

summary of information, data and arguments in support of their pesticide petition. This summary was prepared by Siemer and Associates, Inc., and EPA has not fully evaluated the merits of the petition. EPA edited the summary to clarify that the conclusions and arguments were the petitioner's and not necessarily EPA's and to remove certain extraneous material.

On August 30, 1996 Siemer and Associates on behalf of National Chelating petitioned EPA, under pesticide petition 6F4789, for a permanent exemption from the requirements of a tolerance for ammonium thiosulfate on apples.

Section 408(b)(2)(A) of the amended Federal Food, Drug, and Cosmetic Act allows the EPA to establish an exemption from the requirements for a tolerance only if the Administrator determines that there is a "reasonable certainty that no harm will result from the aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information."

The available information indicates that there is a reasonable certainty that no harm will result from various types of exposure. Requests for waivers from the requirements of performing studies for known chemistry are presented and substantiated. The following is a summary of the information submitted to EPA, to support the establishment, under Section 408(b)(2)(D) of the amended FFDCA, of a tolerance for ammonium thiosulfate on apples.

A. Residue Chemistry

1. *Plant metabolism.* The qualitative nature of the residues of ammonium thiosulfate in apple is adequately understood. The requirement for residue studies was waived by EPA based on the knowledge that ammonium thiosulfate has been used as a soil applied and foliar applied fertilizer for many years. Prior experience and numerous publications teach that ammonium thiosulfate ionizes when placed into water, forming an ammonium ion and a thiosulfate ion which further degrades to form elemental sulfur and a sulfate ion. The sulfur is further oxidized to form a sulfate ion. The ammonium and sulfate ions thus formed are absorbed into the growing plant and moved into the naturally occurring nitrogen and sulfate pools that occur naturally in growing plants. Once applied to the plant, without isotope identification, it is not possible to separate the ammonium and sulfate ions that will occur from those that already occur naturally in the plant. On this basis, an

exemption from the requirements of a tolerance is justified. There is no analytical method needed since there is no practical way to separate the ammonium and sulfate ions from those that naturally occur.

2. *Analytical method.* The need for an analytical method is waived on the basis that there is no need for analyzing for the component of ammonium and sulfate ion applied for blossom thinning purposes.

3. *Magnitude of residues.* No residues of ammonium thiosulfate will be identified separately from those ammonium and sulfate ions naturally occurring. This result supports the proposed exemption from the requirements for a tolerance.

B. Toxicological Profile

A request to waive the battery of mammalian toxicity studies for ammonium thiosulfate is based on and justified by the following:

1. *Acute toxicity.* Based on EPA criteria, ammonium thiosulfate previously registered for a non-food use as an ornamental herbicide has been shown to be relatively non-toxic and has been registered for non-food use purposes as a Category III herbicide. These data have previously been supplied to the agency.

2. *Genotoxicity.* A request for a waiver from the following requirements is made on the basis that sodium thiosulfate is on the Food and Drug Administration's Generally Recognized as Safe (GRAS) list at 21 CFR 184.1807, and ammonium thiosulfate is already exempted from the requirements of a tolerance when used in accordance with good agricultural practices as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest (at 40 CFR 180.1001(c)). Ammonium thiosulfate ionizes to form ammonium ion and thiosulfate ion in water with neither of these ions being mutagenic or genotoxic. On that basis the following tests are requested to be waived.

- i. Gene Mutation - Ames.
- ii. *In vitro* Structural chromosomal aberration assay.
- iii. *In vitro* CHO/HGPRT assay.
- iv. *In vivo* micronucleus aberration assay.

3. *Reproductive and developmental toxicity.* A request for waiving the data requirements for the following is made on the basis of the discussion in paragraph B. above. In addition, all of the tests listed below rely on feeding the test substance, to animals that have acidic stomachs. Placing ammonium thiosulfate into an acidic environment

will cause near instantaneous ion formation giving rise to ammonium and thiosulfate ions, which ultimately breaks down to elemental sulfur and sulfite. These sulfur forms will be quickly oxidized under acidic conditions to sulfate, which will be incorporated into the normal sulfate pool that exists within the metabolic system of the various animal test systems. The ammonium ion will react with the acidic component, most likely forming ammonium chloride which will be metabolized in a well understood pathway in the systems of the various animal test systems. The new moiety formed in this acidic medium is the sulfite ion which also is well understood and is quickly oxidized to sulfate. The FDA instituted studies in 1975 and 1985 on the GRAS status of sulfite and, as a result of these studies, has substantiated the GRAS status except for a few individuals that might be allergic to sulfite. In this proposed usage, however, the sulfite will not reach the possibly allergic people, since the sulfite will be metabolized to sulfate in the plant system before reaching any sensitive people who may consume the treated tissue. The data waivers requested are as follows:

- i. Teratology in rats.
- ii. Teratology in rabbits.
- iii. 2-Generation reproduction in rats.

4. *Subchronic toxicity.* The data requirements listed below are requested to be waived on the basis illustrated above at paragraph B. 3.

- i. 28-Day dermal in rats.
- ii. 13-Week oral feeding in rats.
- iii. 90-Day oral feeding in dogs.

5. *Chronic toxicity.* The data requirements listed below are requested to be waived for reasons listed above at paragraph B. 3.

- i. 1-Year chronic toxicity in dogs.
- ii. 18-month chronic toxicity and carcinogenicity in mice.
- iii. 24-month chronic toxicity and carcinogenicity in rats.

6. *Animal metabolism.* The metabolism of ammonium thiosulfate is well understood in animals. As listed above, this substance rapidly ionizes in the acidic portion of the animal gut, giving rise to ammonium ion and sulfate ion. Both of these substances are required and occur in the metabolism of animals.

7. *Metabolite toxicology.* No toxicologically significant metabolites will be detected in plant or animal metabolism studies using ammonium thiosulfate. Therefore, no metabolites are required to be regulated.

8. *Endocrine effects.* There is no information available that suggest that