EVALUATION OF THE HEALTH ASPECTS OF SULFAMIC ACID AS IT MAY MIGRATE TO FOODS FROM PACKAGING MATERIALS

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Prepared for

Bureau of Foods
Food and Drug Administration
Department of Health, Education, and Welfare
Washington, D.C.

Contract No. FDA 223-75-2004
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Life Sciences Research Office
Federation of American Societies for Experimental Biology
9650 Rockville Pike
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NOTICE

This report is one of a series concerning the health aspects of using the Generally Recognized as Safe (GRAS) or prior sanctioned food substances as food ingredients, being made by the Federation of American Societies for Experimental Biology (FASEB) under contract no. 223-75-2004 with the Food and Drug Administration (FDA), U.S. Department of Health, Education, and Welfare. The Federation recognizes that the safety of GRAS substances is of national significance, and that its resources are particularly suited to marshalling 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 Hearing Clerk, 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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Life Sciences Research Office
FASEB
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I. INTRODUCTION

This report concerns the health aspects of using sulfamic acid as an ingredient of food packaging materials. It has been based partly on the information contained in a scientific literature review (monograph) furnished by FDA (1), which summarizes the world's scientific literature from 1920 through 1973.* To assure 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 April 22, 1976 (41 FR 16848 and 16849) 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 sulfamic acid as an ingredient of food packaging materials. The Select Committee received no requests for such a hearing on sulfamic acid.

As indicated in the Food, Drug, and Cosmetic Act [21 USC 321 (s)], GRAS substances are exempt from the premarking clearance that is required for food additives. It is stated in the Code of Federal Regulations 21 CFR 121.1, revised April 1, 1975, 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. This section of the Code also indicates 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 121.3) that it is impossible to provide assurance that any substance is absolutely safe for human consumption.

The Select Committee on GRAS Substances of LSRO is making its evaluations of these substances in full recognition of the foregoing provisions. In reaching its conclusions on safety the Select Committee, in accordance

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*The document (PB- 228 552/6) is available from the National Technical Information Service, U.S. Department of Commerce, P.O. Box 1553, Springfield, Virginia 22161

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with FDA's guidelines, is relying primarily on the absence of substantive
evidence of, or reasonable grounds to suspect, a significant risk to the
public health. While the Select Committee realizes that a conclusion
based on such reasoned judgment is expected even in instances where the
available information is qualitatively or quantitatively limited, it recognizes
that there can be instances where, in the judgment of the Select Committee,
there are insufficient data upon which to base a conclusion. The Select
Committee, aware that biological testing is dynamic, bases its conclusions
on information now available; it cannot anticipate the results of experiments
not yet conducted or those of tests that may be reconducted, using new
technologies. These conclusions will need to be reviewed as new or better
information becomes available.

In this context, the LSRO Select Committee on GRAS Substances has
reviewed the available information on sulfamic acid and submits its inter-
pretation and assessment in this report, which is intended for the use
of FDA in determining the future status of this substance under the Federal

II. BACKGROUND INFORMATION

Sulfamic acid, \( \text{NH}_2\text{SO}_3\text{H} \), is the monoamide of sulfuric acid. It is
prepared by a commercial process utilizing urea, sulfur trioxide, and sul-
furic acid (2). Sulfamic acid is not found in nature. It occurs as dry, stable,
orthorhombic crystals, melting at \( 200^\circ \text{C} \). It is stable when dry, but in solu-
tion, it slowly hydrolyzes to form ammonium bisulfite. It is soluble in water
to the extent of 14.68 g per \( 100 \text{ ml} \) of water at \( 0^\circ \text{C} \), and 47.08 g per \( 100 \text{ ml} \) of
water at \( 60^\circ \text{C} \). The acid is highly ionized, the pH of a 1 percent solution being
1.18. The principal commercial salt, used as a herbicide, is ammonium
sulfamate. It is a stable compound, melts at \( 125^\circ \text{C} \), and is highly soluble in
water (3).

The acid and its salts are available in commercial grades, but no
manufacturer has been found who lists a food grade product. The acid and its
salts are not listed in the Food Chemicals Codex (4). Sulfamic acid is not used
as a direct GRAS food additive but is authorized as an ingredient of paper and
paperboard products used in food packaging (5) from which it may migrate to
food. The Select Committee has not been able to find any information concern-
ing the amount of sulfamic acid that exists in the paper or paperboard products
used in food packaging or whether it is now used in the manufacture of such
products.

Sulfamic acid is widely used in industry for such purposes as acid
cleaning, electroplating, and bleaching. Of possible significance to human
consumers are its uses as a cleaner in processing plants of the dairy, poultry, meat, sugar, vegetable, and brewing industries (2, 6, 7) and as a component of mixtures used for corrosion inhibition in water supply systems (8, 9). The use of sulfamic acid for these purposes is not being evaluated in this report.

