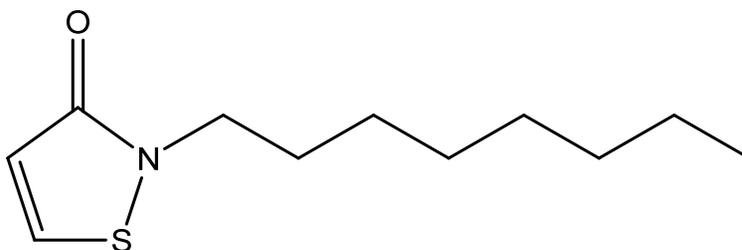


Octhilonone [CASRN: 26530-20-1]

Materials for the July 28-29, 2009 Meeting of the California Environmental Contaminant Biomonitoring Program (CECBP) Scientific Guidance Panel (SGP)

Agenda Item: "Consideration of Potential Designated Chemicals"



Exposure or potential exposure to the public or specific subgroups:

Octhilonone (2-octyl-4-isothiazolin-3-one) [OIT] is a mildewcide, fungicide and bacteriocide used in cooling tower and air washer water systems, as a materials preservative and on wood to prevent mold and sapstain. In California, 444,257 pounds of OIT were used on lumber in 2007 (CDPR, 2007), a large increase from the 9,416 pounds used in 2006 (CDPR, 2006). CDPR (2008) reports that over 2.5 million pounds of OIT were sold in California in 2007. OIT is used as a preservative in various household products including paints, carpets and carpet backings, vinyl floors, mattress covers, rubber/polymer products (including slippers, gloves), foams (e.g., foam used in pillows and mattresses, shoe soles), adhesives, caulks, feather and down fill, textiles (e.g., upholstery, clothing and linens), and leather preservation.

U.S. EPA (2007a) concluded that there was concern for exposure to children from OIT-treated carpets (from both dermal exposure and incidental oral ingestion) and concern for aggregate oral exposure to OIT (includes exposure from mouthing OIT treated toys and mouthing treated clothing/textiles). Under new use conditions, OIT preserved plastics cannot be used in the manufacture of children's toys and OIT can only be used for carpet backing and not carpet fibers (U.S. EPA, 2007a). The extent of OIT transfer from treated clothing/textiles and treated mattress covers is unknown. U.S. EPA has requested a study on the extent of residue transfer and also required that the amount of OIT in mattress covers be reduced (U.S. EPA, 2007a). It is also unknown to what extent carpets, toys, and fabrics manufactured outside of the United States contain OIT.

Known or suspected health effects:

OIT belongs to the isothiazolone (or isothiazolinone) class of chemicals, which, because of structure and electron density, can react with cellular thiols, such as cysteine residues in proteins (King et al., 2009, Du et al., 2002). Methylisothiazolinone (MIT) was found

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to be highly toxic to neurons *in vitro*, which was hypothesized to involve the observed glutathione (GSH) depletion (Du et al., 2002). OIT and MIT were found to significantly increase the amount of oxidized GSH in the human liver cell line Hep G2, although these effects were markedly less than those of two chlorinated isothiazolone analogues (Arning et al., 2008).

OIT is responsible for several cases of occupational allergic contact dermatitis, mostly among paint manufacturers (Thormann 1982; Balaguer et al., 2008; Mathias et al., 1983; Korte-Aalto et al. 2007). Isothiazolones have also been associated with the development of occupational asthma (Bourke et al. 1997).

CDPR (2001) reported that OIT caused a statistically significant increase in chromosomal aberrations in an *in vitro* cytogenic assay, although other genotoxicity studies of OIT did not report positive effects (U.S. EPA, 2007b). An 18-month carcinogenicity mouse bioassay is available for OIT, but this negative study was found to be inadequate by both U.S. EPA (2007b) and CDPR (2001).

As an anti-microbial agent, the toxicological database on OIT meets the requirements for federal registration (Federal Insecticide, Fungicide, and Rodenticide Act, [FIFRA]) and for California registration (Schreider, pers. comm., 2009). However, in a 2007 memorandum, U.S. EPA noted that the database does not contain the following endpoints: carcinogenicity, reproductive toxicity, chronic toxicity, neurotoxicity, and pharmacokinetics/metabolism (U.S. EPA, 2007b). Data on these endpoints would normally be required for a conventional pesticide with the potential for significant exposures. The carcinogenicity and chronic toxicity endpoints were considered important because of OIT's use as a metal-working fluid. The Reregistration Eligibility Decision (RED) for OIT (U.S. EPA, 2007a) referred to a two-generation reproduction study with negative results, but OEHHA was not able to locate a summary of this study. OEHHA is in contact with U.S. EPA to clarify the status of the OIT toxicological database and whether any new studies have been submitted.

Potential to biomonitor:

Physical and chemical properties (U.S. EPA, 2007a):

Molecular weight: 213.34

Vapor pressure: 3.68×10^{-5} mm Hg at 25°C

Water solubility: 525 mg/L at 25°C

Octanol/water partition coefficient: $\text{Log } K_{ow} = 3.42$

Persistence: OIT is stable and persistent in water under abiotic conditions with a half-life of greater than 30 days. It is immobile in soil and binds strongly to top soil surfaces. Microbial degradation occurs in soil within 120 days (U.S. EPA, 2007c).

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Bioaccumulation: BCF = 15 (predicted, PBT Profiler)

Pharmacokinetics and metabolism: No pharmacokinetics or metabolism studies have been identified.

Previous biomonitoring studies: None identified.

Need to assess efficacy of public health actions:

Although 2.5 million pounds of OIT were sold in California in 2007, the extent of OIT exposure is unknown. The U.S. EPA has acted to limit exposure from household and consumer items. Biomonitoring would provide information about exposures in California and help evaluate the necessity for further study of this relatively unknown chemical.

Availability of analytical methods: Methods have not been developed.

Availability of adequate biospecimens: Blood.

Incremental analytical cost: It is unlikely that this chemical can be bundled with other analytes.

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