Isoprene is the 2-methyl analogue of 1,3-butadiene, which is currently classified as a known human carcinogen. While isoprene is synthesized and used in the manufacturing of substances such as synthetic rubber, it is also produced naturally by plants, animals, and bacteria and is one of the main endogenous compounds found in human breath. Following the Texas Commission on Environmental Quality (TCEQ) Guidelines for the development of toxicity factors, a preliminary review and characterization of the carcinogenic potential of isoprene was conducted. Three key animal studies provided adequate data for the dose-response assessment of isoprene’s carcinogenic potential. In order to determine URFs for study endpoints assuming exposure for 24/7,70% for a lifetime, the dose levels and numbers of animals at risk in the data sets were adjusted for differences between the exposure durations and times of response observation. The doses were adjusted to the constant lifetime environmental dose that is equivalent to the time-dependent doses in the studies, based on the multistage theory of carcinogenesis using the Armitage and Doll (1954) mathematical description of carcinogenesis with the number of stages being m = 1, 2, or 3. Similarly, the number of subjects at risk of developing the specified response by necropsy time in the study was adjusted to the equivalent number of animals at risk if the time to necropsy were equal to the normal animal lifetime. The adjusted parameters were used to carry out 217 model fits. The ECbottom for each endpoint was identified using the estimated multistage models, and from there a URF for each endpoint was calculated. Based on the TCEQ Guidelines, only endpoint studies considered relevant to humans and showing a statistical significance were considered for the draft URF. The chosen draft URF was 0.04 ppm for liver carcinoma in a one-stage carcinogenesis process (m=1). From the draft URF, a draft air concentration corresponding to a 1E−5 lifetime excess cancer risk is calculated to be 1.1 ppb.

CARCINOGENIC POTENTIAL

There are currently no human exposure studies available for isoprene; however, there are three chronic animal studies available that provide evidence of carcinogenicity in mice (Mehlman et al. 1994 and Placke et al. 1996) and rats (Mehlman et al. 1996). Increased incidences of neoplasms were observed in the lungs, liver, baderen gland, bone marrow, hematopoietic system, and circulatory system in mice exposed to isoprene via inhalation. In rats, increased incidences of neoplasms were observed in the mammary gland, kidney, liver, and testes. While there are currently no human exposure studies indicating that inhalation exposure to isoprene increases the risk of cancer, due to the formation of tumors at multiple sites in multiple animal species, isoprene has been classified by the National Toxicology Program’s Report on Carcinogens as a potential human carcinogen. As such, it is the policy of the TCEQ to conduct a carcinogenic dose-response assessment for chemicals considered “likely to be carcinogenic to humans.”

MATHEMATICAL ADJUSTMENTS TO THE DATA

DRAFT TOXICITY FACTOR

A draft Unit Risk factor for URF and isoprene air concentration at 1 in 100,000 excess cancer risk were calculated using the above POD. Without strong evidence of a non-linear model, the default procedure is to use a linear approach to this calculation. To determine the best estimate lifetime excess cancer risk resulting from continuous exposure to isoprene at 1 ppb, the following equation is used:

\[
\text{U} = \frac{\text{RID}}{\text{URF}}
\]

U = the 10−5 risk concentration is then calculated based on the URF using the following equation:

\[
10^{-5} \text{ risk concentration} = 1 \times 10^{-5} \times \frac{1}{\text{URF}}
\]

The DRAFT calculated URF and air concentration corresponding to a 1 in 100,000 excess cancer risk are:

- DRAFT URF (risk per ppb) = 0.04
- DRAFT air concentration = 0.04 ppm

REFERENCES