III. CONSUMER EXPOSURE DATA

The report of a National Research Council Subcommittee on the use of GRAS Substances in foods (10) contains no data on possible intakes of sulfamic acid and no information is included in the Handbook of Food Additives (11). United States production or disappearance figures for sulfamic acid are not available. Approximate amounts of sulfamic acid imported in recent years in millions of pounds were: 9.2 in 1970; 5.4 in 1971; and 5.2 in 1972 (12). Although the use of sulfamic acid or its ammonium salt for cleaning equipment in food processing plants, in the brewing and sugar industries, in water supply systems, and as a herbicide (ammonium salt) could lead to human exposure to small amounts of sulfamate ion, this report is concerned only with the use of sulfamic acid as a GRAS substance that might migrate into foods from paper and paperboard packaging materials. The Select Committee is of the opinion that the amount of sulfamic acid which enters the human food supply from the latter source is minute, but there are no data available from which an estimate of the actual amount can be made. One somewhat relevant series of experiments has been found which indicates that only small amounts of paper packaging ingredients are likely to migrate to food. Davison et al. (13) studied the migration of rosin components from sized paper to foods and concluded that foods stored up to several weeks in such packaging materials contain on the average, no more than 9 ppm of rosin.

IV. BIOLOGICAL STUDIES

Acute toxicity

Two of a group of ten rats given oral doses of a 4 percent solution of sulfamic acid at levels of 1.6 g sulfamic acid per kilogram of body weight died in 12 to 20 hours; in similar tests eight of a group of eight rats survived without toxic signs as much as 1.6 g per kilogram of orally administered ammonium sulfamate given in a 4 percent solution (14). It has been noted that Spencer (15) indicated the oral LD₅₀ of sulfamic acid in rats to be 1.6 mg per kg. The author believes that this figure is in error and that it should have been 1.6 g per kg. \(\triangledown\)

\(\triangledown\) Telephone conversation with the author.
The acute oral LD₅₀ of ammonium sulfamate in rats is reported as 3.9 g per kg (16) and 1.6 g to 4.4 g per kg (17).

Based on a rating of sulfamic acid and its salts as moderately toxic substances, the lethal oral dose of sulfamic acid in man is probably between 0.5 and 5.0 g per kg body weight and may be as much as 5 to 15 g per kg body weight for technical grade ammonium sulfamate (18). The Environmental Protection Agency has established a tolerance of 5 ppm for ammonium sulfamate on apples and pears (19) and has recently announced (20) that ammonium sulfamate is one of the substances for which they are seeking additional toxicological data for purposes of re-registration of this herbicide.

**Short-term studies**

Sulfamic acid or ammonium sulfamate in the diet of rats for 15 weeks retarded growth at the 2 percent level but not at 1 percent (estimated intakes varied between 0.5 and 1.0 g per kg per day for the 1 percent level and 1.5 and 2.5 g per kg per day for the 2 percent level) (14). Neither substance was toxic to dogs in oral doses of 100 mg per kg daily over a period of 6 days (21). When fed to cattle at a concentration of one percent in silage, sulfamic acid induced severe diarrhea, but no effect was noted at 0.5 percent of the diet (doses estimated to be 150 mg per kg per day and 75 mg per kg per day, respectively) (22). Sulfamic acid was irritating to human skin when applied as a 4 percent solution (14). The effect was probably due to the high acidity of the solution since ammonium sulfamate does not have the same effect. The dosages used in these studies and in the acute toxicity studies noted above far exceeded the possible levels of human ingestion that might result from the migration of sulfamic acid from paper and paperboard packaging materials.

**Biochemical studies**

Sulfamate ion from sulfamic acid or ammonium sulfamate fed orally to dogs (1 g daily for 6 days) gave no systemic toxic effects, was not metabolized, and was excreted unchanged in the urine (21). Sulfamic acid exerts moderate germicidal activity against gram-negative bacteria and less activity against gram-positive forms (23).

**Long-term and special studies**

No long-term toxicity studies or studies of possible carcinogenicity, mutagenicity, or teratogenicity of sulfamic acid were available to the Select Committee.
V. OPINION

It seems most unlikely that more than minute amounts of sulfamic acid might occasionally enter foods by migration or abrasion from packaging materials. The acute toxicity of sulfamic acid is relatively low; it does not appear to be metabolized but is excreted unchanged in the urine.

The Select Committee has weighed the foregoing and concludes that:

There is no evidence in the available information on sulfamic acid that demonstrates, or suggests reasonable grounds to suspect, a hazard to the public when it is used in food packaging materials as now practiced or as it might be expected to be used for such purposes in the future.
VI. REFERENCES CITED


VII. SCIENTISTS CONTRIBUTING TO THIS REPORT

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Report submitted by:

July 14, 1976
Date

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Select Committee on GRAS Substances