Inspections, Compliance, Enforcement, and Criminal Investigations

CPG Sec. 420.400 Performance of Tests for Compendial Requirements on Compendial Products (CPG 7132.05)

Sec. 420.400 Performance of Tests for Compendial Requirements on Compendial Products (CPG 7132.05)

BACKGROUND:

There have been inquiries from the field and industry concerning the following four items as they apply to the manufacture of compendial (USP/NF) drug products.

1. Does a firm have to use the compendial methodology on a batch release basis, to determine whether its product meets the requirements of the monograph?

2. Does the word, "specifications" as used in 21 CFR 211.165 refer to compendial specifications or those set up by the firm's quality control unit?

3. Does a firm have to test for all requirements listed in the monograph for a compendial product?

4. Are the compendial testing requirements the same for products destined for the commercial market and the military?

POLICY:

1. Compendial methods need only be applied, as a batch release test, where a firm has made specific commitments to do so (as in a new drug application), or where the official method is the only appropriate test. It should be noted that neither the USP/NF nor the CGMP regulations necessarily require a firm to utilize, as a batch release test, the methods and procedures stated in the official compendia.

What is required is that official drug products conform to the appropriate compendial standards. This conformance must be assured by suitable means, including adequate manufacturing process validation and control. Scientifically sound alternative test methods may be acceptable for the purpose of batch release testing. However, in the event of a dispute as to whether or not a drug product meets the standard, the compendial method will be applied as the referee test.

2. The term "specifications" as used in 21 CFR 211.165 refers to the criteria established by manufacturers to assure that their products have the properties they purport to possess. Typically, these specifications are identical to, or more stringent than those contained in the compendia themselves. However, the manufacturer's specifications for standards of strength, quality and purity may be less stringent in those cases in which the differences from the official standards are stated on the product label; such alternate standards must not adversely affect the product's safety or efficacy.

3. Where an official product purports to conform to the standards of the USP/NF the manufacturer must assure that each batch conforms to each monograph requirement. This assurance must be achieved by appropriate means, including process validation and controls and end product testing. However, the nature and extent of end product testing which is needed will depend upon the circumstances. Factors to consider in determining the need to test each batch for a given monograph requirement include: the adequacy of the manufacturer's process validation, adequacy of in-process manufacturing controls, and the nature of the particular product characteristic which is the subject of the specification (e.g. potency, sterility, content uniformity). Therefore, in some cases it may not be necessary for a manufacturer to test each batch for each monograph requirement.

4. Compendial testing requirements are the same for products destined for commercial and military use unless the Defense Personnel Support Center (DPSC) insists upon certain requirements as part of military contracts. For example, DPSC can insist that only compendial methods be used and that each batch be tested for every monograph specification, whereas, as explained above, FDA considers that alternative procedures may sometimes be acceptable. Under the Government Wide Quality Assurance Program FDA must assure that the drug manufacturer abides by the terms of the military contract, including testing requirements.

Issued: 10/1/80