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Ethylene

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TEXAS COMMISSION ON ENVIRONMENTAL QUALITY

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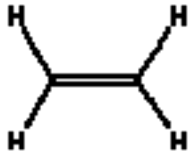
Table 1. Health - and Welfare-Based Values

Short-Term Values	Concentration	Notes
$^{acute}ESL_{veg}$	1,400 µg/m^3 (1,200 ppb) * **Short-Term ESL for Air Permit Reviews**	This value is a sub-threshold concentration that is protective of all crop plants including flowering plants
$^{acute}ESL$ [1 h] (HQ = 0.3)	170,000 µg/m^3 (150,000 ppb)	**Critical Effect**: hepatic damage in male Holtzman rats, based on a free-standing NOAEL
acute ReV (HQ = 1.0)	570,000 µg/m^3 (500,000 ppb) *	
$^{acute}ESL_{odor}$	310,000 µg/m^3 (270,000 ppb) *	50% odor detection threshold
Long-Term Values	**Concentration**	**Notes**
$^{chronic}ESL_{veg}$	34 µg/m^3 (30 ppb) * **Long-Term ESL for Air Permit Reviews**	This value is a threshold concentration that is protective of all crop plants including flowering plants
$^{chronic}ESL_{nonlinear(nc)}$ (HQ = 0.3)	1,800 µg/m^3 (1,600 ppb)	**Critical Effect**: hepatic damage in Fischer 344 rats based on free-standing NOAEL
chronic ReV (HQ = 1.0)	6,100 µg/m^3 (5,300 ppb) *	
$^{chronic}ESL_{linear(c)}$ $^{chronic}ESL_{nonlinear(c)}$	---	No evidence of carcinogenic potential

* Values that may be used for evaluation of air monitoring data

Abbreviations used: **ppb**, parts per billion; **µg/m^3**, micrograms per cubic meter; **h**, hour; **ESL**, Effects Screening Levels; **ReV**, Reference Value; **^{acute}ESL,** acute health-based ESL; **^{acute}ESL$_{odor}$**, acute odor-based ESL; **^{acute}ESL$_{veg}$**, acute vegetation-based ESL; **^{chronic}ESL$_{nonlinear(nc)}$**, chronic health-based ESL for nonlinear dose-response noncancer effects, **^{chronic}ESL$_{linear(c)}$**, chronic health-based ESL for linear dose-response cancer effects; **^{chronic}ESL$_{nonlinear(c)}$**, chronic health-based ESL for nonlinear dose-response cancer effect; and **^{chronic}ESL$_{veg}$**, chronic vegetation-based ESL; **HQ**, Hazard Quotient.; **NOAEL**, no-observed-adverse-effect level

Table 2. Chemical and Physical Data		
Parameter	**Value**	**Reference**
Molecular Structure		ChemFinder 2004
Molecular Formula	C_2H_4	ChemFinder 2004
Molecular Weight	28.05	ChemFinder, 2004
Physical State	Volatile gas, highly flammable and a dangerous fire risk, liquid under pressure	ACGIH 2005[a], ACC 2004[b]
Color	Colorless	ACGIH 2005[a], ACC 2004[b]
Odor	Faint Sweet	ACGIH 2005[a], ACC 2004[b]
CAS Registry Number	74-85-1	ACGIH 2005[a], ACC 2004[b]
Synonyms	Acetene; Elayl; Olefiant Gas; Refrigerant 150; Ethene; UN1038 (refrigerated liquid), UN1962 (compressed liquid), Athyllen [German], Bicarburretted hydrogen; Caswell No. 436; EINECS 200-815-3; EPA Pesticide Chemical Code 041901; Etileno; HSDB 168	ACC 2004[b]
Solubility in water	26 g/L- Slightly soluble	ChemFinder 2004
Log K_{ow} or P_{ow}	Log P_{ow}= 1.13	ACC 2004[b]
Vapor Pressure	760 mmHg @ -104°C	Matheson Tri-Gas[c]
Relative Vapor Density @ 32º F (gas; air =1)	0.975	ACC 2004[b]
Density (liquid) @ Critical Temperature (48.54 ºF)	13.36 lb/ft^3; 1.786 lb/gal; 0.21 g/cm^3	ACC 2004[b]
Melting Point	-169.14°C	ChemFinder 2004
Boiling Point	-103.7°C	ChemFinder 2004
Conversion Factors at 25ºC and 1 atmosphere	1 ppb = 1.15 µg/m^3 1 µg/m^3 = 0.87 ppb	Alberta Environment 2003 Toxicology Section

[a]American Conference of Governmental Industrial Hygienists (ACGIH)
[b]American Chemistry Council (ACC) 2004
[c]Matheson Tri-Gas Material Safety Data Sheet

Chapter 2 Major Uses and Sources

Ethylene is produced through both natural and anthropogenic activity. Microbes and higher plants naturally produce ethylene. Ethylene is also released during forest fires and active volcanic events. In higher plants, ethylene functions as a plant hormone and ethylene production can either increase or decrease in response to a variety of environmental stressors such as flooding, wounding (e.g., mechanical and/or pathogenic attack), chemical exposure (e.g., ozone), and mechanical bending (*e.g.,* lodging) (Health Canada 2001).

