Contains Nonbinding Recommendations

Administrative Procedures for CLIA Categorization

Guidance for Industry and Food and Drug Administration Staff

Document issued on October 2, 2017.

This document supersedes the Administrative Procedures for CLIA Categorization guidance issued on March 12, 2014.

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. The OMB control number for this information collection is 0910-0607 (expires 12-31-2019).

See additional PRA statement in Section IV of the guidance.

For questions about this document, contact Peter Tobin at 240-402-6169 or by e-mail at peter.tobin@fda.hhs.gov, or contact the Office of In Vitro Diagnostics and Radiological Health at 301-796-5711.



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

GRZAN

Preface

Public Comment

You may submit electronic comments and suggestions at any time for Agency consideration to http://www.regulations.gov. Submit written comments to the Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. Identify all comments with Docket No FDA-2008-D-0228**.** Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

Additional copies are available from the Internet. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive a copy of the guidance. Please use the document number 1143 to identify the guidance you are requesting.

GRZAN

Table of Contents

I. Introduction 4
II. Procedures for Determination of CLIA Categorization 6
III. CLIA Waiver Protocols and Applications.....7
IV. Paperwork Reduction Act of 1995 10

Administrative Procedures for CLIA Categorization

Guidance for Industry and Food and Drug Administration Staff

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

On February 28, 1992, the Department of Health and Human Services (DHHS) published laboratory standards regulations (57 FR 7002) implementing the Clinical Laboratory Improvement Amendments of 1988 (CLIA) (42 U.S.C. 263a). The implementing regulations are codified at 42 CFR Part 493. CLIA regulates laboratory testing and requires that clinical laboratories obtain a certificate before accepting materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or the impairment of, or assessment of the health of human beings. The type of CLIA certificate a laboratory obtains depends upon the complexity of the tests it performs. CLIA regulations describe the following three levels of test complexity: waived tests, moderate complexity tests, and high complexity tests. 42 CFR 493.5(a).

On January 31, 2000, the responsibility for categorization of commercially available *in vitro* diagnostic (IVD) tests was transferred from the Centers for Disease Control and Prevention (CDC) to the Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH).[1] This allows IVD manufacturers to submit premarket notifications or applications for tests and requests for complexity categorization of these tests under CLIA to one agency. Per the

[1] 64 FR 73561, December 30, 1999. See also the delegation to FDA to categorize commercially available in vitro diagnostic tests and perform associated functions (69 FR 22849, April 27, 2004).

December 30, 1999, Notice of the Federal Register, FDA/CDRH's responsibility for CLIA complexity categorization explicitly applies to clinical laboratory devices:

- under premarket review by CDRH,
- under premarket review by other FDA Centers,
- exempt from premarket notification, and
- that are legally marketed and for which the sponsor is seeking a waiver categorization.

FDA/CDRH's general administrative procedures vary for each of the categories above and are described within this document. This guidance also includes information regarding FDA's internal administrative processes, including CDRH's e-copy program which is voluntary for CLIA categorizations. This guidance also includes administrative procedures for categorization applicable to IVDs overseen by other FDA Centers.

Performance goals were initially negotiated and agreed to under the Medical Device User Fee Amendments of 2012[2] (now referred to as MDUFA III) for CLIA waiver by application submissions received in FY 2013-2017. New performance goals and process improvements were incorporated in the FDA Reauthorization Act of 2017 (referred to as MDUFA IV).[3] For CLIA waiver by application submissions received during FY 2018-2022, the revised performance goals and process improvements are outlined in the letter from the Secretary of Health and Human Services to Congress[4] and are further described below.

This guidance does not specifically address the recommended content of CLIA waiver applications. For more information on what should be included in CLIA waiver applications, you may refer to the guidance entitled, "Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm079632.htm).

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

[2] Title II of the Food and Drug Administration Safety and Innovation Act of 2012 (Public Law 112-144).
[3] FDA Reauthorization Act of 2017, text available at: https://www.congress.gov/bill/115th-congress/house-bill/2430/text.
[4] MDUFA Performance Goals and Procedures, Fiscal Years 2018 Through 2022 (MDUFA IV), available at https://www.fda.gov/downloads/ForIndustry/UserFees/MedicalDeviceUserFee/UCM535548.pdf.

