

the use of this substance as a flavoring agent. With respect to the natural presence of *cis*-3-hexen-1-ol in food, common sources include: All green leafy plants, cruciferous plants, many fruits and vegetable, particularly tomatoes, and many essential oils. More than 10,000 kg of *cis*-3-hexen-1-ol may be consumed in the United States from its natural presence in tomatoes alone.

Cis-3-Hexen-1-ol is consumed primarily through its use as a flavoring agent. Based on measured concentrations in foods and the use of consumption estimates of various food categories, *per capita* consumption *cis*-3-hexen-1-ol is estimated at about 1 mg/kg body weight/day. About 0.018 mg/kg body weight per day may be consumed as a result of the use of *cis*-3-hexen-1-ol as a flavoring agent.

The residues of *cis*-3-hexen-1-ol on raw agricultural commodities, due to application in paraquat formulations only, are expected to be negligible, particularly in contrast to the human exposures to *cis*-3-hexen-1-ol from its natural presence foods and from its use as a flavoring agent.

Based on the expected relative concentrations of *cis*-3-hexen-1-ol in paraquat formulations and on the chronic dietary intake of paraquat calculated in the RED document (U.S. EPA, 1997) for paraquat dichloride, chronic exposures to residues of *cis*-3-hexen-1-ol of 0.0000076 and 0.000024 mg/kg body weight/day, respectively, were calculated for the U.S. population and for non-nursing infants less than 1-year old. These calculated chronic exposures to *cis*-3-hexen-1-ol residues on food are more than 40,000-fold lower than exposures occurring from the natural presence of *cis*-3-hexen-1-ol in foods (i.e., 1 mg/kg body weight/day from natural occurrence in food / 0.000024 mg/kg body weight/day from possible residues on paraquat-treated food products).

i. *Food*. Chronic dietary exposure to *cis*-3-hexen-1-ol has occurred for centuries due its natural presence in many foodstuffs and due to the use of this substance as a flavoring agent. With respect to the natural presence of *cis*-3-hexen-1-ol in food, common sources include: all green leafy plants, cruciferous plants, many fruits and vegetable, particularly tomatoes, and many essential oils. More than 10,000 kg of *cis*-3-hexen-1-ol may be consumed in the United States from its natural presence in tomatoes alone.

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categories, per capita consumption *cis*-3-hexen-1-ol is estimated at about 1 mg/kg body weight/day. About 0.018 mg/kg body weight per day may be consumed as a result of the use of *cis*-3-hexen-1-ol as a flavoring agent.

The residues of *cis*-3-hexen-1-ol on raw agricultural commodities, due to application in paraquat formulations, are expected to be negligible, particularly in contrast to the human exposures to *cis*-3-hexen-1-ol from its natural presence foods and from its use as a flavoring agent.

ii. *Drinking water*. Exposures to *cis*-3-hexen-1-ol from drinking water are expected to be negligible. Given the volatile nature of *cis*-3-hexen-1-ol, any trace concentrations of *cis*-3-hexen-1-ol that may enter drinking water supplies would be readily off-gassed. In any case, given its toxicological profile, *cis*-3-hexen-1-ol could not be present in drinking water at concentrations of concern for human health.

2. *Non-dietary exposure*. *Cis*-3-Hexen-1-ol, and a number of related alcohols and aldehydes, is a common constituent of the leafy portions of many plant species, hence the name "leaf alcohol". A number of studies have reported the presence of *cis*-3-hexen-1-ol and other compounds in the off-gas emissions from agricultural and non-agricultural (forest) plant species. While emissions from these sources appear considerable, it is not possible to determine the extent of inhalation exposure to *cis*-3-hexen-1-ol from these sources.

D. Cumulative Effects

Cis-3-Hexen-1-ol has been shown in a 98-day toxicity study not to produce overt organ toxicity. In addition, biochemical and metabolic considerations indicate that *cis*-3-hexen-1-ol would be metabolized to the corresponding aldehydes and acids, which, in turn, would be normal substrates for enzymes involved in fatty acid catabolism. Based on these data, there would appear to be no evidence for a "common mechanism" of toxicity with other substances. Simple metabolism along a common metabolic pathway does not constitute a "common mechanism of toxicity". As a result, there is no expectation that the use of *cis*-3-hexen-1-ol as an inert ingredient in paraquat dichloride pesticide formulations (at up to 4 grams/L) would contribute to any cumulative toxicity arising from exposure to other substances having a common mechanism of toxicity.

E. Safety Determination

1. *U.S. population*. The results of the acute toxicity studies, irritation and

sensitization studies, and the 98-day subchronic toxicity study demonstrate that *cis*-3-hexen-1-ol is of a low order of toxicity, with no overt organ toxicity, even at high dosages. *Cis*-3-Hexen-1-ol is not anticipated to be genotoxic, a conclusion consistent with the results reported for similar compounds. Similarly, metabolic considerations provide no evidence of severe toxicity since *cis*-3-hexen-1-ol is likely biotransformed to the corresponding unsaturated carboxylic acid, a compound that would participate in normal fatty acid metabolism.

Use of *cis*-3-hexen-1-ol at up to 4 grams/L in paraquat dichloride pesticide formulations is not expected to produce significant residues in raw agricultural commodities. Based on tolerances established for paraquat and on the anticipated relative concentrations of paraquat and *cis*-3-hexen-1-ol in end use formulations, maximum residues of *cis*-3-hexen-1-ol were estimated to be in the range of 0.0009 ppm. Under field conditions, the residues of *cis*-3-hexen-1-ol are expected to be even lower since *cis*-3-hexen-1-ol is highly volatile with a much higher vapor pressure than paraquat dichloride. At these maximum residue levels, the maximum chronic exposures to *cis*-3-hexen-1-ol were estimated to be 0.0000076 and 0.000024 mg/kg body weight/day, respectively, for the U.S. population and for non-nursing infants less than 1-year old. These calculated chronic exposures to *cis*-3-hexen-1-ol residues on food are more than 40,000-fold lower than exposures occurring from the natural presence of *cis*-3-hexen-1-ol in foods.

Based on the preceding analysis, Syngenta Crop Protection, Inc., believes that there is a reasonable certainty that no harm will result to the general population, including subgroups such as infants and children, from aggregate exposures to *cis*-3-hexen-1-ol.

2. *Infants and children*. Based on the data presented in the preceding sections and on the safety analysis presented above, Syngenta Crop Protection, Inc., believes that there is a reasonable certainty that no harm will result to infants and children from aggregate exposures to *cis*-3-hexen-1-ol.

F. International Tolerances

No tolerances, or exemptions for tolerance, for *cis*-3-hexenol have been previously requested by Syngenta Crop Protection, Inc. A maximum residue level (MRL) for *cis*-3-hexen-1-ol has not been established by the Codex Alimentarius Commission. In the United