Ethylene is also produced endogenously in mammals through lipid peroxidation of unsaturated fats, oxidation of free methionine, oxidation of hemin in hemoglobin, and metabolism of intestinal bacteria (Health Canada 2001). However, ethylene production in mammals is only a minor contributor to atmospheric ethylene when compared to the relative contribution from microbial, vegetative, and industrial sources (Health Canada 2001).

In occupational settings, very high concentrations of ethylene can lower oxygen concentrations and has been reported to function as an asphixiant (Cavender 1994). Ethylene is primarily used as an intermediate in the production of other chemicals and as an agent to enhance the ripening process of fruits, vegetables, and flowers. Ethylene is also a high-production-volume chemical product of the petrochemical industry, produced mainly by the steam-cracking of hydrocarbons. Industrial contribution to ambient ethylene is primarily due to fugitive emissions from stacks, flares, and leaks in pipe fittings that can result in a discontinuous exposure scenario (Health Canada 2001).

Ambient ethylene is also produced during incomplete combustion of biomass and fossil fuels. While gasoline itself does not contain ethylene, the combustion of gasoline causes ethylene to be emitted into the ambient air. A relatively large proportion of ethylene in urban air is due to vehicular traffic emissions (Abeles and Heggestad 1973).

Chapter 3 Acute Evaluation

3.1 Health-Based Acute ReV and ESL

3.1.1 Physical/Chemical Properties and Key Studies

3.1.1.1 Physical/Chemical Properties

Ethylene is a highly-flammable volatile gas that is considered to be a fire hazard at sufficiently high concentrations. It is a colorless gas with a faint sweet odor, is a liquid under pressure, and is slightly soluble in water (Chemfinder 2004). The main physical and chemical properties of ethylene are summarized in Table 2. Ethylene has been reported to be relatively non-toxic, has a low blood-gas partition coefficient and does not accumulate in the body.

3.1.1.2 Essential Data and Key Studies

The inhalation toxicity studies conducted by Conolly et al. (1978) and Guest et al. (1981) were selected as key studies to determine the acute Reference Value (ReV) and the acute Effect Screening Level (^{acute}ESL). The study conducted by Conolly and Jaeger (1977) was selected as a supporting study.

3.1.1.2.1 Conolly et al. (1978)

In the Conolly et al. (1978) studies, a group of male Holtzman rats were exposed to 10,000, 25,000, or 50,000 ppm ethylene for 4 h. A second group of rats were administered a combined exposure protocol with polychlorinated biphenyl (PCB) mixture (300 µmoles of PCB/kg of body weight) *via* gavage once daily for 3 days followed by 4 h of inhalation exposure to the various concentrations of ethylene. In addition, control groups were included with rats exposed to PCB alone.

In the study, hepatic damage was assessed by conducting histopathology of the liver and by measuring the levels of hepatic enzymes including sorbitol dehydrogenase (SDH) and serum alanine-alpha-ketoglutarate transaminase (SAKT). Elevated levels of SAKT and SDH are often indicative of liver damage. The authors reported ethylene concentrations at 10,000 ppm to be hepatotoxic only when the rats were pre-treated with the PCB mixture. Specifically, rats that were exposed to ethylene after exposure to PCB mixture were reported to have elevated levels of SDH and the liver of the rats had severe degenerative necrosis.

The authors reported no increase in hepatic enzymes and no liver damage in rats exposed to ethylene alone. A no-observed-adverse-effect-level (NOAEL) of 50,000 ppm was determined from the exposure group of rats exposed only to ethylene. As the studies did not provide any other toxicological information, such as lowest-observed-adverse-effect-level (LOAEL), the NOAEL will be considered a free-standing NOAEL.

3.1.1.2.2 Guest et al. (1981)

Guest et al. (1981) also studied the toxicity of ethylene alone and in conjunction with PCBs. For the ethylene-only exposure group, the authors exposed Fisher rats for 5 h to 10,000 ppm ethylene. For the combined exposure (i.e., PCB mixture + ethylene), the authors administered 500 mg/kg PCB mixture *via* gavage five days prior to exposing the rats for 5 h to 10,000 ppm of ethylene. Control groups included rats exposed either to ethylene alone or rats exposed to only the PCB mixture.

