

CPG Sec. 420.100 Adulteration of Drugs Under Section 501(b) and 501(c) of the Act. *Direct Reference Seizure Authority for Adulterated Drugs Under Section 501(b)*

BACKGROUND:

Section 501(b) of the Food, Drug, and Cosmetic Act (the Act) deems an official drug (i.e., a drug purported to be or represented as a drug the name of which is recognized in an official compendium) to be adulterated if it fails to conform to compendial standards of quality, strength or purity. Compendial tests or assay methods are used when determining such conformance under 501(b); the standards are stated in individual monographs as well as portions of the General Notices section of the USP/NF. Standards and test methods have been established for such characteristics as potency, sterility, *dissolution*, weight variation and content uniformity.

If an official drug fails to conform to one or more compendial standards of strength, quality or purity, but plainly states on the label how it differs from the standard, then the drug is not deemed to be adulterated under Section 501(b).

Section 501(c) of the Act deems *a drug that is not recognized in an official compendium to be adulterated if it fails to meet the strength, purity or quality which it purports or is represented to possess. The applicable quality standards for a drug not recognized in an official compendium can be determined from such sources as the labeling of the drug (or drug product), the manufacturer's written specifications, and new drug applications. (Test methods are usually contained in the written specifications or new drug application).*

POLICY:

Any official drug which, when tested by compendial methods, fails to conform to compendial standards for quality, strength, or purity, is adulterated unless the differences from such standards are plainly stated on the drug's label.

Any *drug which is not recognized in an official compendium is adulterated if its strength differs from, or its purity or quality falls below that which it purports or is represented to possess, when tested by scientifically sound methods.*

REGULATORY ACTION GUIDANCE:

Recommendations for regulatory action will be considered in the above instances of adulteration. The regulatory action of choice will depend upon the circumstances of each case.

In cases where there is a health hazard, the first choice of action should be recall, particularly for drugs found to be non-sterile, and for narrow therapeutic range drugs that fail potency or dissolution tests. However, where the appropriate division within the Office of Pharmaceutical Quality Operations (OPQO) has advised the firm of such a defective product, and the firm fails to recall, seizure should be considered. Seizure recommendations charging adulteration under section 501(c) should be submitted to the Office of Compliance, Center for Drug Evaluation and Research (HFD-300) (CDER).

Appropriate division offices within OPQO are authorized to submit seizure recommendations, charging adulteration under section 501(b), directly to the OPQO Program Director and Office of Enforcement without CDER review under the following circumstances, provided introduction or delivery for introduction into interstate commerce has been documented:

1. An official sample of either a compendial bulk pharmaceutical chemical or a compendial finished dosage form has been analyzed, using the compendial methods without modification and found to fail both the original and check analyses.
2. The analyzing laboratory has certified in the transmittal memorandum that an unmodified compendial method was used.

Note: No tolerance need be applied beyond that provided by the official compendium.

3. For sterile products, no check analysis is needed provided the compendial sterility test was utilized without modification, the product is one that is required to be sterile, and all relevant laboratory controls (including positive and negative) are satisfactory.

Where the analyzing laboratory deviates from the official compendial analytical method(s), a detailed description of the deviation(s) and justification for such deviation(s) can be submitted to CDER for review. In such cases, CDER will review only the deviation(s) and not the choice of regulatory action or other documentation.

For seizure actions, the charges may be drafted as follows:

That the article of drug was adulterated, when introduced into and while in interstate commerce, and is adulterated while held for sale after shipment in interstate commerce, within the meaning of 21 U.S.C. 351(b), in that it purports to be and is represented as a drug, the name of which is recognized in an official compendium (United States Pharmacopeia) and its strength differs from, and its quality and purity falls below the standard set forth in such compendium because it fails the official (INSERT TYPE OF TEST) test.

or

That the article of drug was adulterated, when introduced into and while in interstate commerce, and is adulterated while held for sale after shipment in interstate commerce within the meaning of 21 U.S.C. 351(c), in that it is a drug not subject to the provisions of 21 U.S.C. 351(b) and its strength differs from, and its purity and quality falls below, that which it purports or is represented to possess because (e.g., the drug contains less than the amount of (INSERT NAME OF INGREDIENT) on the label).

It should be kept in mind that the types of adulteration found under 501(b) and 501(c) may be indicative of a wider problem involving failure of the manufacturer to adhere to current good manufacturing practice that should be addressed.

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