HYDROGEN PEROXIDE

CAS # 7722-84-1

ORAL RISK ASSESSMENT

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EXECUTIVE SUMMARY

Hydrogen Peroxide – Preliminary Oral Risk Assessment CAS # 7722-84-1			
PARAMETER	**LEVEL**	**UNITS**	**DERIVED**
$BMDL_{05}$ (no-observed-adverse-effect level)	49	mg/kg-day	From a subchronic repeated dose study in catalase-deficient mice.
Oral RfD (oral reference dose)	0.5	mg/kg-day	From a subchronic repeated dose study in catalase-deficient mice, with a 100x total uncertainty factor.
TAC (total allowable concentration)	8	mg/L	For a 70 kg adult drinking 2 L/day using a 49% relative source contribution for drinking water
SPAC (single product allowable concentration)	8	mg/L	From the TAC, using 1 source of hydrogen peroxide in drinking water.
STEL (short term exposure level)	Not Derived	-	-

KEY STUDY	Weiner et al. 2000. 13-Week drinking water toxicity study of hydrogen peroxide with 6-week recovery period in catalase-deficient mice. Food Chem Toxicol 38:607-615. Supportive studies: Ito et al. 1981. Induction of duodenal tumors in mice by oral administration of hydrogen peroxide. Gann 72:174-175. Ito et al. 1984. Correlation between induction of duodenal tumor by hydrogen peroxide and catalase activity in mice. Gann 75:17-21.
CRITICAL EFFECT	Duodenal hyperplasia.
UNCERTAINTY FACTORS	Factors applied in calculating the oral RfD include: • 3x for interspecies extrapolation • 10x for intraspecies extrapolation • 1x for subchronic to chronic extrapolation • 1x for LOAEL to NOAEL • 3x for database deficiencies The total uncertainty factor is therefore 100x
TOXICITY SUMMARY	Hydrogen peroxide is irritating and corrosive and will damage any tissue/organism it contacts with time/concentration dependence. The response also depends on tissue levels of catalase, glutathione peroxidase, and glucose-6-phosphate dehydrogenase, making human genetic polymorphisms in these enzymes a factor in hydrogen peroxide toxicity. In subchronic and chronic repeated dose ingestion studies the critical effects were observed in the gastrointestinal tract. The key studies showed dose-dependent increases in glandular stomach erosion, duodenal hyperplasia, and duodenal carcinoma in mice given hydrogen peroxide in their drinking water. These lesions correlated inversely with catalase activity and were associated with the irritant properties of the chemical. Hydrogen peroxide is mutagenic and clastogenic in a wide variety of *in vitro* assays, including forward and reverse mutation, chromosomal aberration, DNA damage/repair, and sister chromatid exchange assays. Genotoxicity is not expressed *in vivo*, which is likely to be related to endogenous levels of catalase, other detoxifying enzymes and radical scavenging substances. Although hydrogen peroxide produced localized duodenal carcinomas upon repeated administration in drinking water to catalase-deficient mice, ECB (2003) suggested development of duodenal carcinomas was a threshold phenomenon, since these tumors failed to metastasize and hyperplasia readily resolved upon cessation of treatment. Under U.S. EPA (2005) guidelines for carcinogen risk assessment, the data support a descriptor classification of *suggestive evidence of carcinogenic potential*. Therefore, hydrogen peroxide was evaluated as a carcinogen with a low-dose nonlinear mode of action in this assessment.
CONCLUSIONS	Based on the status of hydrogen peroxide as an endogenous chemical participating in a number of normal metabolic reactions, effects observed in laboratory animals dosed up to chronic duration that are considered relevant to human health, and use of benchmark dose modeling with application of appropriate uncertainty factors, the derived drinking water action levels are considered protective of human health.

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1.0 INTRODUCTION

This document has been prepared to allow toxicological evaluation of the unregulated contaminant **hydrogen peroxide** in drinking water, as an extractant from one or more drinking water system components evaluated under NSF/ANSI 61 (2010), or as a contaminant in a drinking water treatment chemical evaluated under NSF/ANSI 60 (2009). Both non-cancer and cancer endpoints have been considered, and risk assessment methodology developed by the U.S. Environmental Protection Agency (U.S. EPA) has been used.

Non-cancer endpoints are evaluated using the reference dose (RfD) approach (Barnes and Dourson, 1988; Dourson, 1994; U.S. EPA, 1993; U.S. EPA, 2002a), which assumes that there is a threshold for these endpoints that will not be exceeded if appropriate uncertainty factors (Dourson et al., 1996; U.S. EPA, 2002a; WHO/IPCS, 2005) are applied to the highest dose showing no significant effects. This highest dose is derived from human exposure data when available, but more often is derived from studies in laboratory animals. Either the no-observed-adverse-effect level (NOAEL) taken directly from the dose-response data, or the calculated lower 95% confidence limit on the dose resulting in an estimated 10% increase in response (the LED_{10} or $BMDL_{10}$ from benchmark dose programs) can be used (U.S. EPA, 2009). The lowest-observed-adverse-effect level (LOAEL) can also be used, with an additional uncertainty factor, although the benchmark dose approach is preferred in this case. The RfD is expressed in mg/kg-day. It is defined by the U.S. EPA as "an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime" (Barnes and Dourson, 1988; U.S. EPA, 1993; U.S. EPA, 2007a).

NSF uses the RfD to derive three product evaluation criteria for non-cancer endpoints. The total allowable concentration (TAC), generally used to evaluate the results of extraction testing normalized to static at-the-tap conditions, is defined as the RfD multiplied by the 70 kg weight of an average adult assumed to drink two liters of water per day. A relative source contribution (RSC), to ensure that the RfD is not exceeded when food and other non-water sources of exposure to the chemical are considered, is also applied in calculating the TAC. The relative source contribution should be data derived, if possible. Alternately, a 20% default contribution for water can be used (U.S. EPA, 1991a). The TAC calculation is then as follows:

$$\text{TAC (mg/L)} = \frac{[\text{RfD (mg/kg-day)} \times 70\ \text{kg}] - [\text{total contribution of other sources (mg/day)}]}{2\ \text{L/day}}$$

or

$$\text{TAC (mg/L)} = \frac{\text{RfD (mg/kg-day)} \times 70\ \text{kg}}{2\ \text{L/day}} \times 0.2\ \text{(RSC)}$$

The single product allowable concentration (SPAC), used for water treatment chemicals and for water contact materials normalized to flowing at-the-tap conditions, is the TAC divided by the estimated total number of sources of the substance in the drinking water treatment and