Compressed Gas Association
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CGA TR-6—2022
ARSINE THRESHOLD LIMIT VALUE

FIRST EDITION

PREFACE:

This Technical Report is based on a 2001 study conducted for CGA by Dr. Dean Carter, Professor of Pharmacology and Toxicology at the University of Arizona and Dr. Henry Trochimowicz, Toxicology Consultant and former DuPont Company toxicologist.

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FIRST EDITION: 2022

Contents **Page**

Table

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1 Introduction

The American Conference of Governmental Industrial Hygienists (ACGIH) proposed to change the current threshold limit value (TLV®) for arsine from 0.05 ppm to 0.003 ppm and to classify arsine as a known human carcinogen.

The proposed change to the TLV is primarily based on the data from two subchronic rodent studies. ACGIH's interpretation of these studies is that subchronic exposure to 0.025 ppm arsine (6 hr/day, 5 days/week for 13 weeks) causes significant anemia in rats and hemolysis and hematopoietic system stress in mice [1, 2].[1] In both studies, the latter value (0.025 ppm) was considered to be the lowest observed adverse effect level (LOAEL). Dividing that number by an uncertainty factor of 10 yields a proposed TLV of 0.003 ppm.

There is no human data from which one could estimate an exposure level that would be protective against hematopoietic effects. However, it is important to note that such effects have not been reported in workers protected by the ACGIH TLV of 0.05 ppm since 1948.

The proposed ACGIH change from no carcinogen designation to an A1 confirmed human carcinogen is based on the premise that as arsine passes through the lungs it is metabolized in the body to inorganic arsenic compounds, which are considered to be human carcinogens. The latter compounds have been found in the urine of workers exposed by inhalation to arsine [3]. In addition, the current Environmental Protection Agency (EPA) Maximum Contaminant Level (MCL) of 50 µg/L for arsenic in drinking water is intended to provide protection (against cancer) for the general population of humans. This value represents an arsenic ingestion of approximately 100 µg/day (micrograms per day).

It is also assumed that an equivalent amount of arsenic could be absorbed from the air by workers breathing an atmosphere of 10 $\mu g/m^3$ of arsine (approximately 0.003 ppm, assuming 100% retention), which is another reason for ACGIH's recommendation for a 0.003 ppm TLV with an A1 confirmed human carcinogen designation. ACGIH proposed the cancer designation despite the fact that there are no human or animal data to show that arsine is carcinogenic or genotoxic.

CGA believes that the two ACGIH proposals on arsine appear to be the result of an incomplete and inaccurate risk assessment, believes that the animal studies were conducted on an inappropriate species as detailed in this technical report, and believes that the human data on arsine metabolites is based on mixed arsine/arsenic species exposure. In addition, CGA believes that the decision of the carcinogenicity designation for arsine was premature and is not supported by the scientific literature.

In conclusion, after reviewing the toxicity literature on arsine and inorganic arsenic oxides in both animals and humans and ACGIH's rationale of for its decisions on arsine, CGA concludes that there is no adequate scientific evidence to support a reduction of the current TLV for arsine from 0.05 ppm to 0.003 ppm or to support an A1 confirmed human carcinogen designation. Details on CGA's position are provided in the following sections.

2 Animal studies

The two rodent studies that provide the main basis for lowering the TLV (subchronic hematopoietic effects in rats and mice at 0.025 ppm) have serious limitations and may have been misinterpreted [1, 2]:

- The rodent is not a suitable model for arsine or arsenic toxicity because the metabolism (i.e., methylation pattern of arsenic metabolites), absorption, distribution, and excretion of arsenic in rodents are significantly different from humans. This is particularly true for the rat [4];

[1] References are shown by bracketed numbers and are listed in order of appearance in the reference section.