EVALUATION OF THE HEALTH ASPECTS OF A MIXTURE OF DIFERROUS, DIPOTASSIUM FERROUS, AND POTASSIUM FERROCYANIDES AS A FINING AGENT IN WINE PRODUCTION

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Prepared for

Bureau of Foods
Food and Drug Administration
Department of Health and Human Services
Washington, D.C.

Contract No. FDA 223-78-2100
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Life Sciences Research Office
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This report, one of a series concerning the health aspects of using the Generally Recognized as Safe (GRAS) or prior-sanctioned food substances as food ingredients, is being made by the Federation of American Societies for Experimental Biology (FASEB) under contract no. 223-78-2100 with the Food and Drug Administration (FDA), U.S. Department of Health and Human Services. The Federation recognizes that the safety of GRAS substances is of national significance, and that its resources are particularly suited to marshaling the opinions of knowledgeable scientists to assist in these evaluations. The Life Sciences Research Office (LSRO), established by FASEB in 1962 to make scientific assessments in the biomedical sciences, is conducting these studies.

Qualified scientists were selected as consultants to review and evaluate the available information on each of the GRAS substances. These scientists, designated the Select Committee on GRAS Substances, were chosen for their experience and judgment with due consideration for balance and breadth in the appropriate professional disciplines. The Select Committee's evaluations are being made independently of FDA or any other group, governmental or nongovernmental. The Select Committee accepts responsibility for the content of each report. Members of the Select Committee who have contributed to this report are named in Section VII.

Tentative reports are made available to the public for review in the office of the Dockets Management Branch, Food and Drug Administration, after announcement in the Federal Register, and opportunity is provided for any interested person to appear before the Select Committee at a public hearing to make oral presentation of data, information, and views on the substances covered by the report. The data, information, and views presented at the hearing are considered by the Select Committee in reaching its final conclusions. Reports are approved by the Select Committee and the Director of LSRO, and subsequently reviewed and approved by the LSRO Advisory Committee (which consists of representatives of each constituent society of FASEB) under authority delegated by the Executive Committee of the Federation Board. Upon completion of these review procedures the reports are approved and transmitted to FDA by the Executive Director of FASEB.

While this is a report of the Federation of American Societies for Experimental Biology, it does not necessarily reflect the opinion of all of the individual members of its constituent societies.

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I. INTRODUCTION

This report concerns the health aspects of using mixtures of certain ferrocyanide salts as food ingredients. It has been based partly on the information contained in a scientific literature review (monograph) furnished by FDA (Dailey and Weissler, 1978), which summarizes the world's scientific literature from 1920 through 1978. To ensure completeness and currency as of the date of this report, this information has been supplemented by searches of over 30 scientific and statistical reference sources and compendia that are generally available; use of new, relevant books and reviews and the literature citations contained in them; consideration of current literature citations obtained through computer retrieval systems of the National Library of Medicine; searches for relevant data in the files of FDA; and by the combined knowledge and experience of members of the Select Committee and the LSRO staff. In addition, an announcement was made in the Federal Register of May 29, 1981 (46 FR 28947–28948) that opportunity would be provided for any interested person to appear before the Select Committee at a public hearing to make oral presentation of data, information, and views on the health aspects of using mixtures of certain ferrocyanide salts as food ingredients. The Select Committee received no request for a hearing.

As indicated in the Food, Drug, and Cosmetic Act [21 USC 321(s)], GRAS substances are exempt from the premarketing clearance that is required for food additives. It is stated in the Act and in the Code of Federal Regulations [21 CFR 170.3 and 170.30] (Office of the Federal Register, 1980a) that GRAS means general recognition of safety by experts qualified by scientific training and experience to evaluate the safety of substances on the basis of scientific data derived from published literature. These sections of the Code also indicate that expert judgment is to be based on the evaluation of results of credible toxicological testing or, for those substances used in food prior to January 1, 1958, on a reasoned judgment founded in experience with common food use, and is to take into account reasonably anticipated patterns of consumption, cumulative effects in the diet, and safety factors appropriate for the utilization of animal experimentation data. FDA recognizes further [21 CFR 170.30] that it is impossible to provide assurance that any substance is absolutely safe for human consumption.