Similar to the Conolly et al. studies, Guest et al. (1981) reported no increase in serum enzyme activities and no necrotic tissue for the ethylene only exposure groups. Exposure only to the PCB mixture, without subsequent exposure to ethylene, resulted in slight hypertrophy of centrolobular liver cells with no hepatocellular necrosis. However, animals exposed to 10,000 ppm ethylene after pre-treatment with the PCB mixture, had uniform hepatic centrolobular necrosis. In addition, the authors also reported elevated hepatic enzyme levels in the combined exposure group (PCB mixture + 10,000 ppm ethylene). As no LOAEL information was available, a free-standing NOAEL of 10,000 ppm was determined from the group exposed only to ethylene.

The results from the acute exposure studies indicate that very high doses of ethylene coupled with high doses of the PCB mixture are required to elicit hepatotoxic responses in rats. Guest et al. (1981) hypothesized that the PCB mixture induced the hepatic mixed-function oxidase (MFO) system that then resulted in hepatotoxicity in the rats.

3.1.1.2.3 Conolly and Jaeger (1977)

The study conducted by Conolly and Jaeger (1977) was selected as a supporting study. Similar to Conolloy et al. (1978) studies, Conolly and Jaeger (1977) studied the acute hepatotoxicity of ethylene and other chemicals with and without PCB pre-treatment. Male Holtzman rates were exposed up to 50,000 ppm ethylene. In addition to hepatic injury, the authors also studied the effects of changes in environmental parameters (i.e., changes in temperature during exposure and food deprivation. The authors reported ethylene to be more acutely toxic in rats that were fasted when compared to rats that were fed and PCB –pre-treated. The authors attribute depletion of glutathione to be higher in the fasted rats.

3.1.1.2.4 Other Studies Reviewed by TS

Aveyard and Collins (1997) conducted a reproductive/developmental toxicity screening study with head only exposures to rats. A total of 10 animals/sex/group were exposed to 5,000 ppm of ethylene for 6 h/day for 2 weeks prior to mating and during the mating period. Female rats were also exposed to ethylene until gestational day 20. No effects on weight gain, food intake, fertility, fecundity, sex ratio, and pup weight or pup growth were reported. This study was described in the Organization for Economic Co-Operation and Development (OECD) dossier on ethylene.

3.1.2 Mode-of-Action (MOA) Analysis and Dose Metric

Ethylene is metabolically converted to ethylene oxide (EtO) *via* the cytochrome P-450 pathway (Filser and Bolt 1983). Concern about the potential toxicity of ethylene stems from the fact that EtO is a suspected human carcinogen and a genotoxicant (ACGIH 2005 and Tornqvist 1994). In addition, EtO is also a potent alkylating agent and can form adducts by interacting with cellular macromolecules such as DNA, RNA, and protein (e.g., hemoglobin). Similar adduct formation has been reported on direct exposure to EtO (ACGIH 2005).

While adducts have been used as biomarkers of DNA damage, their use is controversial. There is some controversy in regards to whether adduct formation is indicative of exposure, and if adducts can be unequivocally utilized as precursors of diseases such as cancer (Selinski et al. 2000). A few studies reported the detection of hemoglobin adduct formation on exposure to ethylene. One example is the identification of hemoglobin adducts (i.e., hydroxyethylvaline adducts) in the serum of fruit storage workers exposed to approximately 0.3 ppm ethylene (Tornquist et al. 1989). Similar results have also been reported in plastic industry workers exposed to ethylene (Granath et al. 1996).

Very few human exposure studies using ethylene have been conducted. The majority of ethylene exposure studies have been conducted using animals. When using animal studies, it is beneficial to extrapolate the risks observed in animals to humans using physiologically-based-pharmacokinetic (PBPK) models. Filser et al. (1992) measured ethylene uptake by exposing 6 human subjects for 2 h in controlled chambers to 5 and 50 ppm of ethylene. The authors reported 98% of the ethylene to be exhaled

unchanged and only 2% of the ethylene was absorbed and metabolized to EtO. Similar to humans, most of the inhaled ethylene (83%) in rats was exhaled unchanged. Further, the relatively smaller fraction of ethylene that was actually absorbed was also reported to be eliminated unchanged in rats (Filser and Bolt 1983).

