§ 500.80

anaphylactoid shock. Usual Dosage: Cattle, horses, sheep, and swine—1 cubic centimeter per 100 pounds of body weight. Inject subcutaneously".

(c) The labeling must also bear a description of the symptoms of anaphylactoid shock including glassy eyes, increased salivation, grinding of the teeth, rapid breathing, muscular tremors, staggering gait, and collapse with death following. These symptoms may appear shortly after injection of a bacterin, vaccine, or antibiotic.

Subpart E—Regulation of Carcinogenic Compounds Used in Food-Producing Animals

SOURCE: 52 FR 49586, Dec. 31, 1987, unless otherwise noted.

§ 500.80 Scope of this subpart.

(a) The Federal Food, Drug, and Cosmetic Act requires that sponsored compounds intended for use in food-producing animals be shown to be safe and that food produced from animals exposed to these compounds be shown to be safe for consumption by people. The statute prohibits the use in food-producing animals of any compound found to induce cancer when ingested by people or animals unless it can be determined by methods of examination prescribed or approved by the Secretary (a function delegated to the Commissioner of Food and Drugs under §5.10 of this chapter) that no residue of that compound will be found in the food produced from those animals under conditions of use reasonably certain to be followed in practice. This subpart provides an operational definition of no residue and identifies the steps a sponsor of a compound shall follow to secure the approval of the compound.

(b) The Federal guidelines contain the procedures and protocols FDA recommends for the implementation of this subpart. These guidelines are available from the Dockets Management Branch (HFA-305), Food and Drug Administration, rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857. Requests for these guidelines should be identified with Docket No. 83D-0288.

(b) If FDA concludes on the basis of the threshold assessment that a sponsor shall conduct carcinogenicity testing on the sponsored compound, FDA will also determine whether and to what extent the sponsor shall conduct carcinogenicity testing on metabolites of the sponsored compound. The bioassays that a sponsor conducts must be designed to assess carcinogenicity and to determine the quantitative aspects of any carcinogenic response.

(c) If FDA concludes on the basis of the threshold assessment or at a later time during the approval process that the data show that the sponsored compound and its metabolites should not be subject to this subpart, FDA will continue to consider the compound for approval under the general safety provisions of the act for risks other than cancer.

(d) This subpart does not apply to essential nutrients.


§ 500.82 Definitions.

(a) The definitions and interpretations contained in section 201 of the act apply to those terms when used in this subpart.

(b) The following definitions apply to this subpart:


Essential nutrients means compounds that are found in the tissues of untreated, healthy target animals and not produced in sufficient quantity to support the animal’s growth, development, function, or reproduction, e.g., vitamins, essential minerals, essential amino acids, and essential fatty acids. These compounds must be supplied from external sources.

FDA means the Food and Drug Administration.

Marker residue means the residue selected for assay whose concentration is in a known relationship to the concentration of the residue of carcinogenic concern in the last tissue to deplete to its permitted concentration.

Preslaughter withdrawal period or milk discard time means the time after cessation of administration of the sponsored compound for the residue of carcinogenic concern in the edible product...
§ 500.84 Operational definition of "no residue".

(a) On the basis of the results of the chronic bioassays and other information, FDA will determine whether any of the substances tested are carcinogenic.

(b) If FDA concludes that the results of the bioassays do not establish carcinogenicity, then FDA will not subject the sponsored compound to the remainder of the requirements of this subpart.

(c) For each sponsored compound that FDA decides should be regulated as a carcinogen, FDA will analyze the data from the bioassays using a statistical extrapolation procedure.

(1) For each substance tested in separate bioassays, FDA will calculate the concentration of the residue of carcinogenic concern in the total human diet that represents no significant increase in the risk of cancer to people.

(2) FDA will consider that "no residue" of the compound remains in the edible tissue when conditions of use of the sponsored compound, including any required preslaughter withdrawal period or milk discard time, ensure that the concentration of the residue of carcinogenic concern in the total human diet will not exceed Sm. Because the total diet is not derived from food-producing animals, FDA will designate as Sm the concentration of residue of carcinogenic concern that is permitted in a specific edible product.

§ 500.86 Marker residue and target tissue.

(a) For each edible tissue, the sponsor shall measure the depletion of the residue of carcinogenic concern until its concentration is at or below Sm.

(b) In one or more edible tissues, the sponsor shall also measure the depletion of one or more potential marker residues until the concentration of the
residue of carcinogenic concern is at or below $S_m$.

(c) From these data, FDA will select a target tissue and a marker residue and designate the concentration of marker residue ($R_m$) that the regulatory method must be capable of measuring in the target tissue. FDA will select $R_m$ such that the absence of the marker residue in the target tissue above $R_m$ can be taken as confirmation that the residue of carcinogenic concern does not exceed $S_m$ in each of the edible tissues and, therefore, that the residue of carcinogenic concern in the diet of people does not exceed $S_o$.

(d) When a compound is to be used in milk- or egg-producing animals, milk or eggs must be the target tissue in addition to the tissue selected to monitor for residues in the edible carcass.

(Approved by the Office of Management and Budget under control number 0910-0228)

§ 500.88 Regulatory method.

(a) The sponsor shall submit for evaluation and validation a regulatory method developed to monitor compliance with FDA's operational definition of no residue.

(b) The regulatory method must reliably measure and confirm the identity of the marker residue in the target tissue at concentrations equal to and above $R_m$.

(c) FDA will publish in the Federal Register the complete regulatory method for measuring the marker residue in the target tissue in accordance with the provisions of sections 409(c)(3)(A), 512(d)(1)(H) and (i), and 723(b)(5)(B) of the act.

(Approved by the Office of Management and Budget under control number 0910-0228)

§ 500.90 Waiver of requirements.

In response to a petition or on the Commissioner's own initiative, the Commissioner may waive, in whole or in part, the requirements of this subpart except those provided under §500.88. A petition for this waiver may be filed by any person who would be adversely affected by the application of the requirements to a particular compound. The petition shall explain and document why the requirements from which a waiver is requested are not reasonably applicable to the compound, and set forth clearly the reasons why the alternative procedures will provide the basis for concluding that approval of the compound satisfies the requirements of the anticancer provisions of the act. If the Commissioner determines that waiver of any of the requirements of this subpart is appropriate, the Commissioner will state the basis for that determination in the regulation approving marketing of the sponsored compound.

(Approved by the Office of Management and Budget under control number 0910-0228)

§ 500.92 Implementation.

(a) This subpart E applies to all new animal drug applications, food additive petitions, and color additive petitions concerning any compound intended for use in food-producing animals (including supplemental applications and amendments to petitions).

(b) This subpart E also applies in the following manner to compounds already approved:

(1) For those compounds that FDA determines may induce cancer when ingested by man or animals, i.e., suspect carcinogens, §§500.80(b), 500.82, and 500.90 apply.

(2) For those compounds that FDA determines have been shown to induce cancer when ingested by man or animals, §§500.82 through 500.90 apply.

PART 501—ANIMAL FOOD LABELING

Subpart A—General Provisions

Sec. 501.1 Principal display panel of package form animal food.

501.2 Information panel of package for animal food.

501.3 Identity labeling of animal food in package form.

501.4 Animal food; designation of ingredients.

501.5 Animal food; name and place of business of manufacturer, packer, or distributor.

501.8 Labeling of animal food with number of servings.

501.15 Animal food; prominence of required statements.

501.17 Animal food labeling warning statements.

501.18 Misbranding of animal food.