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December 8, 1971

Hearing Clerk
Department of Health, Education, and Welfare
Room 6-28
5600 Fishers Lane
Rockville, Maryland 20852

Dear Sir:

Buckman Laboratories, Inc., has noted the comments of the Commissioner of the Food and Drug Administration in the *Federal Register* notice of November 2, 1972, on pages 20985-20986, and is surprised that paints containing water-soluble barium are included in the proposed regulation in section 191.5(a)(2)(iii). This proposed regulation pertains to the toxic metals lead, antimony, arsenic, cadmium, mercury, and selenium which are considerably more hazardous than barium. To our knowledge, there have been no reported instances of toxic effects to children or other persons related to the ingestion of paint films containing barium compounds.

The toxicity of compounds of barium, copper, mercury, selenium, cadmium, antimony, arsenic, and lead has been investigated by Dr. A. J. Lehman of the Food and Drug Administration. A copy of Dr. Lehman's paper is included as appendix A. This paper shows that barium chloride fed to rats for 104 weeks at dietary concentrations of 2,000 parts per million did not produce any gross effect or tissue damage. The lowest level of barium chloride that was actually observed to produce gross effects or tissue damage was 10,000 parts per million or one percent of barium chloride in the diet. In contrast, copper chloride, mercuric acetate, phenylmercuric acetate, selenium, cadmium chloride, and antimony trioxide produced gross toxic effects at from one-half (antimony trioxide) to one-two hundredth (mercuric acetate and phenylmercuric acetate) of the concentration of barium chloride. The differences are even more pronounced when one compares the amounts required to produce tissue damage.

The administration of barium chloride to dogs for 56 weeks at the rate of 20 mg. per kg. of body weight produced no gross evidence of injury. In comparison, 0.33 mg. per kg. of lead acetate killed the dogs in 33 weeks. This work by Lehman, in the Food and Drug Administration's own laboratories, shows definitely that the water-soluble barium chloride has a low level of chronic toxicity.

An examination of the toxicology literature further confirms that the acute toxicities of water-soluble barium compounds are considerably less than those of lead, antimony, arsenic,

cadmium, mercury, and selemium compounds. The most striking and the most important difference between barium and the toxic metals listed in section 191.5 is that barium is not a cumulative poison. It does not accumulate in the bone, muscle, kidney, or other tissue. It is actually excreted more rapidly than calcium. Antimony, arsenic, lead, cadmium, mercury, and selenium do accumulate in the body. These metals cause toxic effects when ingested in small quantities over long periods of time. The hazards caused by this cumulative effect are well known. The indicated metals thus are serious contaminants in the environment, and there has been increasing worldwide concern about them, particularly during the past few years.

The metals which have cumulative toxic effects are the only ones which have ever been found to be hazardous in paint films. A child does not consume large quantities of paint film during a 24-hour period. Toxic effects from lead and arsenic in paint films have historically been related to the repeated ingestion of small quantities of paint films over weeks or even months. If the ingestion of large quantities of paint film were a problem, the Food and Drug Administration would have to include in section 191.5 a number of other metals in addition to water-soluble barium. These would include zinc, copper, cobalt, chromium, and molybdenum. In addition, the use of such organic compounds as sodium tetrachlorophenate and sodium pentachlorophenate and possibly other new microbicides currently being developed for the paint industry should also be included in the proposed section 191.5.

Zinc oxide is a widely used paint pigment. Although zinc oxide is not appreciably water soluble, it is soluble in dilute mineral acid such as that present in the stomach. One widely used reference book on clinical toxicology (*2*) (see attached Reference List) states as follows for zinc oxide: "The usually U.S.P. grade has high purity, but some technical grades contain a few tenths of 1% lead. No estimates of acute oral toxicity were located, and it is assumed that no human fatalities have resulted from ingestion of the pure oxide. Because it is soluble in dilute mineral acid (presumably including gastric juice), it probably shares to a limited extent the toxic actions of water-soluble 'zinc salts' (see latter)." Under Zinc Salts, Soluble, e.g., Chloride, sulfate, acetate, the same reference (*2*) states: "Although no longer recommended, the sulfate has been used as an emetic drug (adult dose 0.5-1.0 gm.). Toxicity and toxic actions are like those of copper salts. Produces irritation or corrosion of the alimentary tract with pain, emesis, etc. The chloride appears to be more corrosive and more toxic than the sulfate. A few grams of the chloride has killed an adult, while recovery has been reported after ingestion of 90 gm. Delayed deaths have been ascribed to inanition following severe strictures of the esophagus and pylorus."