The metabolic conversion of ethylene to EtO has been reported to be a rate-limiting step resulting in only an insignificant amount of EtO being produced during the process (Bolt and Filser 1987 and Csanady et al. 2000). At 37 ppm ethylene exposure in rats, Bolt and Filser (1987) estimated a 1 ppm equivalent exposure to EtO in humans, while Csanady et al. (2000) have reported an exposure of 45 ppm ethylene in rats to be equivalent to a 1 ppm EtO exposure in humans.

3.1.3 Points of Departure (PODs) for the Key Studies

A POD of 50,000 ppm based on a free-standing NOAEL was determined from the Conolly et al. studies, and a POD of 10,000 ppm based on a free-standing NOAEL was determined from the Guest et al. (1981) study. In the toxicity study selected as the key study, data on the exposure concentration of the parent chemical are available. Since the MOA of the toxic response is not fully understood and data on other more specific dose metrics are not available (e.g. blood concentration of parent chemical, area under blood concentration curve of parent chemical, or putative metabolite concentrations in blood or target tissue), the exposure concentration of the parent chemical was used as the default dose metric.

3.1.4 Dosimetric Adjustments

3.1.4.1 Default Exposure Duration Adjustments

In accordance to the ESL Guidelines, a duration adjustment for 1 h is recommended if the data are obtained from acute toxicity studies with greater than 1 h exposure (TCEQ 2006). However, as the reported PODs in the key studies were relatively very high (i.e., indicative of low toxicity) and because no adverse effects were observed in the key studies at either the 4 h and/or 5 h study, the Toxicology Section (TS), did not conduct duration adjustments and considered the POD for 1 h to be the same as the POD determined for exposure durations greater than 1 h (i.e., 50,000 ppm from the Conolly et al. and 10,000 ppm from the Guest et al. (1981) study).

The POD determined from the Conolly et al. studies (50,000 ppm) is higher than the POD determined from the Guest et al. (1981) study and is selected by the TS as the POD to derive a health-based acute reference value (acute ReV) and effects screening level (ESL). The TS selected the higher POD based on the fact that the key and supporting studies only determined a free-standing NOAEL and on US. EPA's (2002) definition of a NOAEL,"The highest exposure level at which there are no biologically significant increases in the frequency or severity of adverse effect between the exposed population and its appropriate control". Some effects may be produced at this level, but they are not considered adverse or precursors to adverse effects".

3.1.4.2 Default Dosimetry Duration Adjustments from Animal-to-Human Exposure

As no duration adjustments are required, the POD becomes POD_{ADJ} and is 50,000 ppm. The POD_{ADJ} is then adjusted to human equivalent POD or $POD_{HEC.}$ Ethylene is relatively non-toxic even at high concentrations as it does not produce point of entry (POE) respiratory effects and the critical effect is

hepatotoxicity. The TS will consider ethylene as a Category 3 gas and the duration exposure adjustments from animals to humans will be conducted with the following equation:

$$POD_{HEC} = POD_{ADJ} \times ((H_{b/g})_A / (H_{b/g})_H)$$

Where,
POD_{HEC} = Point of Departure at Human Equivalent Concentration
POD_{ADJ} = Adjusted Point of Departure
$H_{b/g}$ = Ratio of blood:gas partition coefficient
A = Animal
H = Human

According to USEPA (1994), if the animal blood:gas partition coefficient is greater than the human blood:gas partition coefficient, a default value of 1 is used for the regional gas dose ratio [$(H_{b/g})_A$ / $(H_{b/g})_H$], (RGDR). Csanady (2000) reported the tissue:air partition coefficients for rat and humans to be very similar and the blood:gas partition coefficients for rats to be double that of human values. The TS will therefore conservatively consider a default blood:gas partition coefficient of 1. The POD_{HEC} calculated based on the Conolly et al. studies is:

$POD_{HEC} = POD_{ADJ} \times (H_{b/g})_A / (H_{b/g})_H$
POD_{HEC} = 50,000 ppm x 1
POD_{HEC} = 50,000 ppm

3.1.5 Critical Effect and Adjustments of the POD_{HEC}

3.1.5.1 Critical Effect

Potential hepatotoxicity is the critical effect in the animal studies discussed in Section 3.1.1.2, although the POD_{HEC} is a free-standing NOAEL, and no adverse effects were noted in any ethylene-only exposure group.

