Reregistration Eligibility Decision – Inorganic Sulfites

May 2007

Reregistration Eligibility Decision

Inorganic Sulfites

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Introduction

The Environmental Protection Agency (EPA) has completed its Reregistration Eligibility Decision (RED) for the inorganic sulfites case, which includes the chemicals sulfur dioxide and sodium metabisulfite. This assessment provides information to support the issuance of a Reregistration Eligibility Decision for inorganic sulfites. EPA's pesticide reregistration process provides for the review of older pesticides (those initially registered prior to November 1984) under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) to ensure that they meet current scientific and regulatory standards.

In this document, EPA presents the results of its review of the potential human health effects of dietary, drinking water and occupational/bystander exposure to inorganic sulfites, as well as its ecological risk findings. Evaluations performed by the World Health Organization (WHO), the International Agency for Research on Cancer (IARC), and the Agency for Toxic Substances and Disease Registry (ATSDR) were relied upon for this assessment, in addition to peer-reviewed evaluations performed by the Cosmetic Ingredient Review (CIR), the Organization for Economic Cooperation and Development-Screening Information Data Set (OECD-SIDS) and from other open literature sources. Based on this assessment, the Agency has determined that products containing sulfur dioxide or sodium metabisulfite are eligible for reregistration provided the necessary label changes are made. As a result of this assessment, one tolerance has been reassessed.

I. Use Information

The inorganic sulfites reregistration case includes the chemicals sulfur dioxide (CAS No. 7446-09-5) and sodium metabisulfite (CAS No. 7681-57-4). As active ingredients, these chemicals are fungicides typically used to treat for *Botrytis cinerea*, the fungus which causes bunch rot, or gray mold disease on grapes. The sulfur dioxide products are formulated as a compressed liquid that converts to a gas upon release. These products are used in cold-storage warehouses, trucks, vans and train cars for post-harvest grape fumigation. In addition to the fungicidal use against *Botrytis cinerea*, sulfur dioxide is also used in combination with carbon dioxide to treat for black widow spider on grapes in warehouse settings. The black widow spider treatment is not included on any sulfur dioxide product labels, as this use is permitted solely under a FIFRA 24(c) carbon dioxide registration (CA920007). The sodium metabisulfite products are composed of the anhydrous, solid active ingredient contained in semi-sealed pads which are added to containers holding grapes prior to shipping. The pads absorb moisture generated by grapes, and release low levels of sulfur dioxide in the range of 1-5 ppm.

End-use inorganic sulfite products contain sulfur dioxide at 99.9 to 100%, and sodium metabisulfite at 37.5 to 98.5%. The Agency currently has six of the ten sodium metabisulfite products designated as containing sodium bisulfite (078201) as the active ingredient. As of the publication of this RED, the Agency will transfer these registrations to the sodium metabisulfite designation (111409). The tolerance being reassessed in this document, with the respective citation in the Code of Federal Regulations (CFR), and the use pattern as an active ingredient is

listed in Table 1.

Table 1. Tolerance Being Reassessed for Inorganic Sulfites					
Tolerance Expression	CAS No.	40 CFR	PC Code	Limit	Use Pattern
Active Ingredient					
Sulfur dioxide (as sulfite residues)	7446-09-5	§180.444	77601	10 ppm	grape, postharvest/used as fungicide and preservative
Sodium metabisulfite (as sulfite residues)	7681-57-4	§180.444	111409	10 ppm	grape, postharvest/used as fungicide and preservative

Both sulfur dioxide (21CFR §182.3862) and sodium metabisulfite (21CFR §182.3766) are listed as GRAS (Generally Recognized as Safe) by the FDA (Food and Drug Administration) as preservatives in certain foods[1]. Sodium metabisulfite is also used up to a concentration of 1% as an antioxidant in hair care products and as a reducing agent in cosmetic formulations (CIR 2003). Sources of sulfur dioxide include the combustion of fossil fuels, smelting of sulfide ores, volcanic emissions, and other natural sources. Sulfur dioxide is also used to manufacture hydro-sulfites, to bleach wood pulp and paper, to process, disinfect, and bleach food, for waste and water treatment, in metal and ore refining, and in oil refining (ATSDR-MMG 2004).

