT)
7. Intended use (general purpose of device per 21 CFR 892.1360)
8. Applicable standards (e.g. IEC or ANSI) if used.

B. Administrative Information

1. 510(k) Summary of Safety and Effectiveness or Statement (see 21 CFR 807.92 and 807.93)
2. FDA Indications for Use Form (specific use of device, i.e. nuclear medicine or brachytherapy)
3. Truthful and Accurate Statement (see 21 CFR 807.87(j))
4. Declarations of Conformity to Consensus Standards (Abbreviated 510(k) only)
5. Declaration of Conformity to Design Controls (Special 510(k) only)

C. Device Description

The device description should describe the type of detector (gas, pressurized gas, vented, scintillator), the principal components of the system, provide a brief description of the purpose of each component, and provide a diagram illustrating their interconnections.

D. Comparison to a Predicate

A 510(k) submission is a comparison of a new device to a predicate to show that the two devices are substantially equivalent. Therefore, the sponsor must identify at least one class II legally marketed device to which equivalence is claimed. The following information relating to the predicate should be supplied:

1. manufacturer, tradename and 510(k) number;
2. a brief description of the important similarities and differences between the device and predicate;
3. promotional material for the predicate and any other relevant labeling; and
4. a tabular comparison of features and specifications of the new device and predicate including:

    a. type of detector and design
    b. allowable activity ranges;
    c. type of radiation measured;
    d. energy range;
    e. accuracy and reproducibility;
    f. geometry of the sensitive volume;
    g. linearity;
    h. interference from background radiation; and
    i. measurement error to be expected over the calibration range.

Any significant differences should be explained and a rationale given for substantial equivalence.

E. Other information

1. Describe the method of initial calibration, the calibration sources used (NIST derivable), and the strength of these sources.

2. Describe the common sources of error and their magnitude.

The listed items should be supported (appropriate laboratory data and descriptions of methods).

F. Software

If the device uses software, computer chips, or other digital components, provide the information requested in "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices, May 1998." This document is available on the WorldWide Web/CDRH home page: http://www.fda.gov/cdrh/ or CDRH Facts on Demand at 1-800-899-0381 or 301-827-0111 specify number 337 when prompted for the shelf number.

The submission should indicate whether the device is year 2000 compatible and describe how this was determined.

F. Electromagnetic Compatibility

The submission should explain whether the device is susceptible to electromagnetic interference and how this was determined.

G. Labeling

The labeling for an RDC device should consist of a summary specification sheet (i.e. a product data sheet that includes the information provided in paragraph IV, D, 4 for the device; promotional material; and instructions for use.

The instructions for use should contain:

a. the indications for use of the device (e.g. types of sources for which RDC is applicable - nuclear medicine, brachytherapy);
b. any contraindications, warnings, precautions associated with the device;
c. instructions for using the device;
d. a recommended way to calibrate the device for specific isotopes;
e. a recommended way to calibrate the device for a specific isotope for which there is no calibrated national standard available;
f. a recommended way to calibrate the device for new isotopes which were not available at the time of manufacture;
g. the expected uncertainty for each radionuclide for which the RDC is calibrated;
h. the activity range (radionuclide RDC) or air kerma-strength range (brachytherapy RDC) over which the expected accuracy is achieved;
i. the positioning of the source in the RDC, including distances from a reference point over which measurements can be made within a specified accuracy;
j. any limitation on source size or orientation in the RDC during measurement of source output;
k. if the RDC uses software, the functions that are performed by it;
l. recommended minimum specifications or ranges for power source and environment (e.g., temperature, humidity, voltage, etc.);
m. recommended maintenance schedules for the equipment, including a designation of whether they should be performed by the user or company service personnel;
n. reference to NRC requirements for routine calibration; and
o. a discussion of sources of error; including the effect of source size and geometry; and encapsulation thickness, and energy difference from the standard.

Warnings should contain any information concerning the limits on environmental factors and any known sensitivity to electromagnetic interference.

Appendix 1

510(k) Summary/Statement Certification

Re: K_____

CHECK ONLY ONE:

☐ 1. **510(k) Summary**. Attached is a summary of safety and effectiveness information upon which an equivalence determination could be based.

☐ 2. **510(k) Statement**. I certify that, in my capacity as

_____

of _____(company),

I will make available all information included in this premarket notification on safety and effectiveness within 30 days of request by any person if the device described in the premarket notification submission is determined to be substantially equivalent. The information I agree to make available will be a duplicate of the premarket notification submission, including any adverse safety and effectiveness information, but excluding all patient identifiers, and trade secret and confidential commercial information, as defined in 21 CFR 20.61.

_____

[Signature]*

_____

[Typed or Printed Name]

_____

[Date]

* Must be signed by a responsible person of the firm required to submit the premarket notification (e.g., not a consultant for the 510(k) submitter).

Appendix 2

Indications for Use Form

Page___of

510(k) Number (if known):

Device Name:

Indications For Use:

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

_____ _____ _____ _____ _____ _____

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use___ OR Over-The-Counter Use
(Per 21 CFR 801.109)

(Optional Format 1-2-96)

Appendix 3

PREMARKET NOTIFICATION TRUTHFUL AND ACCURATE STATEMENT
(as required by 21 CFR 807.87(j))

I certify that, in my capacity as _____
of _____(company name), I believe, to the best of my knowledge, that all data and information submitted in this premarket notification is truthful and accurate and that no material fact has been omitted.

_____ _____
(Signature)* *(Date)*

_____ _____
(Typed Name) *(510(k) number)*

* Must be signed by a responsible person of the firm required to submit the premarket notification (e.g., not a consultant for the 510(k) submitter).

Appendix 4

Declaration of Conformity

Voluntary Standards in 510ks

Reviewers should rely on a declaration of conformity to the recognized consensus standards if the declaration:

Identifies the applicable recognized consensus standards and specifies those that were met;

Specifies, for each consensus standard, that all requirements were met, except for inapplicable requirements or deviations noted below;

Identifies for each consensus standard any way(s) the standard may have been tailored or modified for application to the device under review, e.g., identifies which of an alternative series of tests were performed;

Identifies, for each consensus standard, any requirements that were not applicable to the device;

Specifies any deviations from each applicable standard that were applied (e.g., deviations from international standards which are necessary to meet U.S. infrastructure conventions such as the National Electrical Code (ANSI/NFPA 70));

Specifies what differences exist, if any, between the tested device and the device to be marketed and justifies the use of test results in these areas of difference; and

If a test laboratory or certification body was employed, provides the name and address of each laboratory or certification body that was involved in the determining the conformance of the device with the applicable consensus standards and a reference to any accreditations of those organizations.