CPG Sec. 480.300 Lack of Expiration Date of Stability Data

BACKGROUND:

The CGMP regulations (21 CFR 211.137) have required that drug products packaged since September 29, 1979, bear an expiration date which is supported by appropriate stability data, with limited exceptions. OTC drug products which have no dosage limitation and which are stable for at least three years as demonstrated by appropriate data are exempt from the requirement to bear an expiration date. Homeopathic drugs, while required to have a limited evaluation of stability, are also exempt from the requirement to bear an expiration date. Additionally, allergenic extracts that are labeled "No U.S. Standard of Potency" are exempt from the requirements to be labeled with an expiration date and the performance of stability studies.

Section 211.166 requires a firm to have a written stability program, the results of which are to be used in determining appropriate storage conditions and a product's expiration date and specifies what must be included in the stability program.

In addition, the USP requires that the labels of all pharmacopeial dosage forms bear an expiration date.

REGULATORY ACTION GUIDANCE:

Appropriate division offices within the Office of Pharmaceutical Quality Operations (OPQO) are authorized to issue *Warning Letters without Office of Compliance, HFD-300*, review under the following circumstances:

1. A non-compendial drug product intended for internal use does not bear an expiration date and is not exempt by regulations.

Charge: 501(a)(2)(B), 21 CFR 211.137.

2. A prescription drug product for which it has been determined that stability studies do not exist.

Charge: 501(a)(2)(B), 21 CFR 211.166

Examples of the wording to be used in a *warning letter* are as follows:

501(a)(2)(B) Your product, (name of product), is adulterated in that the controls used for the manufacture, processing, packing, or holding of this drug product are not in conformance with current good manufacturing practice regulations (Title 21, Code of Federal Regulations, Parts 210 and 211).

Specific Violations are:

There is no assurance that the product meets applicable standards of identity, strength, quality, and purity at the time of use in that it does not bear an expiration date (211.137).

You have not performed stability testing of your product and therefore are unable to appropriately determine storage conditions designed to assure the stability of your drug product (211.166).

NOTE: If appropriate, misbranding [502(g)] may be charged when a USP drug product intended for internal use does not bear an expiration date and is not exempt by regulations. Example of the wording to be used in a *warning letter*:

502(g) The article (name of the drug product) is misbranded in that it purports to be a drug, the name of which is recognized in an official compendium and the label fails to bear an expiration date as prescribed therein.

All other cases should be referred to the Office of Compliance, *HFD-300*, or as identified in *CPG 7132a.04 (See Sec. 480.100) or* specific compliance programs, in the usual manner.

Material between asterisks is new or revised

Issued: 1/16/84
Revised: 9/4/87, 3/95