II. Physical/Chemical Properties

The physical and chemical properties of the inorganic sulfites are provided in Table 2.

Table 2. Physical/Chemical Properties of Inorganic Sulfites				
	Sulfur Dioxide	References	Sodium Metabisulfite	References
Molecular weight	64.06	ATSDR, 1998a (*NIOSH, 1994)	190.109	HSDB, 2005
Color/Form	colorless		white crystals or powder	
Odor	strong odor; suffocating		slight odor of sulfur dioxide	
Melting point	-72.7°C		150° C	
Boiling point	-10° C		Decomposes	OECD, 2001
Density	2.927 g/L (gas) 1.434 g/L (liquid)		1.4	HSDB, 2005
	~~22.8 g/100~~ mL (water at 0° C)		54,000 mg/L water @ 20° C	
	8.5 mL /100 mL (water at 25°		81.7 g/100 mL water @	

[1]Sodium metabisulfite and sulfur dioxide are GRAS when used in accordance with good manufacturing practice, except that it is not used in meats; in food recognized as a source of vitamin B1; on fruits or vegetables intended to be served raw to consumers or sold raw to consumers; or to be presented to consumers as fresh.

Table 2. Physical/Chemical Properties of Inorganic Sulfites				
	Sulfur Dioxide	References	Sodium Metabisulfite	References
Solubilities	C)* 11.3 g/100 mL (water at 20° C) 0.58 g/100 mL (water at 90° C)		100° C	
Vapor Pressure	3000 mm Hg at 20° C		Not available	
Relative vapor density	2.25 (air = 1)	NIOSH, 1994		
Relative density	1.4 at -10° C (water = 1)			
Specific gravity	2.26	MSDS, 1996		

III. Hazard Assessment

A. Acute Toxicity

Sufficient toxicity information is available for both sulfur dioxide and sodium metabisulfite from publicly available sources.

Sodium Metabisulfite

Table 3. Acute Toxicity Data for Sodium Metabisulfite				
Study Type	Species	Lethal Dose (LD_{50}) or Lethal Concentration (LC_{50})	Toxicity Category[1]	Reference
Acute Oral	rat	LD_{50} = 1540 mg/kg, death observed ≥1250 mg/kg LD_{50} = 1131 mg/kg	III	TOXNET, 2005 OECD, 2001
Acute Dermal	rat	LD_{50} > 2000 mg/kg	III	TOXNET, 2005
Acute Inhalation	Not Available			
Dermal Sensitization	guinea pig	Non-sensitizer	----	OECD, 2001
Skin and Eye Irritation	rabbit	Not irritating to the skin; Irritating to the eyes	Not provided	OECD, 2001

[1] The toxicity category ratings were not provided by OECD.

At high oral doses (> 1% or 10,000 ppm in the diet), effects seen in rats were local irritation, including inflammatory changes and hyperplasia in the stomach (WHO, 1999). Although dermal toxicity studies performed with sodium metabisulfite in laboratory animals have not been submitted to the Agency, a report by the Cosmetic Ingredient Review Committee (CIR, 2003) indicates that dermal penetration is unlikely due to the highly charged nature of sulfites. Cosmetic products containing sodium metabisulfite range from shampoos and hair coloring products, to eye and skin lotions, and makeup foundations. Sodium metabisulfite was not

sensitizing in the standard skin sensitization test in the guinea pig.