3.1.5.2 Uncertainty Factors (UFs)

The TS applied the following UFs to the POD_{HEC} of 50,000 ppm to derive an acute Reference Value (acute ReV) under the assumption of a threshold/nonlinear MOA in accordance with the ESL Guidelines (TCEQ 2006). For detailed information on the MOA, please see Section 3.1.2. A interspecies UF of 3 was applied to account for extrapolation from animals to humans (UF_A), a UF of 10 is applied to account for intraspecies variability (UF_H), and a database UF of 3 was applied to account for deficiencies in the database (medium database confidence) of the referenced studies (UF_D). A total UF of 100 (i.e., 3 x 10 x 3 = 100) was applied to POD_{HEC} of 50,000 ppm.

acute ReV = POD_{HEC} / (UF_A x UF_H x UF_D)
= 50,000 ppm/(3 x 10 x 3)
= 50,000 ppm/100
= 500 ppm (500,000 ppb or 570,000 µg/m^3)

A UF_A of 3 was used because default dosimetric adjustments from animal-to-human exposure were conducted which accounts for toxicokinetic differences but not toxicodynamic differences. A UF_H of 10 was used to account for potentially sensitive subpopulations, and a UF_D of 3 was used because of the availability of several toxicity studies with a wide range of end points The confidence in the acute database is medium.

3.1.6 Health-Based Acute ReV and ^{acute} ESL

As discussed in the previous section, UFs were applied to the POD obtained from the Conolly et al. studies to derive the acute ReV. The acute ReV was rounded to two significant figures. Rounding to two significant figures, the 1-h acute ReV is 500,000 ppb (570,000 µg/m^3) The rounded acute ReV was then used to calculate the ^{acute}ESL using a target hazard quotient of 0.3 (Table 3).

^{acute}ESL = 0.3 x acute ReV
^{acute}ESL = 0.3 x 500,000 ppb
^{acute}ESL = 150,000 ppb (170,000 µg/m^3)

Table 3. Derivation of the Acute ReV and ^{acute}ESL	
Key Studies	Conolly et al. (1978)
Study population	Male Holtzman rats
Study quality	Medium-high
Exposure Method	Inhalation
Critical Effects	Hepatic effects
POD (original animal study) NOAEL	50,000 ppm (free-standing NOAEL)
POD_{ADJ} (No adjustment necessary)	50,000 ppm
POD_{HEC}	50,000 ppm (gas with systemic effects based on default RGDR =1)
Exposure Duration	4 h
Total Uncertainty Factors (UFs)	100
Interspecies UF	3
Intraspecies UF	10
LOAEL UF	Not applicable
Incomplete Database UF *Database Quality*	3 Medium
acute Rev[1hr] (HQ = 1)	**570,000 µg/m^3 (500,000 ppb)**
^{acute} ESL [1h] (HQ= 0.3)	**170,000 µg/m^3 (150,000 ppb)**

3.1.7 Information from Other Organizations

The USEPA Office of Prevention, Pesticides and Toxic Substances has reported the maximum exposure rate to ethylene under current use as a pesticide to be 1000 ppm (USEPA 1992). This limit is for the post-harvest exposure of stored commodities (USEPA 1992). The Screening Information Data Set (SIDS) program operated under the auspices of the Organization for Economic Cooperation and Development recommends no further testing of ethylene toxicity based on the reports of low toxicity of ethylene and no

risk to human health either through direct exposure or through indirect exposure *via* the environment (OECD SIDS 1994).

3.2. Welfare-Based Acute ESLs

3.2.1 Odor Perception

Ethylene has a sweet odor and taste. The ACGIH (2005) reported odor threshold is 290,000 ppb and is based on the Amoore and Hautala (1983) study. A 50% odor detection value of 310,000 µg/m^3 (270,000 ppb) has also been reported by Hellman and Small (1974). Since, Hellman and Small (1974) is included in the list of acceptable sources for odor threshold values and is listed in Appendix B of the ESL Guidelines (TCEQ 2006), the $^{acute}ESL_{odor}$ is 310,000 µg/m^3 (270,000 ppb).

3.2.2 Vegetation Effects

3.2.2.1 Summary of Ethylene Induced Vegetative Effects

Interest in ethylene research spiked when it was identified to be phytotoxic to greenhouse plants (Crocker 1948). Later, many investigators documented the adverse effects of ethylene on plant species (Darley et al. 1963, Air Quality Criteria for Hydrocarbons 1970) and reported the effects of ethylene to be dependent on the types of plant species and the stage of plant growth (Tonneijck et al. 2003, Reid and Watson 1985). Fruits (e.g., apples, oranges, and avocados) release ethylene as they approach maturity which in turn promotes the ripening of the fruits.

The majority of ethylene research has been conducted in growth chambers and very few studies exist for field grown plants. Abeles et al. (1992) reported 10 ppb as the threshold concentration for physiological effects from studies in greenhouse experiments with ethylene. However, there is some controversy regarding the relevance of the threshold concentrations reported by Abeles et al. (1992) to field grown plants. Amongst the issues surrounding the applicability of the results reported by Abeles et al. (1992) is the fact that greenhouse plants are normally exposed to very high concentrations of ethylene in a continuous manner. Field grown plants generally experience lower concentrations of ethylene and the exposure pattern is said to be discontinuous (Tonneijck et al. 1999, 2000, and Dueck et al. 2004). Greenhouse plants are also less hardy when compared to the field-grown plants and, may experience more adverse effects (Tonneijck et al. 2003).