II. Procedures for Determination of CLIA Categorization

A. Categorization of Clinical Laboratory Devices Under Premarket Review

CLIA categorization of IVD tests is determined by FDA at the time of review of premarket submission (e.g., a premarket notification submission (510(k)) or a premarket approval application (PMA) under the Federal Food, Drug, and Cosmetic Act or a Biologics License Application (BLA) under the Public Health Service (PHS) Act). Upon receipt of a marketing application in CDRH, FDA will automatically create a second discrete submission tracking number for the CLIA process and notify the sponsor of their CLIA Record ("CR") number in addition to the tracking number for their premarket submission (e.g., 510(k) ("K") or PMA ("P") number). In cases where the premarket submission is reviewed by another FDA Center (e.g., Center for Biologics Evaluation and Research (CBER)), the other Center will notify CDRH at the time of clearance/approval of the IVD test. At that time, FDA will automatically create a discrete CLIA Record ("CR") number to track CDRH's categorization of the test and notify the sponsor of their CLIA Record number.

FDA determines test complexity by reviewing the package insert test instructions in the premarket submission, using the criteria listed in 42 CFR 493.17. The tests that are not waived by regulation under 42 CFR 493.15 and are not cleared or approved for home use or for over-the-counter use, may be categorized either as moderate or high complexity.

FDA will attempt to notify sponsors of the complexity categorization within two weeks of a positive marketing decision (e.g., a substantial equivalence determination for a 510(k) or an approval decision for a PMA). Categorization is effective as of the date of the written notification to the manufacturer (see 42 CFR 493.17(c)(1)(ii)).

A searchable database of CLIA categorizations for IVD devices is available at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCLIA/clia.cfm. FDA periodically posts all categorizations in the public CLIA database with reference to the premarket submission number.

B. Request for Categorization of Legally Marketed Devices

In cases where premarket submission is not needed but CLIA categorization is still appropriate (e.g., devices exempt from premarket notification), manufacturers should submit a request for CLIA categorization, including a copy of the test package insert with test instructions, to the CDRH Document Control Center at the following address:

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, Maryland 20993-0002

To expedite review, FDA strongly encourages submission of an eCopy. See "eCopy Program for Medical Device Submissions." (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313794.pdf).

FDA will assign a discrete CLIA Record ("CR") number to this submission, notify the sponsor of the tracking number, and attempt to notify sponsors of the categorization within 30 days of the request. FDA will post the categorization in the public CLIA database with reference to the CLIA Record ("CR") number.

Additionally, FDA recommends that where the name of an approved or cleared device changes, or the name of the manufacturer or distributor changes, the manufacturer should submit the updated label and request for CLIA categorization to the CDRH Document Control Center at the address listed above so that its record of categorized tests in the public database is accurate. When requesting CLIA categorizations for a name change for multiple IVD tests (e.g., manufacturer or distributor device name change), FDA recommends that this information be presented using a spreadsheet (e.g., Excel). Sponsors may download the information for their current categorized tests from the CLIA database using the "export to Excel" function, add a new column to the spreadsheet after the current test system name, and enter the new test system name in this column. The spreadsheet could be provided to CDRH as part of the eCopy. The application should reference one cleared marketing application in the cover letter to expedite processing of the new categorization letters. Upon receipt of a request for categorization due to a manufacturer or distributor name change, FDA will assign a discrete CLIA Record ("CR") number to this submission, notify the sponsor of the tracking number, and attempt to notify sponsors of the categorization within 30 days of the request. FDA will post the categorization in the public CLIA database with reference to the CLIA Record ("CR") number.

III. CLIA Waiver Protocols and Applications

A test initially categorized as moderately complex might meet the statutory criteria for CLIA waiver if the device is simple to use and the sponsor demonstrates in studies conducted at the intended use sites that the test is accurate and poses an insignificant risk of erroneous results. If a Sponsor of a test categorized as moderate complexity believes their test meets the statutory criteria for CLIA waiver, they may submit a CLIA Waiver by Application to request categorization of the test system as waived. Such a submission should be mailed to the CDRH Document Control Center (DCC) at the address listed above and identified as a CLIA Waiver by Application submission. Note that all such submissions should be directed to CDRH, regardless of the FDA Center responsible for the marketing review. To expedite review, FDA strongly encourages submission of a validated eCopy per the Guidance Document "eCopy Program for Medical Device Submissions." (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313794.pdf).

CLIA Waivers by Application should reference a cleared/approved marketing application (e.g., 510(k), PMA, BLA). As described in the MDUFA III and MDUFA IV Commitment Letters, an applicant should inform FDA that it plans to submit a Dual 510(k) and CLIA Waiver application

through a Pre-Submission. CLIA Waivers by Application are not accepted for devices that are under premarket review at the time of submission. A Dual 510(k) and CLIA Waiver by Application should contain the complete 510(k) and waiver application in a *single* submission and is subject to 510(k) Refuse to Accept (RTA) policies outlined in the Guidance Document "Refuse to Accept Policy for 510(k)s." (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM315014.pdf). FDA/CDRH will assign a discrete CLIA Waiver by Application ("CW") tracking number and notify the sponsor of the tracking number associated with their submission.