Sulfur Dioxide:

Table 4. Acute Toxicity Data for Sulfur Dioxide

Study Type	Species	Lethal Dose (LD_{50}) or Lethal Concentration (LC_{50}) Results	Toxicity Category[1]	Reference
Acute Oral	Not Available			
Acute Dermal	Not Available			
Acute Inhalation	guinea pig	Lowest published LC: 1039 ppm/24 hr (2.7 mg/L/24 hr)	IV	NIOSH, 2004
	guinea pig	LC_{50} = 1000 ppm/20 hr; 130 ppm/154 hr =2620 mg/m^3/20hr or 2.6 mg/L	IV	HSDB, 2005
	mouse	LC_{50}: 3000ppm/30 min (7.9 mg/L/30min)	IV	NIOSH, 2004
	mouse	LC_{50} = 150 ppm/847 hr; 1000 ppm/4 hr (2.6 mg/L)	IV	HSDB, 2005
	rat	Lethal concentration (LC_{50}): 2520 ppm/1 hr or 1.65 mg/L; 2168 mg/m^3; 20 mg/m^3/5 hr; 30 mg/m^3	III	NIOSH, 2004
Dermal sensitization	Not Available			

[1] The toxicity category ratings were not provided by NIOSH.

B. Reproduction/Developmental Toxicity/Endocrine Disruption:

No evidence of reproductive toxicity was observed in rats exposed orally to 942 mg/kg bw/day of sodium metabisulfite (2% in the diet) in a diet supplemented with thiamine (OECD 2001). Developmental studies reported by the CIR 2003 indicate sodium metabisulfite produced no adverse findings, either maternal or fetal, in mice up to 160 mg/kg in a water solution, in rats up to 110 mg/kg in the diet, in hamsters up to 120 mg/kg in the diet, or in rabbits up to 123 mg/kg in the diet. These results are supported by developmental information reported by WHO (1999) in which no effects were observed on implantation, or on maternal or fetal survival in sodium metabisulfite doses of up to 150, 110 and 120 mg/kg bw in mice, rats, and hamsters, respectively (WHO Series 18). Reproductive effects were not observed in rats exposed to 5-30 ppm sulfur dioxide for a period from 9 days prior to mating until 12-14 days of pregnancy; or in mice exposed to 25 ppm sulfur dioxide 7 hours/day on gestation days 6-15; or in rabbits exposed to 70 ppm sulfur dioxide 7 hours/day on gestation days 6-18 (ATSDR, 1998a).

C. Carcinogenicity:

Sulfur dioxide and sodium metabisulfite are currently not classifiable (Group 3) as to their carcinogenicity to humans (IARC 1992). As for laboratory animals, there was limited evidence for the carcinogenicity to sulfur dioxide, based on inhalation studies reviewed by the IARC,

which indicated an increased incidence of lung tumors in female mice after exposure to sulfur dioxide. However, the concentrations of sulfur dioxide evaluated in these inhalation studies were not reported. Conclusions of the OECD SIDS report indicated 2% sodium metabisulfite via feed (20,000 ppm or 1,000 mg/kg/day) for 104 weeks was not carcinogenic in Wistar rats.

D. Genotoxicity/Mutagenicity:

Sodium metabisulfite was negative in an Ames/microsome assay (SRI International 1978b as cited by CIR 2003). Negative results were also reported for a host-mediated assay using mice to test mutagenicity against bacteria and yeast, in a cytogenetic assay using rats (Litton Bionetics 1972 as cited in CIR 2003), and a cytogenetic assay using sulfite oxidase-deficient hamsters and mice (Renner and Wever 1983 as cited in CIR 2003). Sodium metabisulfite was negative in one dominant lethal assay using rats while another study indicated further testing was needed (CIR 2003). However, genetic toxicity studies summarized by the OECD 2001 indicate sodium metabisulfite is equivocal in *in vitro* testing, but is not genotoxic in the *in vivo* testing.

