

§ 201.310

21 CFR Ch. I (4-1-10 Edition)

commerce, began an active investigation of reports of possible toxic effects and renal damage due to misuse of the drug acetophenetidin. This study led to the decision that there was probable cause to conclude that misuse and prolonged use of the drug were in fact responsible for kidney lesions and disease. The Commissioner of Food and Drugs, in December 1963, appointed an ad hoc Advisory Committee of Inquiry on Possible Nephrotoxicity Associated With the Abuse of Acetophenetidin (Phenacetin)-Containing Preparations. This committee, composed of scientists in the fields of pharmacology and medicine, on April 23, 1964, submitted its findings and conclusions in the matter and recommended that all acetophenetidin (phenacetin)-containing preparations bear a warning as provided in section 502(f)(2) of the Federal Food, Drug, and Cosmetic Act.

(b) On the basis of the studies made by the Food and Drug Administration and the report of the Advisory Committee, the Commissioner of Food and Drugs has concluded that it is necessary for the protection of users that the label and labeling of all acetophenetidin (phenacetin)-containing preparations bear a warning statement to the following effect: "Warning—This medication may damage the kidneys when used in large amounts or for a long period of time. Do not take more than the recommended dosage, nor take regularly for longer than 10 days without consulting your physician."

§ 201.310 Phenindione; labeling of drug preparations intended for use by man.

(a) Reports in the medical literature and data accumulated by the Food and Drug Administration indicate that phenindione, a synthetic anticoagulant drug, has caused a number of cases of agranulocytosis (with two fatalities). There are also reports implicating the drug in cases of hepatitis and hypersensitivity reactions. In view of the potentially serious effects found to be associated with preparations of this drug intended for use by man, the Commissioner of Food and Drugs will regard such preparations as misbranded within the meaning of section 502(f) (1) and (2) of the Federal Food, Drug, and Cos-

metic Act, unless the label and labeling on or within the package from which the drug is to be dispensed, and any other labeling furnishing or purporting to furnish information for use of the drug, bear a conspicuous warning statement to the following effect: "Warning: Agranulocytosis and hepatitis have been associated with the use of phenindione. Patients should be instructed to report promptly prodromal symptoms such as marked fatigue, chill, fever, and sore throat. Periodic blood studies and liver function tests should be performed. Use of the drug should be discontinued if leukopenia occurs or if evidence of hypersensitivity, such as dermatitis or fever, appears."

(b) Regulatory action may be initiated with respect to preparations of phenindione intended for use by man found within the jurisdiction of the act on or after November 25, 1961, unless such preparations are labeled in accordance with paragraph (a) of this section.

§ 201.311 [Reserved]

§ 201.312 Magnesium sulfate heptahydrate; label declaration on drug products.

Magnesium sulfate heptahydrate should be listed on the label of a drug product as epsom salt, which is its common or usual name.

§ 201.313 Estradiol labeling.

The article presently recognized in The National Formulary under the heading "Estradiol" and which is said to be "17-cis-beta estradiol" is the same substance formerly recognized in the United States Pharmacopeia under the designation "Alpha Estradiol." The substance should no longer be referred to in drug labeling as "Alpha Estradiol." The Food and Drug Administration would not object to label references to the article as simply "Estradiol"; nor would it object if the label of a preparation containing this substance referred to the presence of "Estradiol (formerly known as Alpha Estradiol)."