WHITE PAPER ON BENZENE TOXICITY

I. Background Information

Benzene is a clear, colorless liquid at ambient temperatures. Benzene has a relatively high vapor pressure and thus evaporates quickly into the air. The odor threshold for benzene has been reported as 12 parts per million. Benzene occurs naturally in crude oil and is widely used in industry as a raw material for the production of other organic chemicals. Most gasolines sold in the United States contain between one and two percent benzene (World Health Organization, 1993; ACGIH, 2001; Bruckner, et al., 2008). Benzene is present in most outdoor and indoor environments. Most benzene exposures to the general public are associated with the use of gasoline powered vehicles and other equipment. Benzene is also found in some consumer products and is present in main stream and side stream tobacco smoke (Wallace, 1996).

II. Summary of Health Effects of Benzene Exposure

A. Non-cancer Health Effects

1. Effects of short-term exposures

The acute effects of over-exposure to benzene are well known in general terms. Effects on the central nervous system predominate, but benzene exposure can also cause irritation, cardiovascular effects, and effects on the kidney. There is little quantitative data in the toxicity literature concerning human health effects associated with acute exposures to benzene.

Volunteers exposed for eight hours to 25 parts per million (ppm) of benzene suffered no ill effects. Headache, lassitude, and weariness were reported when six-hour exposures of 50-150 ppm were encountered. Exposures to 500 or more ppm for one hour caused headache and other ill effects. Acute exposures to high levels of benzene can cause eye, skin, and respiratory irritation; difficulty breathing; cardiovascular effects such as ventricular fibrillation; gastritis; kidney congestion; and neurological effects such as distal neuropathy, abnormalities in nerve conduction velocity, difficulty sleeping, and memory loss (Cavender, 1996). At very high levels of exposure confusion, convulsive movements, paralysis, and death can occur (Cavender, 1996; Galbraith, et al., 2010).

2. Effects of longer-term exposures

Intermediate and chronic exposures to benzene cause a variety of pathological states. These include cytopenia (anemia, leukopenia, or thrombocytopenia) which is a decrease in various cellular elements of the circulating blood; central nervous system effects such as headache, dizziness, fatigue, anorexia, visual disturbances, and hearing loss; and respiratory irritation evidenced by difficulty breathing (ATSDR, 2007;

Cavender, 1996). Benzene has also been shown to be an immunosuppressive agent (Synder, 1984).

B. Cancer

The critical effect of chronic benzene exposure is an increased risk of cancer. Benzene exposure at a high enough level for a long enough time is known to cause acute myelogenous leukemia (AML). Chronic high-level benzene exposure has also been shown to cause myelodysplastic syndrome (MDS) a cancerous condition which can progress to leukemia (Synder, 2002; Bruckner, et al., 2008). More recent studies have shown and increased risk of MDS at lower levels of benzene exposure, but those associations have not been statistically significant (Schnatter, et al., 2012; Stenehjem, et al., 2015). Benzene can also cause chromosomal aberrations in humans. Chromosomal analyses have been used in investigations of benzene exposures (Zhang, et al., 2002).

III. Historical Aspects of Knowledge of Benzene Toxicity

The fact that benzene exposure can cause chronic, as well as acute effects was first noted as early as 1897. Animal experiments and occupational exposure studies conducted in the early part of the 20th century showed long-term benzene exposure particularly affects the hematopoietic system (Ferguson, et al., 1933). An early article published in the Journal of the American Medical Association described the types of effects to be expected from occupational exposures to benzene (McCord, 1929). More reports of benzene toxicity continued to become available in the 1930s and 1940s.

In the early 1940s many industries were abandoning the use of benzene as a solvent (Gafafer, 1943). A widely-quoted report issued in the late 1940s by the American Petroleum Institute noted the effects of acute and chronic benzene exposure. While recommending a 50 parts per million (ppm) occupational standard, they stated the only "absolutely safe" level of benzene exposure was zero (API, 1948).

An association between long-term benzene exposure and human leukemia was suggested by a series of case reports beginning in the 1930s up through the 1960s (Galbraith, et al., 2010). Subsequent epidemiologic studies carried out beginning in the 1970s confirmed those findings (Rinsky, et al., 1981; Rinsky, et. al., 1987). Various organizations have now concluded there is a causal relationship between excess benzene exposure and the development of acute myelogenous leukemia (WHO, 1993; NTP, 2005; ATSDR, 2007).

IV. Health-Based Exposure Standards and Guidelines for Benzene

Benzene is considered to be a known human carcinogen by Occupational Safety and Health Administration (OSHA), the Environmental Protection Agency (EPA), the

National Institute for Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH), and the International Agency for Research on Cancer (IARC) among others.
Occupational exposure guidelines and standards have decreased markedly over the years. Up until 1948, 100 ppm was considered a safe level to which workers could be exposed for 8 hours a day, 5 days a week, over a working lifetime. Exposure guidelines were revised downwards to 50 ppm in 1948; 35 ppm in 1949; 25 ppm in 1957; and 10 ppm in 1972. In 1987 the Occupational Health and Safety Administration (OSHA) reduced the occupational exposure limit to its current value of 1 ppm (Galbraith, et al., 2010).

Other occupational exposure standards and guidelines currently exist for benzene. OSHA has set a Permissible Exposure Limit at 1 ppm as an 8-hour average and a Short Term Exposure Limit (STEL) of 5 ppm as a 15-minute average. The National Institute for Occupational Safety and Health Recommended Exposure Limit is and 8-hour limit of 0.1 ppm and their STEL is 1 ppm (NIOSH, 2007). The American Conference of Governmental Industrial Hygienists has set a Threshold Limit Value of 0.5 ppm as an 8-hour average and a 15-minute average STEL of 2.5 ppm (ACGIH, 2014). These levels have been set to protect workers from the adverse effects of benzene exposure, including cancer.

Other agencies and organizations have also set exposure guidelines for community exposures to benzene. The Agency for Toxic Substances and Disease Registry (ATSDR) has set “Minimal Risk Levels” for benzene of 0.009 ppm for a 24-hour exposure, 0.006 ppm for exposures lasting from 1 to 14 days, and 0.003 ppm for longer exposure periods. These are levels that are believed to be without risk for adverse health effects (ATSDR, 2009). The American Industrial Hygiene Association, in conjunction with the U.S. Department of Defense, has set “Emergency Response Planning Guidelines” based on the acute health effects of benzene exposure. They have established that a one-hour exposure to 50 ppm of benzene can cause mild, transient health effects; a one-hour exposure to 150 ppm could cause serious transient or irreversible health effects; and a one-hour exposure to 1,000 ppm of benzene could be life-threatening (AIHA, 2010).

IV. Summary

Benzene is widely used in industry and is present at low levels in most outdoor and indoor environments. Exposure to elevated levels of benzene can cause a variety of adverse health effects. Non-cancer effects of over-exposure to benzene include effects on the respiratory system, the nervous system, the cardiovascular system, the gastrointestinal system, and the kidney. Benzene is a known human carcinogen. Over-exposure to benzene has been shown to cause acute myelogenous leukemia and myelodysplastic syndrome in humans.

Disclaimer: The information in this white paper is current as of mid-2015. Research into the carcinogenic and non-carcinogenic health effects of benzene is on-going. For the latest information, please contact Dr. Dydek directly at dydek@tox-expert.com.

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