Ethylene is a plant hormone that is produced naturally at many of the stages of plant growth. As a plant hormone, ethylene 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, ethylene can stimulate or inhibit the growth process, influence other plant hormones (e.g., giberillic acid), or itself be influenced by other hormones (Grossmann and Hansen 2001).

Tonneijck et al. (2000) reported epinasty or leaf curling in potatoes grown in the vicinity of polyethylene manufacturing plants. However, the authors reported that the epinasty did not translate to a loss in tuber yield. In a review on the effects of air-borne volatile organic compounds such as ethylene, Cape (2003) reported epinasty to be a reversible effect if the exposure ended. Nutritional deficiencies and stress factors (i.e., water stress, temperatures, and diseases) can cause vegetative effects (i.e., leaf and flower

abscission) that are similar to the effects caused by exogenous ethylene. Also, plants undergoing stress are reported to be more susceptible to ethylene (Munne-Bosch et al. 2004, Guinn 1982, and Jordan et al. 1972). It therefore becomes difficult to differentiate subtle physiological and morphological effects caused by naturally produced ethylene (i.e., endogenous) versus ambient ethylene (i.e., exogenous).

Fugitive emissions from leaks around industrial facilities and vehicular traffic can create a discontinuous exposure scenario in the ambient environment. Meteorological factors (i.e., wind direction and velocity) can further aid in the movement and dispersal of the emissions and result in subsequent exposures to field-grown plants. During the discontinuous exposure, field-grown plants often have a chance to recover from the exposure. Green-house plants on the other hand are constantly exposed to ethylene from generators that are housed within the green-houses. For this reason, Tonneijck et al. (2003) indicated that the field-grown plants may be less responsive to ethylene when compared to the greenhouse plants where continuous exposure is the norm.

3.2.2.2 Summary of Ethylene Induced Effects in Flowering plants

Many investigators consider flowering plants such as petunias (*Petunia nyctaginiflora*), marigolds (*Tagetes erecta*), orchids (*Cattleya spp*), and carnations (*Dianthus caryophyllus L.*) to be sensitive to ethylene (Tonneijck et al. 2003, Posthumus 1983, and Davidson 1949). Leaf senecessence and flower abscission have been reported to occur due to ethylene exposure (Tonneijck et al. 2003). In addition, decreased flower size and increased abortion of flower buds in petunias have been used as indicators of plant response to pollution (Posthumus 1983 and Cape 2004). While petunias have been used as indicator plants to assess ethylene sensitivity, orchids have been reported to exhibit severe dry sepal injury at exposures of 100 ppb of ethylene for up to 8 h (Davidson, 1949).

The flowering plant studies are limited by the fact that they often included relatively high ethylene exposure concentrations (2 to 4 ppm) when compared to what is expected in an ambient setting (Underwood et al. 2005, Onozaki et al. 2004, Woodson et al. 1988). Ambient ethylene levels vary widely. For example, while the median concentration of ethylene was reported to be 10.79 ppb in 39 US cities from 1984 – 1985 (Seila et al. 1989), Abeles and Heggestad (1973) reported a maximum value of 700 ppb of ethylene in Washington DC. In some of the reported flowering plant studies, longer exposure durations ($\geq$ 8 and/or $\geq$ 12 h) were required before adverse effects could be recorded. In a multi-year study conducted by Tonneijck et al. (2003), a quantitative relationship between short-term ethylene exposure and plant response was not adequately addressed. In another short-term exposure study, excised flowering petunias were exposed to 4 ppm ethylene for 0, 2, 4, 8, or 10 h (Underwood et al. 2005). Similar exposure protocols with excised flowers were reported in carnations and geraniums (Evensen K 1991). While the more recent ethylene exposure studies in flowering plants included adequate dose-response information, the inclusion of excised flowers in the exposure protocols in the opinion of TS is not an appropriate scenario to depict normal vegetation conditions. For this reason, TS has not chosen these flowering plant studies as key studies for the development of the short-term vegetation ESL.

Woltering and Van Doorn (1988) conducted an extensive assessment of ethylene flower sensitivity amongst 93 species of plants from 22 plant families. However, the study included high exposure concentrations (3,405 µg/m^3) that are not relevant to ambient conditions. In addition, the reported exposure durations (22-24 h) were greater than the acute exposure scenarios defined in the ESL guidelines (TCEQ 2006). As such, the TS have not chosen the study conducted by Woltering and Van Doorn (1988) as a key study for the development of the short-term vegetation ESL for ethylene.

