Health Based Guidance for Groundwater
Health Risk Assessment Unit, Environmental Health Division
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Chemical Name: Perfluorohexane sulfonate

CAS: 355-46-4

Synonyms: PFHxS, Perfluorohexane-1-sulphonic acid

A single whole animal toxicity study has been conducted for PFHxS. This study, conducted in rats, consists of a combined repeated dose toxicity study with a reproduction/developmental toxicity screening test. Limited toxicokinetic (e.g., half-life information) is also available in rats. Based on the results of the toxicity study, PFHxS exposure resulted in decreases in body weight and cholesterol levels and an increase in prothrombin time at an estimated human equivalent dose that is similar to the human equivalent dose that formed the basis of the chronic RfD and HRL for PFOS. Sensitive effects observed following PFOS exposure included decreased body weight, cholesterol levels and thyroid hormone levels as well as developmental delays and increased liver weight and histological changes. The PFHxS toxicity study did not include thyroid hormone analysis, however, microscopic changes in the thyroid at higher dose levels were reported. Although no reproductive or developmental effects were reported it should be noted that because of the selectivity of the endpoints and the short duration (approximately 40 days) the reproductive/developmental screening assessment does not provide definitive evidence of no reproductive or developmental effects. After a careful review of the available toxicological information, staff have determined that they are unable to recommend risk assessment advice (RAA) for PFHxS based on the limited data currently available.

Acute Noncancer Risk Assessment Advice ($nRAA_{acute}$) = Not Derived (Insufficient Data)

Short-term Noncancer Risk Assessment Advice ($nRAA_{short\text{-}term}$) = Not Derived (Insufficient Data)

Subchronic Noncancer Risk Assessment Advice ($nRAA_{subchronic}$) = Not Derived (Insufficient Data)

Chronic Noncancer Risk Assessment Advice ($nRAA_{chronic}$) = Not Derived (Insufficient Data)

Cancer Risk Assessment Advice (cRAA) = Not Applicable

Cancer classification: PFHxS has not been classified as to carcinogenic potential.

Slope factor: NA

Volatile: Yes (moderate)

Summary of changes since 1993/1994 HRL promulgation:
None.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	Sec. Observations[1]	No	Yes[2]	Yes[3]	Yes[4]
Effects?	-	-	No	No	No

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:

[1] No in vivo studies. Secondary observations - treatment related microscopic changes in the thyroid were observed following exposure to > 3 mg/kg-d PFHxS. However, more sensitive parameters (e.g., serum thyroid hormone levels) were not measured. Alternations in thyroid hormone levels have been observed following treatment with other PFCs. The results of an in vitro study evaluating PFCs ability to compete with thyroxin (T4) for binding to the human thyroid hormone transport protein transthyretin (TTR) indicate that PFHxS has the ability to compete with T4 for binding to TTR.

[2] A single screening level assessment has been conducted. No treatment effects on development were reported at dose levels up to 10 mg/kg-d. Although the results of this study indicate that development is not a sensitive endpoint the selectivity of the endpoints and the short duration the screening assessment does not provide definitive evidence of no developmental effects.

[3] A single screening level assessment has been conducted. No treatment effects on male or female reproductive ability were reported at dose levels up to 10 mg/kg-d. Males were exposed 14 days prior to mating and through study day 42-44. Females were exposed 14 days prior to mating, throughout gestation and lactation (postnatal day 22). Although the results of this study indicate that the reproductive system is not a sensitive endpoint selectivity of the endpoints and the short duration of the screening assessment does not provide definitive evidence of no reproductive effects.

[4] Functional observation battery and motor activity assessments were conducted as part of the toxicological evaluation in the single toxicity study available. No effects were observed at dose levels up to 10 mg/kg-d.

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