

# **HYDROGEN PEROXIDE**

CAS # 7722-84-1

## **ORAL RISK ASSESSMENT**



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## TABLE OF CONTENTS

<b>1.0</b>	<b>INTRODUCTION .....</b>	<b>1</b>
<b>2.0</b>	<b>PHYSICAL AND CHEMICAL PROPERTIES .....</b>	<b>3</b>
2.1	<b>Organoleptic Properties .....</b>	<b>3</b>
<b>3.0</b>	<b>PRODUCTION AND USE .....</b>	<b>3</b>
3.1	<b>Production .....</b>	<b>3</b>
3.2	<b>Use .....</b>	<b>4</b>
<b>4.0</b>	<b>ANALYTICAL METHODS .....</b>	<b>6</b>
4.1	<b>Analysis in Water .....</b>	<b>6</b>
4.2	<b>Analysis in Biological Matrices .....</b>	<b>6</b>
<b>5.0</b>	<b>SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE .....</b>	<b>7</b>
5.1	<b>Sources of Human Exposure .....</b>	<b>7</b>
5.2	<b>Sources of Environmental Exposure .....</b>	<b>7</b>
<b>6.0</b>	<b>COMPARATIVE KINETICS AND METABOLISM IN HUMANS AND LABORATORY ANIMALS .....</b>	<b>8</b>
6.1	<b>Absorption .....</b>	<b>8</b>
6.2	<b>Distribution .....</b>	<b>8</b>
6.3	<b>Metabolism .....</b>	<b>9</b>
6.4	<b>Elimination/Excretion .....</b>	<b>10</b>
6.5	<b>Conclusions Regarding Comparative Kinetics and Metabolism .....</b>	<b>10</b>
<b>7.0</b>	<b>EFFECTS ON HUMANS .....</b>	<b>10</b>
7.1	<b>Case Reports .....</b>	<b>10</b>
7.2	<b>Epidemiological Studies .....</b>	<b>13</b>
7.3	<b><i>In Vitro</i> Studies .....</b>	<b>13</b>
<b>8.0</b>	<b>EFFECTS ON LABORATORY ANIMALS AND <i>IN VITRO</i> TEST SYSTEMS .....</b>	<b>13</b>
8.1	<b>Limited-Exposure Effects .....</b>	<b>13</b>
8.1.1	<b><i>Irritation and Sensitization Studies</i> .....</b>	<b>13</b>
8.1.2	<b><i>Ocular Exposure Studies</i> .....</b>	<b>13</b>
8.2	<b>Single-Exposure Studies .....</b>	<b>14</b>
8.3	<b>Short-Term Exposure Studies .....</b>	<b>14</b>
8.4	<b>Long-Term and Chronic Exposure Studies .....</b>	<b>14</b>
8.4.1	<b><i>Subchronic Studies</i> .....</b>	<b>14</b>
8.4.2	<b><i>Chronic Studies</i> .....</b>	<b>16</b>
8.4.3	<b><i>Initiation-Promotion and Combined Exposure Bioassays</i> .....</b>	<b>18</b>

8.4.4	<i>Effect on Tumor Growth and Life Span</i> .....	20
<b>8.5</b>	<b>Studies of Genotoxicity and Related End-Points</b> .....	<b>20</b>
8.5.1	<i>Mutagenicity Assays</i> .....	21
8.5.2	<i>Assays of Chromosomal Damage</i> .....	21
8.5.3	<i>Other Assays of Genetic Damage</i> .....	23
<b>8.6</b>	<b>Reproduction and Developmental Toxicity Studies</b> .....	<b>34</b>
8.6.1	<i>Studies Related to Reproduction</i> .....	34
8.6.2	<i>Studies Related to Development</i> .....	34
<b>8.7</b>	<b>Studies of Immunological and Neurological Effects</b> .....	<b>34</b>
8.7.1	<i>Immunological Effects</i> .....	35
8.7.2	<i>Neurological Effects</i> .....	35
<b>9.0</b>	<b>RISK CHARACTERIZATION</b> .....	<b>35</b>
<b>9.1</b>	<b>Hazard Assessment</b> .....	<b>35</b>
9.1.1	<i>Evaluation of Major Non-Cancer Effects and Mode of Action</i> .....	36
9.1.2	<i>Weight-of-Evidence Evaluation and Cancer Characterization</i> .....	37
9.1.3	<i>Selection of Key Study and Critical Effect</i> .....	40
9.1.4	<i>Identification of Susceptible Populations</i> .....	41
<b>9.2</b>	<b>Dose-Response Assessment</b> .....	<b>42</b>
9.2.1	<i>Uncertainty Factor Selection</i> .....	45
9.2.2	<i>Oral RfD Calculation</i> .....	48
<b>9.3</b>	<b>Exposure Assessment</b> .....	<b>48</b>
<b>9.4</b>	<b>TAC Derivation</b> .....	<b>50</b>
<b>9.5</b>	<b>STEL Derivation</b> .....	<b>50</b>
<b>10.0</b>	<b>RISK MANAGEMENT</b> .....	<b>50</b>
<b>10.1</b>	<b>SPAC Derivation</b> .....	<b>50</b>
<b>11.0</b>	<b>RISK COMPARISONS AND CONCLUSIONS</b> .....	<b>51</b>
<b>12.0</b>	<b>REFERENCES</b> .....	<b>53</b>
<b>12.1</b>	<b>References Cited</b> .....	<b>53</b>
<b>12.2</b>	<b>References Reviewed but Not Cited</b> .....	<b>66</b>
<b>13.0</b>	<b>APPENDICES</b> .....	<b>76</b>
<b>13.1</b>	<b>Liberation of O<sub>2</sub> at 5 mg/L Hydrogen Peroxide</b> .....	<b>76</b>
<b>13.2</b>	<b>Benchmark Dose Comparison of Chronic and Subchronic Data</b> .....	<b>77</b>
<b>13.3</b>	<b>Cancer Risk Level Comparison with Uncertainty Factor Approach</b> .....	<b>80</b>
13.3.1	<i>Oral Slope Factor Calculation</i> .....	80
13.3.2	<i>Unit Risk and TAC Calculations based on Oral Slope Factor</i> .....	80