3.2.2.3 Key Studies

Since ethylene-related vegetative effects have been documented, a short-term vegetative based ESL for ethylene exposure was determined according to the ESL Guidelines (TCEQ 2006). The Alberta Canada's Ethylene Research Project (i.e., The Alberta Canada Study) was identified as a key study and the study conducted by Pallas and Kays (1982) was identified as a supporting study to develop the vegetation based acute ESL ($^{acute}ESL_{veg}$).

3.2.2.3.1 The Alberta Canada Study

The Alberta Canada Study was a multi-stake holder initiative that was jointly sponsored by the Provisional Government and petrochemical industries in Alberta, Canada (Alberta Research Council 2001). The project was initiated to determine the concentration threshold at which short-term exposures to ethylene would cause significant effects on vegetative and reproductive parameters in selected cultivars of agricultural crops of interest to Alberta, Canada. Archambault and Li, the investigators of the Alberta Canada study, conducted extensive preliminary screening experiments with Ethephon ((2-Chloroethyl) phosphonic acid) to determine which plant species in each of 3 plant categories (i.e., cereal, legumes, and oilseeds) and 2 tree species were most sensitive to ethylene (Archambault et al. 2006, Archambault and Li 2001, 1999a, and 1999b). In their studies with field crops, sensitivity of seed yield to ethylene was the critical effect that was used to determine the relative sensitivity of the crop species. However, for the tree species, sensitivity to ethylene was based on the vegetative characteristics because vegetative characteristics are important parameters that determine the marketability of seedlings.

Table 4: Information on the Plants and Trees included in the Alberta Canada Study

Category	Plant	Species	Sensitive Stage of Growth	Vegetative Effects
Cereal	Barley	*Hordeum vulgare* cv. Harrington	Spike emerging stage	Decrease in photosynthesis, vegetative effects, and decreases in seed yield.
Legumes	Field pea	*Pisum sativum* cv. Carrera	Flat pod stage	
Oilseeds	Canola	*Brassica napus* cv. Quantum	Many flowers open stage	
Trees	White spruce	*Picea gluca*	Vegetative growth	Effects on seed germination, seedling vigor, growth, and seedling marketability.
Trees	Lodgepole pine	*Pinus Contorta*		

Information on the plants and trees included in the Alberta Canada Study is provided in Table 4. All the plants included in the experiment were grown in the greenhouse until the appropriate stage was reached at which time they were transferred to exposure chambers and left for one day to acclimate prior to the start of the exposures. Plants were moved back to the greenhouse and grown to maturity after exposures were completed. For a detailed description of the treatments and exposure regimens, please see the Alberta's Ethylene Crop Research Project Report titled, "Response of Barley, Field peas, Canola, and Tree seedlings to Ethylene Exposure (2001)".

Treatments included exposing barley, field pea, canola, white spruce, and lodgepole pine to six concentrations of ethylene (10, 75, 150, 300, 600, and 1,200 ppb) at four exposure durations (1.5, 3, 6, and 12 h). In their studies, the investigators defined short-term exposures as being equal to or less than 12 h. In all the experiments, the order of exposures was randomly selected. In addition, the investigators of the Alberta Canada Study considered the 10 ppb exposure concentration as a background concentration based on the findings by Reid and Watson (1985), who reported that complete removal of ethylene from atmosphere would lead to detrimental effects on plant growth.

The investigators of the Alberta Canada Study reported barley from the cereal category, field pea from the legume category, and canola from the oil seed category to be the most sensitive species in their respective categories. In addition, the investigators also reported white spruce and lodgepole pine to be the most sensitive tree species for ethylene exposure.

The investigators conducted analysis of variance (ANOVA) and reported no significant effects on photosynthetic rates or vegetative, or reproductive effects for all exposure durations (up to 12 h) at all the exposure concentrations (up to 1,200 ppb) for all the plant species (barley, field peas, and canola). In the case of the trees (i.e., lodge pine and white spruce), the investigators reported no effects on seed germination, seedling vigor, growth, or seedling marketability after an exposure to 1,200 ppb of ethylene for exposure durations up to 12 h. The investigators reported that after short-term exposures ($\leq$ 12 h) the plants and trees recovered from decreases in photosynthesis and growth.

In addition, the investigators also conducted additional statistical analysis (e.g., linear regression) to further understand the relationship between several plant parameters and ethylene dose expressed as a product of ethylene concentration (ppb) and exposure duration (h). The investigators reported a poor correlation between the various plant parameters measured and the ethylene dose. In the case of the tree seeds/seedlings, the investigators reported a poor correlation between germination and ethylene indicating that there was no significant dose effect.

