Guidance for Industry

Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators

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This document replaces In Vitro Diagnostic Calibrators, July 20, 1998

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

Chemistry, Toxicology, and Hematology Branch
Division of Clinical Laboratory Devices
Office of Device Evaluation

Preface

Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to, Division of Clinical Laboratory Devices, HFZ-440, Office of Device Evaluation, 9200 Corporate Blvd., Rockville, MD, 20850. 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 Dr. Joseph Hackett at 301-594-3084 or by electronic mail, at JLH@cdrh.fda.gov.

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World Wide Web/CDRH home page: http://www.fda.gov/cdrh, or CDRH Facts on Demand at 1-800-899-0381 or 1-301-827-0111, specify number 1247 when prompted for the document shelf number.

Use of Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators

The suggested content of abbreviated 510(k) submissions is identified in guidance prepared by the Center for Devices and Radiological Health on March 20, 1998, titled, "The New 510(k) Paradigm; Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notification." The guidance document is available on theWorld Wide Web/CDRH home page: http://www.fda.gov/cdrh, or CDRH Facts on Demand at 1-800-899-0381 or 1-301-827-0111.

Abbreviated 510(k) submissions for In Vitro Diagnostic Calibrators should include the following:

- A coversheet clearly identifying the application as an "Abbreviated 510(k)";
- Items required under 21 CFR 807.87, including a description of the device, the intended use of the device, and the proposed labeling for the device;
- For a submission that relies on a guidance document (e.g., IVD calibrators) and or special control(s), a summary report (see item III below) that describes how the guidance and or special control(s) were used to address the risks associated with the particular device type;
- Indications for Use enclosure.

Guidance Document for Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators

Device: In Vitro Diagnostic Calibrators

I. Device Description

Common Name(s): Calibrator
Class: II
Classification Panels: Clinical Chemistry (75), Hematology (81), Immunology (82), Microbiology (83), or Toxicology (91)

Product Codes:	JIX,	Calibrator, Multi-Analyte Mixture
	JIS,	Calibrator, Primary
	JIT,	Calibrator, Secondary
	JTW,	Calibrator, Surrogate
	DKB,	Calibrators, Drug Mixture
	DLJ,	Calibrators, Drug Specific
	DNN,	Calibrators, Ethyl Alcohol
	KRX,	Calibrator for Cell Indices
	KRZ,	Calibrator for Hemoglobin and Hematocrit Measurement
	KRY,	Calibrator for Platelet Counting
	KSA,	Calibrator for Red-Cell and White-Cell Counting
	GJZ,	Cyanomethemoglobin Reagent and Standard Solution
	GFX,	Fibrinogen Standard

Regulation numbers: 21 CFR 862.1150, 21 CFR 862.3200, 21 CFR 864.8150, 21 CFR 864. 8165, 21 CFR 864.7340, 21 CFR 864.7500, 21 CFR 864.8175, 21 CFR 864.8185

II. Indications for Use

IVD device calibration is most commonly performed using calibrators (reference materials) specifically intended to be used as a standard curve or cut-off point for an assay.

A calibrator has an assigned value that is established by the manufacturer by a reference method. Calibrators exist in a variety of matrices such as simulated aqueous, serum, plasma or other types of specimens.

Primary reference calibrators are highly purified chemicals that can be directly weighed or measured to produce a solution of known concentration. Alternatively, they may be more complex biological materials having received a value assignment using reference (standard) methodology. They are supplied with a certificate of analysis for each lot (For

example, standard reference materials (SRMs) from the U.S. National Institute of Standards and Technology (NIST)).

Secondary reference materials are those materials or solutions with which the test sample is compared in order to determine the concentration of analytes or other substances. The value of secondary reference materials is usually determined by the manufacturer through cross-over studies of the secondary reference material performed against the primary reference material. This guidance deals with the secondary calibrators which play a key role in the performance characteristics of the IVD device technology method, particularly the accuracy, stability, reproducibility, and linearity.

Suggested indications for use statement

- Clinical Chemistry (75) or Toxicology (91) or Immunology (82) or Microbiology (83) – The (trade name) calibrator is a device intended for medical purposes for use in (specify the test system) to establish points of reference that are used in the determination of values in the measurement of (specify the analyte(s) or drug(s)) in (specify the matrix).

- Hematology (81) – The (trade name) calibrator for (red cell, or white cell, or platelet) counting is a device that resembles (red cells, or white cells, or platelets) and is used to set (specify the instrument(s)) intended to count (red cells, or white cells, or both, or platelets). It is a suspension of particles or cells whose size, shape, concentration and other characteristics have been precisely and accurately determined.

III. Labeling

Include proposed labeling that conforms with 21 CFR 809.10 and reflects the performance data described in the "summary report".

Other: For a multi-purpose instrument used for diagnostic purposes, refer to 21 CFR 809.10(b) (1), (2), (6), (14) and (15).

The labeling must meet the requirements of 21 CFR 809.10. It is recommended that the labeling (package insert) for In Vitro Diagnostic products include intended use and type of procedure (qualitative or quantitative); summary and explanation of test (including literature references, special merits, limitations, deviations from original methods and its effects on results); and test principle (chemical, biological, microbiological, or immunological reactions and techniques).

IV. Summary Report

a. Describe the protocol(s) for real time and accelerated stability studies.

b. Include a description of the process for value assignment and validation.

c. Include a description of any specific instrument applications used for the validation studies including the number of runs and instruments used, the statistical analysis by which the assayed values and ranges were established.

d. Where applicable, identify or define traceability or relationship to a domestic or international standard reference material and/or method.

e. Describe the methodology being used to transfer performance of the primary calibrator to the secondary calibrator. A summary of the results should be presented in a tabular or template form to show that the calibrator as tested evaluates all the preanalytic and analytic components of the total test system.

Note: The assigned values should be clinically relevant and should be set at or near the medical decision levels for the analyte. For qualitative tests, it is recommended that positive and negative cut-offs be carefully identified and that the calibrators be designed to be near these cut-offs.

Checklist and reference to page in 510(k):

1. Proprietary and Established name.

2. Intended Use (include: specific intended instrumentation; quantitative or qualitative methodology; and intended specimen matrix).

3. Summary and explanation, including special merits, limitations.

4. Test Principle.

5. Description of the calibrator material.

- matrix base
- constituents
- appropriate standardization/relationship/traceability
- warnings and precautions
- appropriate testing of human source material (e.g., HBV, HIV warnings)
- "For In Vitro Diagnostic Use" statement

6. Assigned values and value(s) assignment process.

7. Storage instructions/stability - opened/closed shelf-life (include physical, chemical or biological indications or deteriorations).

8. Directions for use, including reconstitution/preparation.

9. Limitations.

10. Bibliography/references.

11. Name and place of manufacturer, packer or distributor.

12. Date of labeling revision.