E. Special Considerations for Infants and Children

There is sufficient toxicological information for sulfur dioxide and sodium metabisulfite to address FQPA considerations. The available information indicates that there is no evidence of increased quantitative or qualitative susceptibility of the offspring after *in utero* or post-natal exposure. Based on this information, there is no concern, at this time, for increased sensitivity to infants and children to sulfur dioxide and sodium metabisulfite when used on postharvest grapes.

F. Incident Data

In evaluating incidents to humans from sulfur dioxide and sodium metabisulfite exposure, the Agency evaluated data from the National Pesticide Information Center, the National Institute of Occupational Safety and Health (NIOSH), National Poison Control Centers, the California Department of Pesticide Regulation (CDPR), and the Agency's Incident Data System. The CDPR sulfur dioxide search identified 87 incident reviews from 1982 through 2003, many of which resulted from non-pesticidal uses. The NIOSH system search indicated that 19 incidents were reported involving sulfur dioxide from 1998 through 2003. Most of these cases involved effects such as chest pains, dizziness, numb hands, teary eyes, blurred vision, itching, and rashes. A 1991 report from the CDPR system also identified a case involving a delivery worker developing an asthmatic response following exposure to sulfur dioxide drift from a nearby fumigation facility. No incidents were reported for sodium metabisulfite; however, sodium bisulfite was implicated in the deaths of three workers using sodium bisulfite with a non-pesticidal use pattern.

IV. Occupational Risk Assessment

Regulatory exposure levels for inhalation exposure to sulfur dioxide include the OSHA PEL, NIOSH IDLH, and AIHA ERPG-1. The OSHA PEL (permissible exposure limit) is set at 5 ppm and is based on a time weighted average over an 8 hour workshift. The NIOSH IDLH

(immediately dangerous to life or health) is 100 ppm and the AIHA ERPG-1 is 0.3 ppm. The AIHA (American Industrial Hygiene Association) ERPG-1 is the maximum airborne concentrations below which it is believed that nearly all persons could be exposed for up to 1 hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined, objectionable odor.

Sodium Metabisulfite

Products which contain sodium metabisulfite as the active ingredient are comprised of the solid, anhydrous active ingredient contained in semi-sealed pads, which are placed in containers holding grapes for shipping and storage. In each crate the sodium metabisulfite pads are separated from the grapes by a layer of tissue paper and a layer of kraft paper, and then the entire contents are wrapped in a porous polyethylene liner bag before the crate is closed. As the pads absorb ambient moisture, they release sulfur dioxide to a level of 1-5 ppm within the crate. Since
the crates are partially open on the sides and top, the free exchange of low levels of sulfur dioxide with the surrounding air occurs continuously. Grapes are usually kept in these containers for 4-6 weeks before arrival at retail establishments. Once the grapes arrive for retail sale, the pads are removed from the crates and discarded. The low level of sulfur dioxide present in the crates or released to the surrounding environment is not expected to result in an occupational inhalation exposure of concern, as any exposure is expected to be of short duration and at or below the 8 hour OSHA PEL. Furthermore, since the sodium metabisulfite is contained in sealed pads, the likelihood of either oral or dermal exposure to the solid is considered minimal, providing the pads stay intact.

Pad disposal directions vary among the product labels; therefore, the Agency has determined that standardization of the labeling on the pad itself, is necessary. This labeling will include revised handling and disposal statements, in addition to a statement for asthmatics and sulfite sensitive individuals which identifies the presence of sulfites in these products. These label statements are detailed in Section XIII of this document. Based on the product use patterns, the low levels of sulfur dioxide released and the additional label requirements included in this document, the Agency expects occupational exposures to sodium metabisulfite to be below levels of concern.

Sulfur Dioxide

Products which contain sulfur dioxide as the active ingredient are formulated as a liquid under pressure which forms a gas upon release for grape fumigation. These products are stored in steel cylinders and applied to the treatment area via a hose system with a detector tube at a maximum rate of 1% concentration (based on measured volume of the fumigation chamber) for the initial fumigation, and up to 0.5% gas concentration for maintenance fumigations. Grapes are fumigated on a 7-10 day interval, and may be treated up to 20 times. Fumigation may occur in various types of cold-storage warehouses, or in truck trailers, vans and railcars.

