

US EPA ARCHIVE DOCUMENT



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES, AND TOXIC SUBSTANCES

DATE: January 13, 2005

ACTION MEMORANDUM

SUBJECT: Inert Reassessments: 2-Methyl-4-isothiazolin-3-one and 5-Chloro-2-methyl-4-isothiazolin-3-one

FROM: Pauline Wagner, Chief *Pauline Wagner 1/17/06*
Inert Ingredient Assessment Branch
Registration Division (7505C)

TO: Lois A. Rossi, Director
Registration Division (7505C)

I. FQPA REASSESSMENT ACTION

Action: Reassessment of two inert exemptions from the requirement of a tolerance. The reassessment decision is to maintain each of the two inert tolerance exemptions "as-is."

Chemicals: 2-Methyl-4-isothiazolin-3-one and 5-Chloro-2-methyl-4-isothiazolin-3-one.

Table 1. Tolerance Exemptions Being Reassessed in this Document				
Citation as it Appears in the CFR				CAS Registry Number and Name
40 CFR 180 ^a	Tolerance Exemption Expression	Limits	Uses	
920	2-Methyl-4-isothiazolin-3-one (in combination with 5-chloro-2-methyl-4-isothiazolin-3-one)	Not more than 0.0022% (22.5 ppm) in the formulation; 0.00022% (or 2.25 ppm) in the final solution applied to growing crops.	Preservative	2682-20-4 3(2H)-Isothiazolone, 2-methyl- (9CI)
920	5-Chloro-2-methyl-4-isothiazolin-3-one (in combination with 2-methyl-4-isothiazolin-3-one)			26172-55-4 3(2H)-Isothiazolone, 5-chloro-2-methyl- (9CI)

a. Residues listed in 40 CFR 180. 920 are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops only.

Reassessment: A Reregistration Eligibility Decision (RED) was completed in April 1996 for Methylisothiazolinone. The RED is available on the Agency's website at

www.epa.gov/pesticides/reregistration/status.htm. The RED assessed the risks of two chemicals, which are the two inert ingredients being evaluated here (Table 1).

The Agency is not aware of any additional recent information that substantially changes the risk findings of the RED in a way that would impact the application of the conclusions to inert ingredient uses. Therefore, the toxicity findings of the RED are being used here for reassessment. The following excerpts are from the RED. Please note that in the RED, the word "methylothiazolinone" refers to both of the chemicals:

"From its review of the mammalian toxicology data, the Agency determined that methylothiazolinone is highly to very highly toxic, especially corrosive, by acute routes of exposure. In subchronic studies with oral and inhalation dosing of rats, the most significant toxicological effect was microscopic lesions in the nasal turbinates from inhalation exposure (NOEL of 0.34 $\mu\text{g}/\text{l}$), which is a typical physiological response to a respiratory irritant. Developmental and chronic/carcinogenicity studies resulted in no significant effects, with the Agency classifying methylothiazolinone as a group D carcinogen. Results from mutagenicity studies were equivocal."

In discussing the results of a developmental toxicity study on the rat, the RED concluded: "Methylothiazolinone was not found to be fetotoxic, embryotoxic, or teratogenic in rats. The maternal toxicity NOEL is 10 mg/kg/day. The maternal LOEL is 30 mg/kg/day, based on decreased body-weight gains, with support from the dose-related increase in deaths. The NOEL for developmental toxicity was 100 mg/kg/day, the highest dose tested."

The RED summarized ecological risks as follows: "Methylothiazolinone is moderately toxic to practically non-toxic to birds, and highly toxic to freshwater and estuarine/marine organisms." Both 2-methyl-4-isothiazolin-3-one and 5-chloro-2-methyl-4-isothiazolin-3-one are rapidly degraded in the environment by hydrolysis and by photochemical and biological action. Therefore, no contribution to drinking water is anticipated.

