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Health- and vegetative-based effect screening values for ethylene

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ABSTRACT

Ethylene (ET) is ubiquitous in the environment and is produced both naturally and due to anthropogenic sources. Interestingly, the majority of ambient ET contribution is from natural sources and anthropogenic sources contribute only a minor portion. While microbes and plants naturally produce a large amount of ET, mammals are reported to produce only a small amount of ET endogenously. Anthropogenic sources of ET include the combustion of gas, fuel, coal and biomass. ET is also widely used as an intermediate to make other chemicals and products and is also used for controlled ripening of fruits and vegetables. Although, a review of human and laboratory animal studies indicate ET to be relatively non-toxic, there is concern about the potential toxicity of ET because ET is metabolically converted to ethylene oxide (EtO). EtO has been classified to be carcinogenic to human by the inhalation route by the International Agency for Research on Cancer (IARC) cancer. ET, however, has been classified as a Group 3 chemical which indicates it is not classified as a human carcinogen by IARC. Several studies have reported ET to cause adverse effects to plant species (vegetation effects) at concentrations that are not adverse to humans. Therefore, the Texas Commission of Environmental Quality (TCEQ) conducted detailed health and welfare (odor and vegetation) based assessments of ET to develop both health and vegetative based toxicity factors in 2008 in accordance with TCEQ guidelines. The health assessment based on well-conducted animal toxicity studies resulted in identification of higher points of departures and subsequently higher effect screening levels (ESLs) that were more than a magnitude higher than the threshold adverse effect level for vegetative effects for ET. Further, based on a weight-of-evidence evaluation of potential mutagenic and carcinogenic mode-of-actions for ET it appears the metabolic conversion of ET to EtO is of insufficient magnitude to cause concern of potential cancer risk. Therefore, the short-term ESL for air permit reviews and air monitoring evaluations is the vegetation-based ESL of 1200 ppb as it is more than a magnitude lower than the health-based acute ESL of 150,000 ppb. Similar to the acute derivation, the chronic evaluation resulted in the derivation of a chronic vegetation based ESL of 30 ppb that was much lower than the chronic ESL of 1600 ppb. In summary, the TCEQ's acute and chronic ESLs for vegetation will protect the general public from short-term and long-term adverse health and welfare effects. The general public includes children, the elderly, pregnant women, and people with pre-existing health conditions.

1. Introduction

ET (CAS No. 74-85-1) is produced both naturally and due to anthropogenic sources. The Organization for Economic Co-operation and Development (OECD) reports the majority of the global ET emissions (approximately 74%) to be from natural sources whereas the remainder (approximately 26%) of global ET emissions comes from anthropogenic sources [38]. All types of vegetation including plants, microbes and marine algae naturally produce ET. In addition decomposition of organic matter by soil microorganisms and burning of wood and biomass during forest fires can release ET. Volcanic emissions and natural gas leakage release a relatively small amount of ET [38]. A relatively small amount of ET is produced endogenously in mammals through lipid peroxidation of unsaturated fats, oxidation of free methionine, oxidation of hemin in hemoglobin, and metabolism of intestinal bacteria [26].

ET has been reported to be the largest volume organic chemical produced worldwide and is produced mainly by the steam-cracking of hydrocarbons. It is considered a basic building block in the

Abbreviations: AMCV, Air Monitoring Comparison Value; DSD, Development Support Document; EPA, Environmental Protection Agency; ESL, effects screening level; ET, ethylene; EtO, ethylene oxide; ReV, reference value; TCEQ, Texas Commission on Environmental Quality.

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chemical and petrochemical industries because it is an essential intermediate in the production of other industrial chemicals and polymers such as polyethylene, ethylene oxide, ethylene dichloride and ethylbenzene, styrene, and vinyl chloride [4]. Burning of hydrocarbons and biomass can also produce significant amounts of ET [38].

ET is a colorless gas (at ambient temperatures) with a faint sweet odor, is a liquid under pressure, and is slightly soluble in water. ET has a low blood-gas partition coefficient and does not accumulate in the body [38]. ET is also a highly flammable volatile gas that is considered to be a fire hazard at sufficiently high concentrations. In occupational settings, very high concentrations of ET can lower oxygen concentrations and has been reported to function as an asphyxiant [14].

ET is widely used as a fruit and vegetable ripening agent and as a pesticide. In the past, ET was widely used as an anesthetic agent but was discontinued because of its flammable properties and its ability to cause asphyxiation at high concentrations. Even though ET has been used as an anesthetic in the past and its continued and prevalent use as an artificial ripening agent indicate it to be non-toxic, there is concern about the potential toxicity of ET because ET is metabolically converted to ethylene oxide (EtO) (CAS No 75-21-8). EtO has been classified by the IARC to be carcinogenic to humans by the inhalation route (Group 1) [29,30]. EtO is also a genotoxicant and is a potent alkylating agent that can form adducts by interacting with cellular macromolecules such as DNA, RNA, and protein, although adduct detection does not necessarily translate to cancer [20,60,11,44,46,47].