Current sulfur dioxide end-use product labels require various levels of personal protective

equipment (PPE) during application and while checking hose connections. Workers must use sulfur dioxide detection devices (Draeger handpumps, Sensidyne or Kitagawa syringe samplers) to monitor the concentration in the fumigation area. If concentrations exceed 2.0 ppm in the fumigation area, the use of a NIOSH/MSHA approved respirator is required for "short exposures of limited duration." Labels also require a self-contained breathing apparatus (SCBA) or combination air-supplied respirator/SCBA for exposures to unknown concentrations, re-entry into a treated area with concentrations in excess of 2.0 ppm, and for emergencies. Other PPE requirements on current labels include protective clothing, gloves and boots impervious to sulfur dioxide, in addition to eye protection. These PPE requirements, as well as the respirator requirements, however, are inconsistent among product labels. Respirator requirements are also not clear regarding when a standard respirator (with an organic-vapor-removing cartridge) is acceptable or when a SCBA respirator is required. In order to clarify when SCBA respiratory protection is necessary and to address other PPE inconsistencies, the Agency has developed standard personal protective equipment (PPE) label requirements as stated in Section XIII of this document.

The Agency believes that the current PPE requirements with the additional labeling language required in this reregistration decision are adequate to ensure that workers are not exposed to sulfur dioxide levels of concern.

V. Bystander Inhalation Risk Assessment

Several regulatory endpoints and standards for ambient air concentrations of sulfur dioxide have been established at the state, Federal and international levels (see Table 5). The endpoint selected by the Agency for the bystander inhalation risk assessment is 0.25 ppm sulfur dioxide, with a 1-hour exposure duration. The 0.25 ppm concentration is based on an ambient air quality standard set by the California Air Resources Board. This endpoint is deemed most applicable to this exposure scenario, as it is based on effects of concern for bystanders (such as broncho-constriction, shortness of breath, wheezing, and chest tightness during physical activity in persons with asthma), and is recognized by the State in which nearly all grape treatments occur. Further, considering the 15-30 minute aeration period used with the grape treatment, an endpoint based on an exposure duration of 1-hour is considered appropriate. The following table lists additional regulatory and guideline concentrations for sulfur dioxide in ambient air.

Table 5. Sulfur Dioxide Air Concentrations used for Regulatory/Guideline Purposes

Exposure Limit	Agency/Group	Regulatory/Guideline Level (ppm)
1-hour	WHO	0.13
	California Air Resources Board	0.25
	AIHA (ERPG-1)	0.3
	State of Washington	0.25
	State of North Dakota	0.27
	State of Montana	0.5
3-hour	US EPA	0.5
	State of Florida	0.5

	State of Maine	0.4
	State of New Mexico	0.5
	State of New York	0.25
	State of Oregon	0.02

Based on the Probabilistic Exposure and Risk Model for Fumigants, version 2.1.1 (PERFUM2) and available incident data, the Agency has concerns for bystander exposure during grape fumigations which involve the release of high levels of sulfur dioxide during aeration. For *Botrytis cinerea* treatments, a practice known as "total utilization" is almost exclusively employed. Total utilization involves circulating the sulfur dioxide gas (typically 1000 to 2500 ppm) within the fumigation chamber until it is almost completely absorbed into the grapes, packaging material and any ambient moisture. As a result, only very low concentrations (i.e., less than 30 ppm) of sulfur dioxide are typically released from the ventilation stack during the aeration phase. However, current product labels do not limit sulfur dioxide release concentrations for this treatment; therefore if total utilization is not employed and much higher levels of sulfur dioxide are vented to the atmosphere, bystander exposure is a concern. To address this concern, the Agency is establishing a maximum release concentration for *Botrytis cinerea* warehouse treatments of 30 ppm, and truck/trailer treatments of 2 ppm. The disparity between these two release concentrations is based on the fact that the release of treated air following warehouse fumigation is performed at a flow rate of 2700 to 8100 ft^3/min and at a typical height of 15 feet above ground level, thereby further reducing the potential for bystander exposure. Based on the results of the PERFUM2 model, this 30 ppm release concentration level is expected to limit bystander exposure potential with this use to sulfur dioxide concentrations at or below 0.25 ppm. This bystander exposure scenario is considered "worst-case," in that it assumes the ventilation stack is at the edge of the treatment warehouse, and the warehouse is in close proximity to the fumigation facility property line.