The Select Committee on GRAS Substances of LSRO reviewed and evaluated the available information on mixtures of certain ferrocyanide salts in full recognition of the foregoing provisions. In reaching its conclusions on safety, the Committee, in accordance with FDA's guidelines, relied primarily on the absence of substantive evidence of, or reasonable grounds to suspect, a significant risk to the public health. This report is intended for the use of FDA in determining the future status of these substances under the Federal Food, Drug, and Cosmetic Act. The Committee anticipates that its conclusions will be reviewed as new information becomes available.
II. BACKGROUND INFORMATION

Ferrocyanide salts are a diverse group of synthetic compounds widely used in industry. None occur naturally and only a few inorganic ferrocyano salts are used in food processing (Dailey and Weissler, 1978). The ferric ferrocyano salt (C.I. Pigment Blue 27; Prussian Blue) was first synthesized in 1704 by Diesback, and was the first of a series of synthetic pigments that are used in printing inks, paints, linoleum, rubbers, plastics, leathercloth, and similar material (Dailey and Weissler, 1978; The Merck Index, 1976).

Potassium ferrocyano is produced by heating a mixture of potassium carbonate, metallic iron, and organic matter; the salt is obtained by evaporating the solution leached from the above mixture (Dailey and Weissler, 1978). The sodium salt is produced similarly, using sodium carbonate in the reaction mixture. Insoluble ferric ferrocyano is prepared by addition of a soluble ferric salt to a solution of potassium or sodium ferrocyanide. The calcium and dipotassium ferrous ferrocyano salts have been prepared in an analogous manner.

The only prior-sanctioned or GRAS use of ferrocyano salts appears to be as a fining agent in wine to remove excess iron and copper (Office of the Federal Register, 1980b), and this report of the Select Committee is concerned solely with the use of ferrocyano salts as fining agents.

While the trade name of one proprietary product occurs in the Code of Federal Regulations, the Select Committee is aware of two products that are used as fining agents (Crantz, 1979; Scott, 1979). Both proprietary products, Cufex* and Metafine*, are reformulations of a product originally known as Fessler Compound (Amerine et al., 1972; Scott, 1979). The proprietary products are considered GRAS for use as fining agents in removing trace metals from wine, provided no insoluble or soluble residue in excess of 1 ppm remains in the finished wine, and "the basic character" of the wine is not changed by this treatment [27 CFR 240.1051 and 240.1052] (Harvey, 1959; Office of the Federal Register, 1980b). Both products are pastes that contain insoluble complexes formed by the reaction of potassium ferrocyano and ferrous sulfate in aqueous solutions. Prior to treatment with the fining agents, wines may have copper and iron contents ranging from 0.1-0.2 ppm and 4-12 ppm, respectively (Crantz, 1979; Scott, 1979). One pound of the proprietary product added to 1000 gal of wine will reduce its iron content by 1 ppm and essentially eliminate the trace amounts of copper. The finely divided particles in the paste sequester trace amounts of the metals and are subsequently removed by settling and filtration (Crantz, 1979; Scott, 1979).
According to label statements, both proprietary products consist of a minimum of 45% dipotassium ferrous ferrocyanide, $K_2Fe[Fe(CN)_6]$, and approximately 2.5% each of diferrous ferrocyanide, $Fe_2[Fe(CN)_6]$, and potassium ferrocyanide. The first two compounds are insoluble in water, whereas potassium ferrocyanide is water-soluble (Thorne and Roberts, 1954). One pound (454 g) of the proprietary product contains about 11 g potassium ferrocyanide. The addition of 1 lb of either product to 1000 gal of wine would add 1.2 ppm or less of potassium to the wine, depending on the extent of reaction with trace metals present and the composition of the insoluble ferrocyanides formed in the process. Presumably, either of the insoluble salts, $K_2Fe_2[Fe(CN)_6]$ or $Fe_2[Fe(CN)_6]$, or both might be formed by reaction with ferrous ions present in the wine (Thorne and Roberts, 1954). The natural potassium content of wine is in the range 360-1100 ppm (Amerine et al., 1972). Marsh (1952) reported experiments in which 100,000 gal of wine were treated with a ferrocyanide preparation using up to 10 times the required amount. No cyanogenetic or cyanide residues were detected (Marsh, 1952; Amerine et al., 1972).

Other ferrocyanide salts used in the food industry in this country or abroad are as follows:

Sodium ferrocyanide decahydrate, $Na_4[Fe(CN)_6]$·10$H_2O$, is a regulated food additive used as an anticaking agent [21 CFR 172.490] (Office of the Federal Register, 1980a). The additive, yellow prussiate of soda, is used as an antica
ing agent in salt and as an adjuvant in the production of dendritic crystals of salt (National Research Council, 1981). However, its use is limited to 13 ppm calculated as anhydrous sodium ferrocyanide.

