

The circumstances involved with the iron poisonings parallel in many significant respects those that led the agency to require a warning on protein products. The use of iron-containing products in households where children are present is in no way an unusual practice. Multi-vitamin/mineral supplements with iron are taken routinely by children, and products of this type specifically intended for use by children are widely available and commonly sold. Iron supplements and iron-containing drug products are frequently recommended by physicians for pregnant women (often with a prescription) and other women of child-bearing age to meet their dietary requirement (these groups require more iron than other adults). Yet, the evidence on poisonings and deaths shows that the presence of iron-containing products in households with young children can lead to accidental injury or death if the children gain access to the products. Thus, FDA tentatively concluded that a warning about the risk of accidental pediatric poisoning from iron-containing products in solid oral dosage form is necessary in the labeling of all iron-containing products.

Second, FDA proposed to require that all iron-containing drugs and dietary supplements in solid oral dosage form that contain 30 mg or more iron per dosage unit be packaged in unit-dose packaging. In the proposal, FDA tentatively concluded that full compliance with CPSC's child resistant packaging requirements, even if there are warning statements in labeling of iron-containing products and appropriate educational programs, is not adequate to ensure the safe use of certain iron-containing drugs and dietary supplements if bottle and closure packaging were to continue as the predominant means of packaging such products. FDA recognizes that each of these measures either has been successful in limiting the number of poisonings or can be reasonably expected to be effective in reducing the number of poisonings. However, given the potentially fatal outcome that can result from pediatric iron poisoning, FDA stated that it is not persuaded that these measures are adequate to ensure the safety of the use of certain iron-containing drugs and dietary supplements. To reduce the incidence of pediatric iron poisonings to a level that would permit the agency to conclude that the use of these products is safe, or generally recognized as safe (GRAS), FDA tentatively concluded that it was necessary to require a specific

type of physical barrier to access dietary supplements that contain 30 mg or more of iron. Therefore, FDA tentatively concluded that an additional packaging requirement was necessary.

FDA proposed this packaging requirement for iron-containing dietary supplements based on its authority under the act, with the provisions available at that time, to ensure that food ingredients are safe. In particular, the act requires, in sections 402 and 409 (21 U.S.C. 342 and 348), that the safety of each food ingredient be established, either because the ingredient is GRAS, or because it is listed under the food additive or other relevant provisions, before it is added to food.

Section 409(a) of the act deems a food additive to be unsafe unless its use conforms to the conditions specified in the listing regulation. These conditions include, but are not limited to, specifications as to the particular food or classes of food to which the additive may be added, the manner in which the additive may be added to such food, and any directions or other labeling or packaging requirements for such additive deemed necessary to assure the safety of such use (section 409(c)(1)(A) of the act). Thus, under the act, the agency is authorized to specify packaging requirements for a food additive when it finds that use of such packaging is necessary to ensure the safe use of the additive.

Section 201(s) of the act provides an exemption to the "food additive" definition for substances that are GRAS under the conditions of their intended use. FDA has issued regulations delineating conditions under which the use of certain substances is GRAS. In the proposal, FDA tentatively concluded that those conditions could include packaging. Thus if a dietary supplement contained an iron salt whose use would be GRAS except for the fact that its packaging would not ensure that its use would be safe, the product would be considered to contain an unsafe food additive and thus to be adulterated.

FDA proposed the packaging requirement for iron-containing drugs based on its authority under section 501(a)(2)(B) of the act (21 U.S.C. 351(a)(2)(B)). This section states that a drug shall be deemed to be adulterated if the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to, or are not operated or administered in conformity with, current good manufacturing practice (CGMP) to assure that such drug meets the requirements of the act as to safety and has the identity and strength, and meets the quality and purity

characteristics, which it purports or is represented to possess.

Under section 501(a)(2)(B) of the act, manufacturers are responsible for preventing intentional misuse of a drug product. For example, in 1982, in response to a series of capsule tamperings, FDA issued a regulation (§ 211.132), under the authority of this section, that requires tamper-resistant packaging for all over-the-counter (OTC) human drug products except dermatologics, dentifrices, and insulin (47 FR 50442, November 5, 1982). The agency's action assured greater package integrity and product security beyond the point of manufacture.

The recent data available to FDA demonstrate that the current manner of holding iron-containing drug products until their use by the intended consumer fails to ensure that the drug products will be safe because large numbers of children are ingesting such products and suffering serious injuries or death. Existing technology permits additional safeguards, such as child-resistant blister packs, to be used for holding iron-containing drug products. Given the known dangers and the ability to minimize or eliminate such dangers through the use of existing technology, FDA tentatively concluded that CGMP dictates that unit-dose packaging be used.

## II. The Dietary Supplement Health and Education Act

On October 25, 1994, President Clinton signed into law the DSHEA (Pub. L. 103-417). The DSHEA contains two provisions that bear on FDA's packaging proposal with respect to dietary supplements. First, section 3(b) of the DSHEA added section 201(s)(6) to the act. This provision excludes minerals, such as iron, that are used in dietary supplements from the definition of a "food additive." Second, section 9 of the DSHEA added section 402(g) to the act. Under this provision, a dietary supplement is adulterated unless it has been prepared, packed, and held under conditions that comply with the CGMP (section 402(g)(1) of the act). Under section 402(g)(2), the Secretary (and, by delegation, FDA) is authorized to prescribe CGMP's for dietary supplements by regulation.

The DSHEA does not bear on any aspect of this rulemaking other than the proposed packaging requirement for dietary supplements. Dietary supplements are deemed to be food and thus are subject to sections 201(n), 403(a), and 701(a) of the act (see section 201(ff) of the act). Thus, the proposed labeling requirement for iron-containing dietary supplements is not affected by