Treatment for black widow spider, however, is performed at a much higher concentration of sulfur dioxide (up to 10,000 ppm) than is used for *Botrytis cinerea* treatments. Further, due to the potential for damaging the fruit, these high concentrations may not be held in contact with the grapes for more than approximately 30 minutes; thus total utilization is not feasible. As a result, much higher sulfur dioxide concentrations are released during aeration for treatment of black widow spider; therefore, the Agency has bystander exposure concerns for this use. To address bystander concerns during black widow spider treatment, the Agency is also placing a limit of 30 ppm on the sulfur dioxide release concentration during the aeration phase of black widow spider treatment. As stated above, based on the results of the PERFUM2 model, this release restriction is expected to limit bystander exposure potential with this use to sulfur dioxide concentrations at or below 0.25 ppm. The Agency has been working with the California Table Grape Commission (CTGC) and the California Grape and Tree Fruit League (CGTFL) to determine the feasibility of using air scrubbers during black widow spider treatments to reduce the release concentrations. However, the use of scrubbers requires additional time, which results in the treated grapes being exposed to high concentrations of sulfur dioxide for longer than 30 minutes, risking damage to the fruit. Hence, CTGL and CGTFL have indicated a need to perform a comprehensive fumigation study in order to determine the lowest sulfur dioxide release concentration which can be achieved using scrubbers or other such equipment, without

damaging the fruit. If such a fumigation study is performed, the Agency may reconsider the 30 ppm release limit for black widow spider treatment if the study findings indicate that 30 ppm cannot be achieved without damaging the treated fruit. However, any reconsideration of the release limit would be in conjunction with the use of higher ventilation stacks, a buffer zone to protect bystanders, or other measures to ensure that bystanders are not exposed to sulfur dioxide levels above 0.25 ppm as a result of this use. As reference, the following table details the correlation between buffer zone size and release concentration for the sulfur dioxide grape fumigation scenario.

Table 6. PERFUM2 Sulfur Dioxide Grape Fumigation Parameters for 0.25 ppm Endpoint

Buffer Size (meters)	Release concentration (ppm)
15	55
30	90
65	150

The details of the PERFUM2 assessments supporting the 30 ppm release rate, as well as the findings in Table 6 are attached as Appendix III. Required label language resulting from the release limits implemented in this section are detailed in Section XIII of this document.

VI. Dietary Exposure Assessment

Both sulfur dioxide (21CFR 182.3862) and sodium metabisulfite (21CFR 182.3766) are listed as GRAS by the FDA, with limitations, as food preservatives. Sulfites are found in many foods, primarily as a result of the GRAS preservative use. It is estimated that sulfite concentrations of >100 ppm may be found in dried fruits (excluding dark raisins and prunes), lemon and lime juices, wine, molasses, and sauerkraut juice. Dried potatoes, grape juice, wine vinegar, gravies, fruit topping, and maraschino cherries may contain between 50 and 100 ppm sulfur dioxide. Foods containing between 10 ppm and 50 ppm include pectin, fresh shrimp, corn syrup, sauerkraut, pickled foods, corn starch, hominy, frozen potatoes, maple syrup, imported jams and jellies, and fresh mushrooms (Lester 1995 as cited in CIR 2003).