Calcium, potassium, and sodium ferrocyanides, $Ca_2[Fe(CN)_6]$·$12H_2O$, $K_4[Fe(CN)_6]$, and $Na_4[Fe(CN)_6]$ have been considered as food additives for use as anticaking agents by the Joint FAO/WHO Expert Committee on Food Additives (1974). The Committee also estimated the acceptable daily intake to be 0-0.025 mg/kg body wt. However, no information concerning usage of ferrocyanide salts as anticaking agents with FDA sanction in the United States beyond the use of the decahydrate sodium salt has been brought to the attention of the Select Committee. The potassium salt has been used commercially to precipitate metal ions interfering with citric acid formation in molasses production (Clark et al., 1965). This technique involves the addition of an aqueous solution of the salt to the molasses mash,
providing 20 ppm potassium ferrocyanide in excess of the amount required to precipitate the metal ions. However, the Select Committee has no information on the current use of this technique in molasses production.

Ferrocyanide salts are also permitted for use in certain drugs and cosmetics. For example, ferric ammonium ferrocyanide, FeNH₄[Fe(CN)₆], is listed in the Code of Federal Regulations [21 CFR 73.1298] for use without certification as a color additive in externally applied drugs and cosmetics, including those intended for use near the eye (Food and Drug Administration, 1979a,b). Ferric ferrocyanide, Fe₄[Fe(CN)₆]₃, is listed as a color additive [21 CFR 73.1299] for use in drugs and cosmetics for external use only (Food and Drug Administration, 1978). Use as a color additive in these products also includes external use in the region of the eyes.
III. CONSUMER EXPOSURE DATA

The Select Committee has no data on actual consumption of residual soluble ferrocyanide salts left in wine after fining and filtration. However, sales of one product to the wine industry were estimated to average 20,000–25,000 lb/yr (Crantz, 1979). Assuming an average application rate of 4 lb/1,000 gal, then approximately 6,000,000 gal of wine would be treated annually. Thus, if 1 ppm ferrocyanide (the maximum allowable) were present, the total residual ferrocyanide in wine would be 23 kg each year. If the quantity of the second proprietary product used annually in wine is similar to that of the first, then the total daily/capita consumption of ferrocyanide derived from use of both products would be about 0.6 μg. The Select Committee believes that this estimate is misleading because only those persons who consume wine would consume residual ferrocyanide salts from fining agents. However, on the basis of the above figures, the average consumption of soluble ferrocyanide remaining in wine after fining is approximately 600 times less than that from consumption of the sodium decahydrate salt which is used as an anticaking agent.

This comparison is derived from the 1970 and 1977 surveys of the food industry conducted by a subcommittee of the National Research Council which provide information on the use of ferrocyanide salts in foods (Subcommittee on Review of the GRAS List--Phase II, 1972; Committee on GRAS List Survey--Phase III, 1979). The 1970 survey indicates use of ferrocyanide salts in three food categories: cheese, meat and meat products, and seasonings and flavorings. The Subcommittee on Review of the GRAS List--Phase II (1972) states that the functional use of ferrocyanide salts in products in each category was as an anticaking agent; however, the identity of the ferrocyanide salts is not specified. This functional use of these salts was confirmed in the 1977 survey (Committee on GRAS List Survey--Phase III, 1979); in addition, the 1979 report refers specifically to the use of sodium ferrocyanide decahydrate as an anticaking agent in baked goods, breakfast cereals, fats and oils, cheese, meat and meat products, as well as seasonings and flavorings.

Use of sodium ferrocyanide decahydrate by the food industry in 1976 was reported to be 60,000 lbs (27,273 kg) (Committee on GRAS List Survey--Phase III, 1979). On this basis, the per capita daily consumption of the soluble sodium ferrocyanide as a regulated food additive (anticaking agent) was 0.35 mg.

The 1977 survey provides no data on the calcium or potassium ferrocyanide salts; however, these are used as anticaking agents in other countries (Joint FAO/WHO Expert Committee on Food Additives, 1974). The Joint FAO/WHO Expert Committee set an acceptable daily intake for calcium, potassium, and sodium ferrocyanides at 0-0.025 mg/kg body wt. This range would result in a maximum daily intake of 1.75 mg for a 70 kg adult.
IV. BIOLOGICAL STUDIES

Absorption, metabolism, and excretion

Most of the information on ferrocyanide salts available to the Select Committee was derived from clearance studies. Intravenous administration of the soluble sodium salt was utilized experimentally in both animals and man as a method of assessing extracellular water space. Evidence for absorption and metabolism was derived from these studies of distribution and excretion.

