

Compliance Policy Guide CPG Sec. 280.100: Stability Requirements - Licensed In Vitro Diagnostic Products

Guidance for FDA Staff

This guidance is for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(4)(i). Submit one set of either electronic or written comments on this guidance at any time. Submit electronic comments to <https://www.regulations.gov/>. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. You should identify all comments with docket number FDA-2020-D-1716.

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 800-835-4709 or 240-402-8010, or email ocod@fda.hhs.gov, or from the Internet at <https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances>.

For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

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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 responsible for this guidance as listed on the title page.

I. INTRODUCTION:

The purpose of this Compliance Policy Guide (CPG) is to provide guidance to FDA staff on stability studies for in vitro diagnostic products (IVDs) licensed by the Center for Biologics Evaluation and Research (CBER).

In general, FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the FDA'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 FDA's guidances means that something is suggested or recommended but not required.

II. BACKGROUND:

In vitro diagnostic products may be approved or cleared through the medical device authorities of the Federal Food, Drug, and Cosmetic Act or licensed under the Public Health Service Act, depending on their intended use and active substances. Licensed IVDs must meet the requirements in the Quality System Regulation at Title 21 of the Code of Federal Regulations (CFR) Part 820, the provisions for in vitro diagnostic products in 21 CFR Part 809, the requirements in the biologics regulations at 21 CFR Parts 600-660, and the requirements in the approved biologics license application (BLA) for the particular product at 21 CFR Part 601.

IVDs regulated as biological products are subject to a number of different provisions that pertain to stability testing prior to product approval. The regulations for biological products require that data establishing the stability of the product through the dating period be included in the BLA (21 CFR 601.2(a)). The IVD regulations, at 21 CFR 809.10(a)(5) and (b)(5)(iv), require that the

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product label and labeling include appropriate storage instructions which are based on reliable, meaningful, and specific test methods to protect the stability of the product¹.

III. POLICY:

CBER requires, as a condition of licensure, that stability studies must be conducted before the BLA for a new IVD product is approved to ensure it will meet the expiration dating and storage conditions stated on the label and labeling (21 CFR 601.2 (a) and (d)). Post-approval stability studies generally are not required for licensed IVDs. Exceptions to this may include:

1. Stability studies that are required as a condition of approval of the biologics license application;
2. Stability studies for products that have undergone changes or deviations in the manufacturing process or formulation changes (21 CFR 601.12(a)(2)); and
3. Stability studies that are indicated as part of a corrective and preventive action plan developed in response to a failure investigation conducted by the firm that would then support a previously established expiration date (21 CFR 820.100).

IV. REGULATORY ACTION GUIDANCE:

Investigators may cite a licensed IVD manufacturer on a Form FDA 483 for failing to perform post-approval stability studies when: (1) the manufacturer is required to perform the post-approval studies as a condition of licensure; (2) the manufacturer has made a formulation or manufacturing change; or (3) the manufacturer has committed to perform post-approval stability studies as part of a corrective and preventive action plan. Investigators should refer any questions regarding a firm's need to perform stability studies post-approval to CBER's Office of Compliance and Biologics Quality using the email CBERInspections@fda.hhs.gov.

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¹ The guidance issued by the Center for Devices and Radiological Health entitled "[Shelf Life of Medical Devices](#)" dated April 1991, provides some background information on the development of stability studies for device products. <https://www.fda.gov/media/72487/download>