Guidance for Industry

Drug Stability Guidelines

(This version of the guidance replaces the version that was made available in December 1990. This guidance document has been revised to correct the contact information, address formatting issues and to add missing text linked to the table of contents.

For questions regarding this guidance document, contact Dr. Dennis M. Bensley, Jr., Center for Veterinary Medicine (HFV-140), Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855, (240) 276-8268.

Additional copies of this guidance document may be requested from the Communications Staff, HFV-12, Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, and may be viewed on the Internet at http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Veterinary Medicine (CVM)
December 9, 2008

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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 the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the appropriate FDA staff. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

The guideline is to be used as an aid in designing and conducting studies to establish drug stability in support of original, abbreviated or supplements to new animal drug applications (NADAs/ANADAs). The guideline will provide a framework within which stability studies can be conducted to provide meaningful and sufficient data. The concept of the guidelines is applicable to studies on drug substances and the actual dosage form. The guideline is not intended to restrict experimentation. The guideline applies to pharmaceutical dosage forms and medicated feed products.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the FDA'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 FDA's guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

Section 512(b) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 360b) establishes the requirements for new animal drug approval. 21 CFR 514.1 specifies the proper form and the information required to be submitted. Included is a requirement under section 514.1(b)(5)(x) that an applicant submit data from stability studies completed as well as information about studies that are underway to substantiate the request for a specific expiration date and provide information on the stability of the drug products.

CGMP regulations under 21 CFR Part 200 also require stability testing for pharmaceutical dosage forms (21 CFR 211) and Type A Medicated Articles (medicated premixes) (21 CFR 226). This guideline can be used as an aid to conduct the required stability testing.

The agency advises that this final guideline represents its current position on the development of stability studies to meet the requirements of the submission of original or abbreviated new

animal drug applications and the corresponding CGMP regulations. The guideline may be useful to manufacturers of new animal drug products. A person may follow the guideline or may choose to use alternate procedures even though they are not provided for in the guideline. If a person chooses to use alternate procedures, that person may wish to discuss the matter further with the agency to prevent an expenditure of money and effort on activities that may later be determined to be unacceptable by FDA. This guideline does not bind the agency, and it does not create or confer any rights, privileges, or benefits for or on any person.

III. GENERAL CONSIDERATIONS

A. PROTOCOLS

Prior to the submission of an original or supplemental NADA, an applicant may wish to submit a stability protocol for comment before committing to studies that will become a permanent part of the NADA.

The protocol should contain an outline of the proposed plan to be used in generating stability data. The protocol should describe the type of product being tested, sampling process, duration and frequency of testing, number of samples and replicates per time interval, storage conditions (length of storage, type of storage, temperatures and packaging), methods of analysis (description or reference of published methods) with accompanying support data, if available, and other tests. The information listed in these guidelines should be incorporated as appropriate in the development of a plan.

The Center's review scientists will evaluate and comment on the proposed protocols or assist an applicant (upon request) in the design of a study.

It should be noted that the Center for Veterinary Medicine does not approve protocols.

Applicants or drug firms proposing to conduct stability studies should refer to the following texts:

- "Chemical Stability of Pharmaceuticals" by K. Connors, G. Amidon and L. Kennon, John Wiley & Sons (1979).
  and
- "Formulation of Veterinary Dosage Forms", vol. 17, Drugs and The Pharmaceutical Sciences, Blodinger, J., Marcel Dekker Inc., NY. (1983). Chapter 5.

These texts provide information on the various aspects of establishing a stability program.

B. GENERAL STABILITY CONSIDERATIONS

1. Definition of Active Ingredient

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