ET is a unique chemical because it is both an air toxic and an important regulatory plant hormone. As an air toxic, ET can cause adverse vegetation effects in plants and crop species at concentrations not harmful to humans. As a plant hormone, it is produced naturally at many of the stages of plant growth, and has been reported to regulate both the morphological (e.g., leaf abscission and epinasty (leaf curling)) and physiological effects (e.g., bud formation, inhibition of flowering, photosynthesis, senescence, sprouting of buds, seed germination, and flower formation). In addition, ET can stimulate or inhibit the growth process. Interestingly, fruits (e.g., apples, oranges, and avocados) naturally release ET during maturation, which in turn promotes the ripening of the fruits.

Interest in ET research spiked when it was identified to be phytotoxic to greenhouse plants [17]. Later, Abeles et al. [1] reported 10 ppb as the threshold concentration for physiological effects from studies in greenhouse experiments with ET. It was soon realized it was important to confirm if the extremely low threshold concentrations reported by Abeles and co-workers are relevant to field grown plants. Among the issues surrounding the applicability of the results reported by Abeles et al. [1] is the fact that greenhouse plants are normally exposed to very high concentrations of ET in a continuous manner, unlike field grown plants that generally experience lower concentrations of ET, and the exposure pattern is said to be discontinuous [51,52]. Greenhouse plants are also less hardy when compared to the field-grown plants and may experience more adverse effects [53].

Texas has a large petrochemical industry and there is potential for point sources of ET emissions to influence ambient ET levels, and subsequently, there is potential for community exposures from point sources of ET emissions. The TCEQ relies on its large air permitting program and extensive ambient monitoring network to both permit and monitor a suite of chemicals including ET [13]. The air permitting program and the air monitoring program use TCEQ's science-based chemical specific values (Effect Screening Levels (ESLs) and Air Monitoring Comparison Values (AMCVs)) to permit and evaluate the potential for community exposures from point sources [50]. If the ambient monitoring reports exceedances, then the exceedances are reviewed for their magnitude and frequency, prior to recommending if additional scrutiny is warranted.

Systematic reviews of diverse streams of data (human chamber, animal, and mechanistic) are recognized to be integral to risk assessments by many entities [37,41]. ET is a well-studied chemical and there are well-conducted human chamber, animal toxicological, mechanistic, and vegetation studies. Because of the potential human exposure and adverse vegetation effects, the TCEQ in 2007 decided to conduct hazard assessments of both the health and vegetation end points to determine both health and vegetation based ESLs for ET. Specifically, the TCEQ's assessments resulted in deriving up to four comparison levels: (1) acute health-based ESL, (2) acute vegetation-based ESL, (3) chronic health-based ESL and (4) chronic vegetation-based ESL. A detailed discussion of the hazard assessments is available in a Development Support Document (DSD) that also underwent an internal review and an external public comment period [49]. Since the DSD was prepared in 2008; a review of the current literature was conducted to determine whether the procedures to develop health and vegetation ESLs need to be updated. The purpose of this paper is to briefly present the procedures and ESLs determined for the chronic health and vegetation hazard assessments of ET and are based on TCEQ guidance developed in 2006 [48]. Due to space restriction, the results of the acute health and vegetation hazard assessments are only discussed briefly.

2. Methods

Chronic and acute health-based and vegetation-based ESLs were derived after conducting hazard assessments following the TCEQ guidelines [48]. ESLs are intended to be comparison levels and are used in the TCEQ's air permitting process to help ensure authorized emissions of air contaminants do not cause or contribute to a condition of air pollution. Specifically, chronic ESLs protect against chronic health effects and vegetation effects and acute ESLs protect against short-term health effects, nuisance odor conditions, and vegetation effects. Acute ESLs also consider that ambient exposure is dependent on meteorology and source emission patterns, and peak exposure could occur several times per day. Additional TCEQ guidance is available that describes how ESLs are used in the air permitting process [50,48].

2.1. Development of health-based ESLs for ET

For the health-based ESLs the TCEQ guidelines employed the four-step risk assessment process formalized by the National Research Council [34,35] and procedures recommended in numerous U.S. EPA risk assessment guidance documents and the scientific literature [55,56,57,39,36]. While, there are a few human exposure studies using ET these were mainly conducted to understand EtO burden in ET-exposed humans and hence did not provide adequate information to identify critical effects and consequently an appropriate point of departure (POD). The majority of ET exposure studies have been conducted using laboratory animals, and these studies were selected as key studies for both the chronic and acute health-based ESL determinations.

The following analytical approach was used for hazard identification and dose-response assessments to derive health-based ESLs for ET: (1) conduct comprehensive literature review including physical/chemical properties and select key studies; (2) conduct human relevant mode of action (MOA) analysis; (3) choose the appropriate dose metric; (4) determine the POD for the key study(s); (5) conduct appropriate dosimetric modeling (i.e., duration adjustments) and determine the human equivalent POD (POD_{HEC}); (6) select the critical effect and apply appropriate