The World Health Organization has emphasized the use of appropriate labeling for alerting individuals who cannot tolerate sulfites. After receiving and reviewing reports of adverse reactions in certain individuals following ingestion of sulfiting agents used as preservatives in food products, beverages, and fresh fruits and vegetables, the FDA required ingredient labels to list sulfite concentrations in excess of 10 ppm.

The uses of products containing inorganic sulfites are limited to use as indoor fumigants and as fungicidal control agents on grapes. A tolerance limit of 10 ppm (expressed as sulfite) for sulfur dioxide is established in 40 CFR 180.444, and sufficient data are available to support the reassessment of this tolerance. This 10 ppm tolerance is relatively low compared to concentrations of sulfites in many common foods and viewed as “GRAS” by FDA. Further this

level is below the level for which FDA requires labeling to alert sulfite-sensitive individuals. Therefore, residues resulting from the postharvest use of sulfur dioxide and sodium metabisulfite on grapes are not expected to be at a level of concern for the general population or any population subgroups.

VII. Drinking Water

Based on the use pattern and fate characteristics of these chemicals, the Agency does not have any drinking water concerns for sulfur dioxide and sodium metabisulfite.

VIII. Aggregate Assessment

The aggregate risk assessment integrates the assessments conducted for dietary, drinking water, and residential exposure if applicable. Currently there are no residential uses for either sulfur dioxide or sodium metabisulfite, as the use of inorganic sulfites is limited to fumigation of postharvest grapes, and bystander inhalation exposure concerns are being addressed in this decision document. Further, no common effects were seen in inhalation and oral toxicity studies. Based on environmental fate information for both chemicals, concentrations of concern are not expected in drinking water. Therefore, based on the uses of sulfur dioxide and sodium metabisulfite, no anticipated presence in drinking water, expected low residues on grapes, and consideration of the presence of sulfites in other common foods as a result of an FDA GRAS determination, the Agency has determined that aggregate exposure to sulfites does not pose a risk concern.

IX. Cumulative Exposure

Section 408(b)(2)(D)(v) of the FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." EPA does not have, at this time, available data to determine whether inorganic sulfites have a common mechanism of toxicity with other substances. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to inorganic sulfites and any other substances, and inorganic sulfites do not appear to produce a toxic metabolite produced by other substances.

For the purposes of this tolerance action, therefore, EPA has assumed that inorganic sulfites do not have a common mechanism of toxicity with other substances. For information regarding the Agency's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

X. Human Health Risk Characterization

Taking into consideration all available information on sulfur dioxide and sodium metabisulfite, including the specific use pattern and limited exposure potential, FDA's classification of generally recognized as safe (GRAS), as well the historical presence of sodium metabisulfite in cosmetics and hair care products, the use of sulfur dioxide and sodium metabisulfite on postharvest grapes is unlikely to pose a significant risk to the general population or any population subgroup. Potential bystander exposure concerns have been addressed, and anticipated occupational exposures are not expected to pose a risk of concern to workers.

XI. Ecological Risk Assessment

Sulfur dioxide (SO_2) is a nonflammable, colorless gas. It is very soluble in water, with its solubility varying from 5.88 % at 104 °F to 22.9% at 32 °F. In moist air or fogs, it combines with water to form sulfurous acid (H_2SO_3), but it is only very slowly oxidized to sulfuric acid. Sulfur dioxide has a high vapor pressure (3,000 mm Hg at 20°C) and, thus is typically present in a gaseous phase. It can be absorbed in soil, with uptake being dependent on the pH and moisture content of the soil (ATSDR, 1998a). The Environmental Fate and Effects Division (EFED) has reported that the only environmental fate data potentially needed for sulfur dioxide would be a hydrolysis study; however, the Agency has determined that the chemistry of sulfur dioxide is so well documented in the open literature that an additional study is not necessary (EPA, 1993b). Sodium metabisulfite dissolves in water and forms sodium cations, disulfite anions and sulfur dioxide (OECD, 2001).