A British reference book (*1*) has a comment on zinc and carcinogenesis: "It has been suggested that malignant tumors contain high concentrations of zinc and that liver tissue, when invaded by metastases, shows an increased zinc content of the uninvolved areas but low amounts of zinc in the tumor itself and that similar changes of the metal pattern are seen in many varieties of the carcinogenic process. Some of this information is contradictory and the findings need much further confirmation and investigation before a specific role of zinc in carcinogenesis can be postulated."

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The publication Water Quality Criteria (*3*) summarizes the chemical constituents in the drinking water standards of the World Health Organization and the U.S. Public Health Service in tabular form. A copy of this table is included as appendix B. It should be noted that the World Health Organization does not even establish maximum levels for barium but does set up standards for arsenic, cadmium, lead, and selenium.

The maximum allowable concentrations in drinking water as established by the U.S. Public Health Service are as follows:

Arsenic	0.05 mg. per liter
Barium	1.0 mg. per liter
Cadmium	0.01 mg. per liter
Lead	0.05 mg. per liter
Selenium	0.01 mg. per liter

The amount of mercury now established as the maximum allowable concentration in water by the Environmental Protection Agency is 0.005 mg. per liter. Barium is allowable at 20 times the concentration of arsenic and lead, 100 times the concentration of cadmium and selenium, and 200 times the concentration of mercury.

Proposed regulation 191.5 would allow the unrestricted use of lead at concentrations of 0.5 percent of the dried paint film even though lead is a cumulative poison and has caused deaths or toxic symptoms in children who have eaten paint films containing lead. On a comparable basis, water-soluble barium should then be allowed in paints at concentrations up to 10 percent of barium based on the dried paint film since the U.S. Public Health Service has established a maximum level in drinking water at 20 times the level of lead. As mentioned earlier, the World Health Organization does not even establish maximum levels for barium.

Mercury will be allowed at 0.05 percent of dried paint film. Using the same reasoning as above, a 200-fold increase in the tolerance for barium would be 10 percent based on the dried film.

In this assembly, we have presented evidence that the presence of water-soluble barium compounds in paint films does not make the paint film hazardous to children. Water-soluble barium compounds have never been implicated in cases of poisoning to children who have ingested paint films. Barium is not a cumulative poison such as the other metals included in the proposed regulation. Barium compounds possess the same order of magnitude of toxicity as zinc, which is a widely used metal in paints. Drinking water standards for barium as established by the U.S. Public Health Service also reflect that barium is much less toxic than lead, mercury, arsenic, cadmium, and selenium.

Among the metals listed in the proposed regulation, lead, arsenic, antimony, cadmium, mercury, and selenium are cumulative poisons and should be included as a group. In

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comparison, barium is not a cumulative poison and should be considered along with such metals as zinc and copper, which are not included in the proposed regulation.

In view of the information presented in this assembly, Buckman Laboratories, Inc., requests that the reference to water-soluble barium compounds be deleted from the proposed regulation in section 191.5(a)(2)(iii).

Sincerely yours,

BUCKMAN LABORATORIES, INC.

J. D. Pera

Vice President—Research & Development

J. D. Pera
FJC
Attachments

LITERATURE CITED

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2. Gleason, M. N., Gosselin, R. E., and Hodge, H. C.
   1957. Clinical Toxicology of Commercial Products, p. 103, Williams & Wilkins Co., Baltimore

3. McKee, J. E., and Wolf, H. W.
   1963. Water Quality Criteria, 2nd, ed., p. 91, California State Water Quality Control Board, Sacramento