The inert ingredient use of these chemicals in 180.920 s significantly limited: Not more than 0.0022% (22.5 ppm) in the formulation; 0.00022% (or 2.25 ppm) in the final solution applied to growing crops. Although both chemicals have toxicity, the small amount that is permitted for use as inert ingredients in pesticide formulations is expected to result in no effects of concern for all endpoints, including residential exposures.

Because the RED was finalized in 1994 -- prior to FQPA, additional safety findings are now required and are found below.

Special Considerations for Infants and Children: Based on the available information, 2-Methyl-4-isothiazolin-3-one and 5-chloro-2-methyl-4-isothiazolin-3-one are of low toxicity for developmental and reproductive effects of concern. They were not found to be fetotoxic or embryotoxic in the developmental study, where the NOEL was

100 mg/kg/day (the highest dose tested) in the presence of maternal toxicity (NOEL of 10 mg/kg/day and a LOEL of 30 mg/kg/day). Therefore, there is no concern for potential sensitivity to infants and children. Based on this information, a safety factor analysis has not been used to assess the risks resulting from the use of 2-methyl-4-isothiazolin-3-one and 5-chloro-2-methyl-4-isothiazolin-3-one, and, therefore, an additional tenfold safety factor for the protection of infants and children is unnecessary.

Aggregate Exposures: In examining aggregate exposure, FFDCA section 408 directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures, including drinking water from ground water or surface water and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses). In developing this assessment for 2-methyl-4-isothiazolin-3-one and 5-chloro-2-methyl-4-isothiazolin-3-one, a qualitative assessment for all pathways of human exposure (food, drinking water, and residential) is appropriate given the lack of human health concerns associated with exposure to these chemicals.

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." 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 2-methyl-4-isothiazolin-3-one and 5-chloro-2-methyl-4-isothiazolin-3-one and any other substances, and these chemicals do not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that 2-methyl-4-isothiazolin-3-one and 5-chloro-2-methyl-4-isothiazolin-3-one have a common mechanism of toxicity with other substances. For information regarding EPA'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/>

Human Health Risk Characterization: Taking into consideration the available information on 2-methyl-4-isothiazolin-3-one and 5-chloro-2-methyl-4-isothiazolin-3-one (including the tolerance exemptions' use limitations), there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure when considering dietary exposure and all other non-occupational sources of pesticide exposure for which there is reliable information. Therefore, it is recommended that the two exemptions from the requirement of a tolerance established for residues of 2-methyl-4-isothiazolin-3-one and 5-chloro-2-methyl-4-isothiazolin-3-one in/on raw agricultural commodities under 40 CFR 180.920 can be considered reassessed as safe under section 408(q) of the FFDCA.

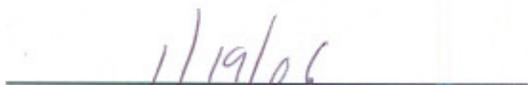
List Reclassification Determination: The current List Classification for 2-methyl-4-isothiazolin-3-one and 5-chloro-2-methyl-4-isothiazolin-3-one is 3. Because EPA has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to 2-methyl-4-isothiazolin-3-one and 5-chloro-2-methyl-4-isothiazolin-3-one when used as inert ingredients in pesticide formulations, the List Classification for will change from List 3 to List 4B.

II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the two exemptions from the requirement of a tolerance for the inert 2-methyl-4-isothiazolin-3-one (CAS Reg. No. 2682-20-4) and 5-chloro-2-methyl-4-isothiazolin-3-one (CAS Reg. No. 26172-55-4), and with the List reclassification determination, as described above. I consider the two exemptions established in 40 CFR part 180.920 to be reassessed for purposes of FFDCAs section 408(q) as of the date of my signature, below. A Federal Register Notice regarding this tolerance exemption reassessment decision will be published in the near future.



Lois A. Rossi, Director
Registration Division



Date:

cc: Debbie Edwards, SRRD
Joe Nevola, SRRD