
SUPPLEMENTAL POLICIES

**POLICY ON STERILIZATION OF NEW ANIMAL DRUG
PRODUCTS AND CONTAINERS BY IRRADIATION**

INTRODUCTION:

Sterilization by irradiation, in general, is permitted for use with drug products. The administration policy with regard to irradiated drugs is stated in 21 CFR 310.502(a)(11). This regulation addresses only human drug products. However, the policy is also applicable to drugs subject to Section 512 of the Federal Food, Drug, and Cosmetic Act (FFDCA) which includes drugs for animal use. There are no other specific regulatory requirements at this time for using this procedure.

POLICY:

In order to assure that the irradiation/sterilization process is properly conducted, there are specific areas of control concerning the procedure that should be addressed to provide the information required under 21 CFR 514.1(b)(5)(v). Since both drug products and containers can be sterilized, the information below is related to both.

1. Process:

The following items regarding the sterilization process used should be addressed:

- a. The method and level of irradiation, time of irradiation and temperature(s) used.
- b. The radiation source used.
- c. Evidence that the proposed contract sterilizer has proper federal, state and local credentials and the proper approvals to operate the radiation facility.

2. Safety and Effectiveness:

Safety and effectiveness data (21 CFR 514.1(b)(8)) may need to be submitted for irradiated products. The applicant may also need to demonstrate that a) residual radiation in the product is safe for the treated animal, and b) residual radiation does not persist in the food product from a food-producing animal treated with the irradiated product. If it does persist, the effect of irradiation on human safety should be determined to provide the information and data required under 21 CFR 514.1(b)(7):

- a. Residual radioactivity in the product or in the product container at time 0, 12, 24 hours post-irradiation or until the radioactivity dissipates.
- b. The effects of irradiation on the physical nature of the sterilized product, including degradation of antibacterial, the active ingredient, the product matrix, or the container.

3. Manufacturing and Control Information (21 CFR 514.1(b)(5)):

The following manufacturing and control information should be provided:

- a. A description of the irradiation process, facilities (including the irradiation chamber), and name and address of contractor who will conduct the process. References to master files are acceptable.
- b. Results of investigations conducted to establish that the irradiation dose to be used could achieve sterilization (using the maximum allowed irradiation dose).
- c. Validation data for the irradiation process including dose mapping, biological indicators, load configuration, number and placement of dosimeters, etc. Refer to FDA's "Sterilization Process Validation Guideline." Validation studies should be conducted with the minimum allowed dose and should include inoculation of product or containers with spore suspensions.
- d. Stability data on representative irradiated market-ready packages. These data should cover at least a six- to nine-month period to establish the long-term effect on the physical or chemical parameters of the dosage unit. Product degradation or any alteration of the product by interaction with container components should be determined. Samples of non-irradiated material should be run in parallel as controls. Evidence of non-detrimental effect on product (identity, strength, quality or purity) and container should be submitted.
- e. For terminally sterilized finished dosage forms, results of the microbial count before irradiation to assure the initial bioburden is at or below the established bioburden limit for that product.
- f. Performance of the customary sterility tests required for sterile dosage forms produced in a sterile environment.
- g. A description of the method of testing the sterility of the product.
- h. A description of the container used. The information should indicate if the product is sterilized in bulk or in the immediate container.

- i. For irradiated containers a description of the packaging to protect the sterile containers from recontamination should be provided. Additionally, an expiration time should be established for the sterile containers. Validation data to document the proposed expiration time should be submitted.

GENERAL

The above represents some of the major concerns relating to sterilization by irradiation. The list should not be considered comprehensive or complete. Each product or container undergoing this process (and the process itself) is evaluated on an individual basis.

Additionally, the sponsor of the NADA provides assurances of occupational and user safety.

General Statement of Policy on Sterilization of Animal Drugs by Irradiation:

There is a current interest in the utilization of radiation for the sterilization of animal drugs. Prior to the marketing of an animal drug sterilized by such means, it is necessary in the interest of protecting the public health to establish by adequate investigations that the irradiation treatment does not cause the animal drug to become unsafe or otherwise unsuitable for use. Accordingly, all animal drug products, including injections, ophthalmic solutions, and intrauterine infusions sterilized by means of irradiation are regarded as new animal drugs within the meaning of section 201(v) of the Federal Food, Drug, and Cosmetic Act. An effective new animal drug application pursuant to section 512 of the act is therefore a prerequisite to interstate shipment of such articles, except as provided by section 512(j).