**13.4 Benchmark Dose Results ..... 81**

*13.4.1 Duodenal Hyperplasia – Ito et al. (1981b), Human Equivalent Dose, 10% effect ..... 81*

*13.4.2 Duodenal Hyperplasia – Weiner et al. (2000), Human Equivalent Dose, 10% effect ..... 84*

*13.4.3 Duodenal Hyperplasia - Weiner et al. (2000), 5% Response ..... 87*

*13.4.4 Duodenal Hyperplasia - Weiner et al. (2000), Human Equivalent Dose, 5% Response ..... 89*

*13.4.5 Glandular Stomach Erosion/Ulcer ..... 91*

*13.4.6 Localized Duodenal Carcinoma ..... 92*

**14.0 PEER REVIEW HISTORY ..... 93**

## **AUTHORS, PEER REVIEWERS, AND ACKNOWLEDGEMENTS**

### **Author:**

NSF Toxicology Services  
1.800.NSF.MARK  
NSF International  
789 Dixboro Road  
Ann Arbor, MI 48105

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### **Internal NSF Peer Reviewers:**

Clif McLellan, M.S.

### **External Peer Reviewers:**

NSF gratefully acknowledges the efforts of the following experts on the NSF Health Advisory Board in providing peer review. These peer reviewers serve on a voluntary basis, and their opinions do not necessarily represent the opinions of the organizations with which they are affiliated.

Edward Ohanian, Ph.D. (Chairman, NSF Health Advisory Board)  
Associate Director for Science  
Office of Water  
U.S. Environmental Protection Agency

Michael Dourson, Ph.D., DABT (Vice Chairman, NSF Health Advisory Board)  
President  
TERA (Toxicology Excellence for Risk Assessment)

David Blakey, D.Phil.  
Director, Environmental Health Science and Research Bureau  
Safe Environments Programme  
Health Canada

Steven Bursian, Ph.D.  
Professor  
Michigan State University

Craig Farr, Ph.D., DABT  
Consultant

Robert Hinderer, Ph.D.  
Senior Consultant, Product Safety & Compliance  
The Lubrizol Corporation

Ernest E. McConnell, D.V.M., M.S. (Path)  
ToxPath, Inc.

Jennifer Orme-Zavaleta, Ph.D.  
Interim National Program Director for Safe and Sustainable Water Resources  
Office of Research and Development  
US Environmental Protection Agency

Calvin Willhite, Ph.D.  
Department of Toxic Substances Control  
State of California

## EXECUTIVE SUMMARY

Hydrogen Peroxide – Preliminary Oral Risk Assessment CAS # 7722-84-1			
PARAMETER	LEVEL	UNITS	DERIVED
<b>BMDL<sub>05</sub></b> (no-observed-adverse-effect level)	49	mg/kg-day	From a subchronic repeated dose study in catalase-deficient mice.
<b>Oral RfD</b> (oral reference dose)	0.5	mg/kg-day	From a subchronic repeated dose study in catalase-deficient mice, with a 100x total uncertainty factor.
<b>TAC</b> (total allowable concentration)	8	mg/L	For a 70 kg adult drinking 2 L/day using a 49% relative source contribution for drinking water
<b>SPAC</b> (single product allowable concentration)	8	mg/L	From the TAC, using 1 source of hydrogen peroxide in drinking water.
<b>STEL</b> (short term exposure level)	Not Derived	-	-
<b>KEY STUDY</b>	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.		
<b>CRITICAL EFFECT</b>	Duodenal hyperplasia.		
<b>UNCERTAINTY FACTORS</b>	Factors applied in calculating the oral RfD include: <ul style="list-style-type: none"> <li>• 3x for interspecies extrapolation</li> <li>• 10x for intraspecies extrapolation</li> <li>• 1x for subchronic to chronic extrapolation</li> <li>• 1x for LOAEL to NOAEL</li> <li>• 3x for database deficiencies</li> </ul> The total uncertainty factor is therefore 100x		
<b>TOXICITY SUMMARY</b>	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 <i>in vitro</i> assays, including forward and reverse mutation, chromosomal aberration, DNA damage/repair, and sister chromatid exchange assays. Genotoxicity is not expressed <i>in vivo</i> , 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 <i>suggestive evidence of carcinogenic potential</i> . Therefore, hydrogen peroxide was evaluated as a carcinogen with a low-dose nonlinear mode of action in this assessment.		
<b>CONCLUSIONS</b>	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.		

1

## 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<sub>10</sub> or BMDL<sub>10</sub> 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