The Joint FAO/WHO Expert Committee on Food Additives (1974) referred to an unpublished study in which rats (strain not identified) received a single oral dose of potassium ferrocyanide at 200 mg/kg body wt. Forty-seven percent of the administered dose was excreted unchanged in the feces and 3% was found in the urine. Fecal and urinary excretions were maximal from day 1 to day 3, declining thereafter. A Joint FAO/WHO Expert Committee on Food Additives (1974) report made no mention of other observations on absorption, metabolism, or toxicity in regard to these studies.

Gersh and Stieglitz (1934) utilized rabbits (not otherwise identified) weighing 1.6–2.2 kg to determine the route and mechanism of ferrocyanide ion elimination. They administered 10% solutions of ferrocyanide salts intravenously and, following sacrifice, monitored ferrocyanide presence in the kidney histologically. The salts and doses/kg body wt studied were anhydrous sodium ferrocyanide, 0.16 and 0.31 g; anhydrous calcium ferrocyanide, 0.14 and 0.28 g; and anhydrous magnesium ferrocyanide, 0.14 and 0.27 g. Only the magnesium salt caused cardiac and respiratory dysfunction, and both were transient. Regardless of the salt used or its concentration, excretion occurred via the glomeruli, especially those of the deep cortex near the medulla. Some precipitated ferrocyanide was seen in the terminal portion of the proximal tubules, more was present in the loops of Henle, and still greater amounts were evident in the collecting ducts. Ferrocyanide was not observed in tubule epithelial cells. However, when elimination of the ferrocyanide salts was complete, as evidenced by absence of ferrocyanide in the urine, some ferrocyanide granules were seen in the cytoplasm of the epithelial cells of the proximal convoluted tubules. Gersh and Stieglitz (1934) noted no toxic effects of the sodium or calcium salt and referred to "unsuccessful attempts to produce renal injuries specific to the tubule of the glomerulus."

Similar studies were performed by Van Slyke et al. (1935) using rabbits and dogs (number and breed not specified). The experiments on dogs with one extirpated kidney demonstrated that sodium ferrocyanide at an intravenous dose of 0.5 g/kg was excreted via the glomeruli without damage to the glomeruli or apparent adverse effects, as evidenced by the absence of hematuria, albuminuria, or cylindruria for several weeks after injection. The authors
observed that the erythrocytes were devoid of ferrocyanide, and based their calculations of clearance on colorimetric analyses of plasma and urine. Berliner et al. (1950) obtained essentially similar results in studies of eight 12–20 kg female dogs receiving intravenous infusions of a ferrocyanide (presumably the sodium salt) solution.

Calcagno et al. (1951) used inulin and sodium ferrocyanide to measure extracellular fluid space in six human infants with congenital nervous system defects. The infants were 9 d–14 mo of age. The investigators infused continuously a 0.1% sodium ferrocyanide solution intravenously for periods of 45 min at the rate of about 0.75–1.0 ml/min (estimated dosage 3.3–4.5 mg sodium ferrocyanide). They reported glomerular excretion without renal injury and no evidence of damage to the urinary system. Because of the relatively rapid equilibration time observed, Calcagno et al. (1951) suggested that tubular reabsorption of ferrocyanide probably followed glomerular filtration.

Miller and Winkler (1936) administered aqueous solutions containing up to 6.2 g sodium ferrocyanide to seven adult subjects. Single doses were injected intravenously; clearance was followed by blood and urinary analyses. They reported marked albuminuria, the presence of numerous granular casts, white cells, epithelial cells, and red blood cells in one male subject who received 1.4 g sodium ferrocyanide. Other subjects receiving doses of 1.9, 2.8, or 6.2 g exhibited the same urinary abnormalities to a lesser degree. Urinary changes were transient and absent after 2 wk. Subjects exhibited no systemic reactions during the clearance studies. Miller and Winkler (1936) concluded that doses of 20 mg/kg body wt sodium ferrocyanide were nephrotoxic and suggested the possibility that lower doses might be harmful, particularly in patients with renal insufficiency.

