

Contains Nonbinding Recommendations

Compliance Policy Guide

Sec. 420.500 Interference with Compendial Tests

Guidance for FDA Staff¹

You may submit either electronic or written comments regarding this guidance at any time. Submit electronic comments to <http://www.regulations.gov>. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document contact the Center for Drug Evaluation and Research (CDER) at 301-796-3100.

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1 This guidance has been prepared by the Office of Compliance in the Center for Drug Evaluation and Research (CDER) and the Office of Strategic Planning and Operational Policy at the Office of Regulatory Affairs (ORA) at the Food and Drug Administration.

2 Note that USP distinguishes between “official articles,” “official products,” and “official substances.” Here, the term, “official product” means a finished dosage form.

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This guidance represents the Food and Drug Administration's (FDA'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 FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This Compliance Policy Guide (CPG) provides guidance to FDA staff regarding compendial drugs for which added substances interfere with compendial assays or tests of the products. This CPG applies to drug products under the jurisdiction of the Center for Drug Evaluation and Research (CDER). A previous version of this CPG, numbered Section 420.500, published in FDA's Compliance Policy Guides Manual in 1980. This CPG supersedes that document.

FDA's guidance documents, including this Compliance Policy Guide, 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.

II. BACKGROUND

Section 501(b) of the Federal Food, Drug, and Cosmetic Act states that a drug is deemed to be adulterated if it is recognized in an official compendium and its strength differs from, or its quality or purity falls below the standards set forth in the compendium. Under the Act, determination of strength, quality, or purity is made in accordance with the tests or methods of assay set forth in the relevant compendium.

The United States Pharmacopeia (USP) indicates that certain added substances, excipients, and ingredients, "such as antimicrobial agents, pharmaceutical bases, carriers, coatings, flavors, preservatives, stabilizers, and vehicles may be added to an official product to enhance its stability, usefulness, or elegance, or to facilitate its preparation, unless otherwise specified in the individual monograph." USP General Notices, Section 5.20.202. However, such added substances, excipients, and ingredients are not suitable for inclusion in an official article if they

1 2

interfere with the assays and tests prescribed for determining compliance with compendial standards. USP General Notices, Section 5.20.

III. POLICY

A compendial drug containing an added substance that interferes with the compendial assay or test of the product is adulterated under 501(b) of the Act.

IV. REGULATORY ACTION GUIDANCE

Regulatory action is indicated for adulterated compendial drugs when such products contain an added substance that interferes with the compendial assay or test of the product, even if the product is fully compliant under other methods of analysis.

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