Inspections, Compliance, Enforcement, and Criminal Investigations

CPG Sec. 460.600 Content Uniformity Testing of Tablets and Capsules

BACKGROUND:

There has been some misunderstanding surrounding the applicability of content uniformity testing requirements to tablets and capsules, particularly for non-official products, i.e., those not recognized as official in the United States Pharmacopeia (USP). Added to this is the confusion created by recent changes in the USP test requirements for official products. In addition to the existing standard for the individual dosage unit assay, the USP included a specification for relative standard deviation to limit large variations in test results. However, many firms have been reluctant to incorporate the relative standard deviation specification into their standard operating procedures.

POLICY:

The following policy is applicable to tablet or capsule dosage forms.

1. Official Products

Any drug product recognized in the USP must comply with the USP requirement for content uniformity if such requirement is included in the monograph for the drug. The product must comply with the specifications for individual dosage unit assay and for relative standard deviation. Both requirements are applicable regardless of whether or not the product in question is subject to a new drug application (NDA). If an approved NDA does not currently provide for complete content uniformity testing, or provides specifications that are inconsistent with the USP monograph, the NDA holder must submit a change to provide for such testing, pursuant to 21 CFR 314.70(d)(1).

2. Non-official Drug Products

The Food, Drug, and Cosmetic Act requires that drug products which are not official (and therefore not subject to compendial requirements) nonetheless meet standards of strength and quality which they purport or are represented to possess. Current good manufacturing practice regulations (21 CFR 211.160) require the establishment of scientifically sound and adequate specifications to assure those product attributes. Specifications for content uniformity are required, within this context, for tablets and capsules which contain less than 50 mg of any active ingredient. Requirements for content uniformity include individual dosage unit assays and establishment of specifications for relative standard deviation.

Any non-official tablet or capsule dosage form which contains less than 50 mg of any active ingredient and such ingredient(s) has not been tested for content uniformity is in violation of Section 501(a)(2)(B) of the Act. In evaluating the appropriateness of test specifications for a non-official product, it must be emphasized that although USP specifications are acceptable, and may be adopted by a firm, they are not specifically required. Scientifically sound alternative specifications may be used.

Issued: 10/2/87

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