Concentration of sulfur dioxide as low as 1-2 ppm have been reported to cause severe stress to green plants, and dissolved sulfur dioxide could be toxic to aquatic life. A few acute toxicity tests for sodium metabisulfite have been reported. The 96-hour LC_{50} was 100 mg/L for fish and the 72-hr EC_{50} for algae was 48.1 mg/L. An acute 48-hr EC_{50} for daphnids has been reported to be 88.76 mg/L and a chronic NOEC of >10 mg/L was reported. In addition, a memo from the Ecological Effects Branch of EFED (EPA 1992), stated that all ecotoxicological studies for the indoor food uses of sodium bisulfite were waived, as it was determined that there would be little likelihood of a hazard to non-target organisms. Therefore, based on the high vapor pressure, the current use pattern (indoor food-use) and limits established for sulfur dioxide release in this decision document, the Agency has no ecological risk concerns resulting from the pesticidal use of sulfur dioxide and sodium metabisulfite.

XII. Tolerance Reassessment

The Agency is proposing no changes in the level or definition of the existing tolerance. Therefore, the current tolerance established at 40CFR 180.444 for sulfur dioxide residues (expressed as sulfite) in grapes is now considered reassessed under section 408(q) of the FFDCA.

XIII. Labeling for End-Use Products

The following tables have been developed by the Agency, and indicate the required label statements for sulfur dioxide and sodium metabisulfite end-use products:

Table 7. Label Revisions
Label Statements for Sulfur Dioxide End-Use Products
"When treating grapes for *Botrytis cinerea* (bunch rot/gray mold) or black widow spider in a warehouse fumigation chamber, do not release treated air into the atmosphere containing concentrations of sulfur dioxide in excess of 30 ppm (as determined by a Sensidyne or Kitagawa syringe sampler, or a Draeger handpump)."
"When treating grapes in a truck, trailer or other transport vehicle, do not release treated air into the atmosphere containing concentrations of sulfur dioxide in excess of 2 ppm (as determined by a Sensidyne or Kitagawa syringe sampler, or a Draeger handpump)."
"Sulfur dioxide concentration in transport vehicles must be below 2 ppm before moving over public roads or highways."
"Before moving or using this product, handlers must be trained how to appropriately use respirators which conform to OSHA requirements (described in 29 CFR Part 1910.124) and how to appropriately handle and use sulfur dioxide."
"When making gas applications or checking connections wear a NIOSH/MSHA approved full face respirator with an organic-vapor removing cartridge, in addition to sulfur dioxide-impervious gloves, boots and coveralls over long-sleeved shirt and long pants."
"If a sulfur dioxide concentration of 2 ppm is exceeded at any time, all persons working in the fumigation area must wear a NIOSH/MSHA approved full face respirator with an organic-vapor removing cartridge. If sulfur dioxide concentrations of 10 ppm are exceeded, or when concentrations are unknown, an approved self-contained breathing mask (SCBA) or combination air supplied SCBA respirator must be used by all persons working in the fumigation area."
"Do not perform sulfur dioxide aerations concurrently from multiple chambers."

Table 8. Label Revisions
Label Statements for Sodium Metabisulfite End-Use Products (pad labeling)
"This pad contains sodium metabisulfite which may trigger an asthmatic response in sulfite sensitive individuals."

"This pad must be removed and disposed of prior to displaying grapes for sale. Do not allow consumers access to pads."
"If pad is torn: Carefully dispose of pad, pad contents, and grapes which have contacted pad contents."
"For Disposal: Place pad in a plastic bag, seal bag and place in an outdoor trash receptacle (dumpster)."

XIV. References

Agency for Toxic Substances and Disease Registry. 1998a. Toxicological Profile for Sulfur Dioxide. http://www.atsdr.cdc.gov/toxprofiles/tp116.html

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