Kleeman et al. (1955) measured distribution and fate of intravenous injections of sodium ferrocyanide in anesthetized female mongrel dogs. Using doses of 1.0 g of the ferrocyanide ion in each of 7 dogs, they found that 94–98% of the dose was recovered in the urine within 24 h. Ferrocyanide could not be detected in erythrocytes, gastric juice, or feces, and at least 80% of the administered doses was excreted within 3 h after injection. In a second study with five of the seven dogs bilaterally nephrectomized and eight additional female dogs similarly prepared, the investigators observed that, while total extracellular ferrocyanide space was smaller in nephrectomized dogs, equilibrium of the ion in plasma was reached in approximately the same length of time as in the non-nephrectomized dogs. In further studies with [59Fe] ferrocyanide, Kleeman and Epstein (1956) administered doses of 30–50 mg intravenously to three bilaterally nephrectomized dogs and nine human subjects (four normal, five with renal and/or hepatic disease). No significant radioactivity was found in pooled samples of feces, saliva, or gastric juice of dogs or human subjects. In
the four normal subjects, 68-87% of the administered radioactivity was recovered in the urine in 24-48 h; decreased rates of clearance were shown in subjects with renal disease. Kleeman and Epstein (1956) also noted that the labeled ferrocyanide was bound to plasma albumins. For this reason, and because of the rapid rate of kidney excretion of ferrocyanide, they concluded that use of the ferrocyanide ion was unsuitable for measuring extracellular body water.

**Acute toxicity**

Fassett (1958) indicated that potassium ferrocyanide was "only slightly toxic" and reported the oral LD$_{50}$ in rats to be 1.6-3.2 g/kg body wt. Solutions of sodium ferrocyanide used in photographic bleaching, toning, and fixing, and subsequently discharged into natural waters, are reported to be toxic to fish at concentrations of 2 ppm and above (The Merck Index, 1976).

Human data are limited to cases of accidental poisoning. Nagaratnam et al. (1974) reported gastrointestinal abnormalities and hyperventilation in a 16-yr-old male after consumption of 14.8 ml of potassium ferrocyanide solution (actual concentration not reported). Premature ventricular beats, varied cardiac rate, and changes in blood electrolytes were noted; acute renal failure occurred in 48 h. Treatment with intravenous sodium thiosulfate, hydrocortisone, and penicillin, in addition to oxygen inhalation therapy and peritoneal dialysis, resulted in complete recovery within 24 d. Nagaratnam et al. (1974) noted that Piotrowski (1925) had reported a case of human poisoning and recovery following ingestion of 20 g of a paste containing potassium ferrocyanide, potassium hydroxide, and sulphocyanide.

**Short-term toxicity**

The Joint FAO/WHO Expert Committee on Food Additives (1974) indicated, on the basis of review of data available at that time, that calcium, potassium, and sodium ferrocyanide, at a level of 25 mg/kg body wt in the diet, would have no toxic effects on rats.

The Joint FAO/WHO Expert Committee also made reference to unpublished reports on feeding studies with rats (strain not identified) and beagle dogs. Groups of 10 male and 10 female rats were fed diets containing 0, 0.05, 0.5, and 5% sodium ferrocyanide (approximately 0, 25, 250, and 2500 mg/kg) for 13 wk. There was slight growth depression, as well as lowered hematocrit and hemoglobin levels at the 5% feeding level. After 13 wk, kidney weights of males and females fed the 5% diet and those of females fed the 0.5% diet increased. Weights of male adrenal and female pituitary
glands also increased in animals fed diets with 5% sodium ferrocyanide. Renal-tubule damage occurred in both sexes fed at the 0.5% and 5.0% levels; granular casts and calcified deposits were observed. These effects were more severe in animals fed the 5% diet than in those fed the diet with 0.5% sodium ferrocyanide, while no effects were noted in animals fed the diet with 0.05% sodium ferrocyanide.

Groups of four male and four female beagle dogs received diets containing 0, 10, 100, or 1000 ppm sodium ferrocyanide. The average intake was approximately 0, 0.26, 2.6, or 26 mg/kg body wt/d, respectively, for an undisclosed but apparently short length of time. Body weights, food consumption, urinalyses, hematology, and organ weights of animals in all four groups were similar. Histopathological examination was negative in all animals except one dog fed the 0.26 mg/kg dietary level, where chronic liver and renal inflammation were noted.

Long-term toxicity

The Select Committee is not aware of any published data on long-term feeding studies or chronic toxicity testing of ferrocyanide salts.

