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List of Subjects

Environmental protection, Agricultural commodities, Feed additives, Food additives, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: July 2, 2003.

Debra Edwards,

Director, Registration Division, Office of Pesticide Programs.

Summary of Petition

The petitioner's summary of the pesticide petition is printed below as required by FFDCA section 408(d)(3). The summary of the petition was prepared by the petitioner and represents the view of the petitioner. EPA may have edited the summary if the terminology used was unclear, the summary contained extraneous material, or the summary unintentionally made the reader conclude that the findings reflected EPA's position and not the position of the petitioner. The petition announces the availability of a description of the analytical methods available to EPA for the detection and measurement of the pesticide chemical residues or an explanation of why no such method is needed.

Syngenta Crop Protection

PP 3E6569

EPA has received a pesticide petition (PP 3E6569) from Syngenta Crop Protection, Inc., P.O. Box 18300, Greensboro, NC 27419 proposing, pursuant to section 408(d) of the FFDCA, 21 U.S.C. 346a(d), to amend 40 CFR part 180 to establish an exemption from the requirement of a tolerance for *cis*-3-hexen-1-ol when used as an inert ingredient in pesticide formulations containing the active ingredient paraquat dichloride. EPA has determined that the petition contains data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

A. Residue Chemistry

1. *Plant metabolism.* The plant metabolism of *cis*-3-hexen-1-ol has not been investigated. However, *cis*-3-hexen-1-ol has been commonly detected as a volatile organic emission from a

number of plant species. *Cis*-3-Hexen-1-ol is also a naturally occurring aromatic substance in a number of food products. *Cis*-3-Hexen-1-ol, is a terminal metabolite of the fatty acid/lipoxygenase pathway catalyzing the normal oxidative breakdown of plant membrane lipids.

2. *Analytical method.* No specific analytical method is provided since the petition is for an exemption from the requirement of establishing a tolerance for *cis*-3-hexen-1-ol. However, *cis*-3-hexen-1-ol has been routinely detected in both raw agricultural commodities and in processed foods by gas chromatography, mass spectroscopy, or a combination of both. These methods could be readily developed and adapted to detect *cis*-3-hexen-1-ol in food products to which paraquat dichloride may be applied.

3. *Magnitude of residues.* Potential residues of *cis*-3-hexen-1-ol in raw and or processed agricultural commodities are expected to be minimal. *Cis*-3-hexen-1-ol would be present at a concentration of up to 4 grams/L only in pesticide formulations containing paraquat dichloride. The maximum concentration of *cis*-3-hexen-1-ol (4 grams/L) in paraquat dichloride formulations is much lower than the concentration of the co-formulated active ingredient (paraquat dichloride). Based on data presented in the re-registration eligibility document on paraquat dichloride, and on the expected relative concentrations of paraquat and *cis*-3-hexenol in end use formulations, residues of *cis*-3-hexen-1-ol on agricultural commodities would be at least 50-fold lower than paraquat dichloride. Under field conditions, the residues of *cis*-3-hexen-1-ol are expected to be even lower since *cis*-3-hexen-1-ol is a volatile organic compound with a substantially higher vapor pressure than paraquat dichloride.

B. Toxicological Profile

1. *Acute toxicity.* The acute oral toxicity of *cis*-3-hexen-1-ol has been evaluated in both rats and mice. The oral lethal dose (LD)₅₀ for *cis*-3-hexen-1-ol in rats was reported to be 4,700 milligrams/kilograms (mg/kg) body weight, with a 95% confidence interval of 3,820 to 5,580 mg/kg body weight. In this study, most deaths occurred within 3 hours of dosing, with all deaths occurring within the first 24 hours post-dosing. Clinical signs observed prior to death included ataxia followed by decreased spontaneous movement and development of a comatose state. Necropsy evaluations revealed no specific abnormalities in any of the rats,

including decedents. Oral lethal dose (LD)₅₀ values of between 7,000 and 10,000 mg/kg body weight have also been reported for both rats and mice. Rats and mice were considerably more sensitive to the intraperitoneal administration of *cis*-3-hexen-1-ol, with reported i.p. LD₅₀ values of 600 and 400 to 500 mg/kg body weight, respectively.

Cis-3-Hexen-1-ol was essentially non-toxic by the dermal route, with a dermal LD₅₀ value of greater than 5,000 mg/kg body weight (the highest dose tested) in rabbits. Similarly, the application of neat solutions of *cis*-3-hexen-1-ol, held under an occlusive dressing for 24 hours, to both the intact and abraded skin of rabbits was found to be non-irritating. In human subjects, no dermal irritation was reported following application of a 4% *cis*-3-hexen-1-ol preparation in petrolatum held under an occlusive patch for 48 hours. In addition, the *cis*-3-hexen-1-ol preparation produced no evidence of sensitization in a maximization test conducted with 25 human volunteers.

The acute toxicity data available for *cis*-3-hexen-1-ol are consistent with the data on related linear and branched chain aliphatic unsaturated/unconjugated alcohols, aldehydes, and esters, showing this class of substances to be of low toxicity when administered orally.

2. *Genotoxicity.* The genotoxicity of *cis*-3-hexen-1-ol has not been formally investigated. However, *cis*-3-hexen-1-ol contains no structural alerts for genotoxic potential. *Cis*-3-Hexen-1-ol is expected to be oxidized to the corresponding aldehyde and carboxylic acid by high capacity carbohydrate metabolic pathways (i.e., NAD⁺/NADH-dependent metabolism to *cis*-3-hexenal followed by aldehyde dehydrogenase-mediated conversion to *cis*-3-hexenoic acid). Products of these metabolic pathways are not anticipated to show genotoxic activity. Information available on substances structurally related to *cis*-3-hexen-1-ol provides no evidence of mutagenic or chromosome-damaging potential. For example, in various reverse mutation assays conducted in bacterial cultures, oleic acid, methyl linoleate, and 2,6-dimethyl-5-heptenal were reported to show no evidence of mutagenic activity. Similarly, 2,6-dimethyl-5-heptenal was reported to show no genotoxic activity in an *in vitro* unscheduled DNA synthesis test or in an *in vivo* mouse micronucleus test. Also, the longer chain saturated aliphatic alcohols octadecan-1-ol and tetradecan-1-ol have been reported to be non-mutagenic in the Ames test conducted with *Salmonella*