Performance goals for CLIA Waiver by Applications filed from FY 2013 through FY 2017 (MDUFA III) are defined as follows in the MDUFA III Commitment Letter.

Action	Review Time (FDA days)	Performance Level FY2013 – FY2017
Substantive Interaction	90	95%
MDUFA Decision		
No Panel	180	95%
With Panel	330	95%
Dual (510(k) and CLIA Waiver by Application) [5]	210	90%

Performance goals for CLIA Waiver by Applications filed from FY 2018 through FY 2022 (MDUFA IV) are defined as follows in the MDUFA IV Commitment Letter.[6]

Action	Review Time (FDA days)	Performance Level FY2018 – FY2022
Substantive Interaction	90	90%
MDUFA Decision		
No Panel	150	90%
With Panel	320	90%
Dual (510(k) and CLIA Waiver by Application)	180	90%

[5] Note that this performance goal applies to both the CLIA Waiver by Application and the 510(k) marketing submission.
[6] If in any one fiscal year, the number of submissions in any CLIA Waiver by Application category is less than 10, then it is acceptable to combine such submissions with the submissions for the following year(s) in order to form a cohort of 10 or more submissions, upon which the combined years' submissions will be subject to the performance goal.

A Substantive Interaction may be a request for Additional Information (via letter or email), a notification that review will Proceed Interactively (via email), or a notification of Waiver Granted (via formal letter). A MDUFA Decision may be a notification of Waiver Granted (via formal letter), notification of Wavier Denial (via formal letter), or withdrawal by the sponsor. The goals for Substantive Interaction and MDUFA Decisions are in terms of FDA Days, which are defined in the MDUFA III and MDUFA IV Commitment Letters as those calendar days when a submission is considered to be under review at the Agency for submissions that have been accepted. FDA Days begin on the date of receipt of the submission.

For all CLIA waiver by application submissions and dual submissions that do not reach a decision by 20 days after the applicable FDA Day goal, FDA will provide written feedback to the applicant to be discussed in a meeting or teleconference, including all outstanding issues with the application preventing FDA from reaching a decision. The information provided will reflect appropriate management input and approval, and will include action items for FDA and/or the applicant, as appropriate, with an estimated date of completion for each party to complete their respective tasks. Issues should be resolved through interactive review. If all of the outstanding issues are adequately presented through written correspondence, FDA and the applicant can agree that a meeting or teleconference is not necessary.

Upon notification of a Waiver Granted, FDA will post the waiver categorization in the public CLIA database with reference to the premarket submission number per current practice.

For additional information regarding data to support a CLIA Waiver by Application, refer to the guidance entitled, "Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices" (http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm079632.htm).

Manufacturers have the option to submit their planned protocols or study designs to support CLIA waiver in order to obtain feedback from FDA prior to conducting the study. These planned protocols or study designs should be submitted to the CDRH Document Control Center (DCC) at the address listed above and identified as a Pre-Submission.

For manufacturers considering either a CLIA Waiver Application following a 510(k), or a Dual 510(k) and CLIA Waiver by Application, FDA welcomes discussion of both the 510(k) and CLIA Waiver processes in Pre-Submissions, including discussion of the appropriate reference/comparator for both 510(k) and CLIA waiver submissions.

In addition, FDA encourages manufacturers considering modification of a test system previously waived by application to contact FDA to discuss planned modifications, and study designs and analyses to validate that the modified test system meets the statutory criteria for CLIA waiver.

For additional information on the Pre-Submission process, please refer to the Guidance "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff" (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocu

ments/UCM311176.pdf). Pre-Submissions for CLIA Waiver by Applications should include a reference to the tracking number for the premarket submission granting marketing authorization (e.g., original 510(k) or PMA number), the protocol/study design, and a valid eCopy.

IV. Paperwork Reduction Act of 1995

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520).

The time required to complete this information collection is estimated to average one hour per response, including the time to review instructions, search existing data sources, gather the data needed, and complete and review the information collection. Send comments regarding this burden estimate or suggestions for reducing this burden to:

FDA PRA Staff,
Office of Operations,
Food and Drug Administration,
PRAStaff@fda.hhs.gov

This guidance also refers to previously approved collections of information found in FDA regulations. The collections of information in 21 CFR Part 801 have been approved under OMB control number 0910-0485; the collections of information in 21 CFR Part 807, subpart E have been approved under OMB control number 0910-0120; and the collections of information for CLIA waiver by application have been approved under OMB control number 0910-0598.

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. The OMB control number for this information collection is 0910-0607 (expires 12/31/2019).