Special studies

Nishioka (1975) used the "rec-assay" procedure with Bacillus subtilis strains H17 and M45 to assess the mutagenic potential of a number of metal salts. The "rec-assay" procedure is based on differential growth sensitivity in normal (Rec-) and mutant cells deficient in DNA repair capacity (Rec+). No mutagenic activity was found in B. subtilis cells exposed to 0.5 M solutions of sodium ferrocyanide.

The Select Committee has no information on studies testing ferrocyanide salts for fetotoxicity, carcinogenicity, or teratogenicity.

Ferric ferrocyanide is recognized as the treatment of choice in cases of accidental or intentional ingestion of thallium-containing substances such as rodenticides (Dailey and Weissler, 1978; Stevens et al., 1974). For example, Barckow and Jenss (1976) administered orally 3 g/d potassium ferric ferrocyanide to one adult with thallium intoxication. Stevens et al. (1974) gave ferric ferrocyanide orally, or by duodenal intubation in four doses which totaled 250 mg/kg body wt, to 11 patients who had ingested thallium accidentally or intentionally. Both groups of investigators indicated no side effects from oral administration of the ferrocyanide salts in these clinical efforts to treat thalliumosis. Stevens et al. (1974) concluded that ferric ferrocyanide was the "first effective and harmless antidote" in the treatment
of thallotoxicosis. Potassium ferrocyanide (0.3-1.3 g doses) is used as an antidote for ingestion of toxic quantities of copper (Wheater, 1979).

Similarly, a number of studies have shown that ingestion of ferric ferrocyanide in feed or tap water enhances excretion of 137Cs (Dailey and Weissler, 1978). The ferrocyanide salt binds cesium in the gastrointestinal tract, thus preventing reabsorption of the cesium ion.
V. OPINION

Food uses of ferrocyanide salts in the United States include the regulated food additive sodium ferrocyanide decahydrate as an anticaking agent in salt with a limit of 13 ppm as the anhydrous salt, and the prior-sanctioned use of two proprietary products containing mixtures of ferrocyanide salts as fining agents in wine production. The proprietary products are prior sanctioned with the stipulation that no insoluble or soluble residue in excess of 1 ppm remain in the finished wine and that the fining treatment not alter "the basic character" of the wine. These two products are mixtures of diferrous ferrocyanide, dipotassium ferrous ferrocyanide, and potassium ferrocyanide. The first two substances are insoluble, while the third reacts with iron and copper to form insoluble complexes. The calculated daily/capita consumption of ferrocyanide derived from use of fining agents in wine production is less than 0.6 µg.

Relevant information on the biological properties of ferrocyanide salts available to the Select Committee was limited. Data on acute toxicity include the rat LD$_{50}$ (1.6-3.2 g/kg body wt), and clinical reports of accidental poisoning of two adults by unknown amounts of potassium ferrocyanide. Most short-term studies have been related to use of sodium ferrocyanide in measuring extracellular body water space. Two short-term feeding trials with rats and dogs have been reported. One short-term study on glomerular filtration of ferrocyanide salts by adult rabbits suggested that the magnesium salt in large amounts induces transient cardiac and respiratory dysfunction. However, all investigations on absorption and excretion of the calcium, potassium, and sodium salts administered intravenously indicate that these ferrocyanides are metabolized and partially excreted unchanged in the feces and urine. Where renal effects were observed, they were transient and dose levels employed in these studies were several orders of magnitude higher than those encountered by persons who might consume soluble ferrocyanide salts from the residual ferrocyanides remaining in wine after fining.

No long-term feeding studies were available. Special studies were limited to tests for mutagenicity of the sodium salt and the use of ferric ferrocyanide salts as an antidote in thalloomnosis. The Select Committee found no reports of studies of fetotoxicity, carcinogenicity, or teratogenicity of the several ferrocyanide salts discussed in this report.
In the light of these considerations, the Select Committee concludes that:

There is no evidence in the available information that demonstrates, or suggests reasonable grounds to suspect, a hazard when a mixture of diferrous, dipotassium ferrous, and potassium ferrocyanides is used in wine production as a fining agent in the manner now practiced or that might reasonably be expected in the future.
VI. REFERENCES CITED


Food and Drug Administration. 1979b. Listing of color additives exempt from certification; ferric ammonium ferrocyanide; confirmation of effective date. Fed. Regist. 44:52189.

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