However, the Alberta Research Council established a different short-term (i.e., 1-h) Ambient Air Quality Objective when compared to the results of the Alberta Canada Study. The Alberta Research Council established a short-term Ambient Air Quality Objective of 1,200 $\mu g/m^3$ (1,044 ppb) to be protective of all plant species (Alberta Research Council Report 2001).

3.2.2.3.2 Pallas and Kays (1982) Study

Pallas and Kays (1982) studied the effect of ethylene on photosynthesis by exposing leaves of a variety of plants to 1 microliter per liter (µl/L) or 1,000 ppb of ethylene for 0, 0.25, 0.5, 1, 2, 4, and 6 h (Table 5). The investigators also reported including a day without treatment between the treatments to measure any "carry-over effects" on photosynthesis. The Pallas and Kays study (1982) is a well-conducted study as the inhibition of photosynthesis was examined in many plants at exposure durations representative of short-term exposure scenarios. However, in the TS's opinion, the study is limited because it included only a single exposure concentration (1,000 ppb). For this reason, the TS considered the Pallas and Kays (1982) study as a supporting study to develop the $^{acute}ESL_{veg}$.

Table 5: Information on the Plants Included in the Pallas and Kays Study	
Green bean	*Phaseolus vulgaris* L. cv. Contender
Pea	*Pisum sativum* L. cv. Wando
Peanut	*Arachis hypogea* L. cv. Florunner
Scarlet runner bean	*Phaseolus coccineus* L.
Sensitive plant (according to the study authors)	*Mimosa Pudica L.*
Irish Potato	*Solanum tuberosum* L.
Sunflower	*Helianthus annus* L. line CM90RR
White Clover	*Trifolium repens L.*
Jerusalem artichoke	*Helianthus tuberosus* L.

Pallas and Kays (1982) reported a wide range of responses in photosynthesis amongst the various cultivars exposed to ethylene. The net decrease in photosynthesis was dependent both on the genotype of the cultivar and the exposure duration. Pallas and Kays (1982) reported a decrease in photosynthesis with an increase in the exposure duration from 0.25 to 6 h in peanuts. In addition, the authors also reported a net decrease in photosynthesis when Jerusalem artichoke, sunflower, and sweet potato were exposed to 1,000 ppb ethylene for 2.5 h. However, the authors reported no effects on photosynthesis in green bean, scarlet runner bean, pea, Irish potato, or white clover. Amongst the various plant species tested in the study, peanut cultivars were reported to be relatively more sensitive to ethylene exposure. With an increase in the duration of exposure, the inhibitory effect on photosynthesis increased, especially for peanut. Pallas and Kays (1982) reported a 68% decrease in photosynthesis after a 6 h exposure period. However, the investigators also reported a rapid recovery after short–term exposure durations and the plants did not exhibit any carry-over effect on photosynthesis. The photosynthetic rates after the short-term exposure treatments (0.5 - 6 h) returned to normal or pre-exposure levels within 24 h following treatments. Plants in the 6 h treatment required an additional day for recovery. Overall, Pallas and Kays (1982) concluded the decrease in photosynthesis to be a reversible effect.

3.2.2.4 Derivation of the $^{acute}ESL_{veg}$

According to the ESL Guidelines, $^{acute}ESL_{veg}$ is set at a threshold concentration for adverse effects (TCEQ 2006). However, the results from the Alberta Canada Study and the Pallas and Kays (1982) study indicate that short-term exposures ($\leq$ 12 h and/or $\leq$ 6 h) of plants to ethylene either at 1,200 ppb or 1,000 ppb respectively to result in no adverse vegetative effects. While the TS acknowledges the absence of adverse vegetative effects at the reported exposure concentrations and durations in both the key and supporting studies, TS conservatively recommends a 1-h $^{acute}ESL_{veg}$ of 1,400 µg/m^3 (1,200 ppb) as a sub-threshold concentration to be protective for all plant species.

The $^{acute}ESL_{veg}$ of 1,400 µg/m^3 was rounded to the two significant figures and is based on the results of the short-term exposures from the Alberta Canada Study (Table 6). In recommending a 1-h $^{acute}ESL_{veg}$ of 1,400 µg/m^3 (1,200 ppb), the TS has taken into consideration that the reported exposure concentration (1,200 ppb) was the highest exposure concentration at exposure durations up to 12 h (i.e., 1.5, 3, 6, and 12 h) and the limited database of well-conducted ethylene exposure field studies for crops. The proposed screening value should also adequately protect vegetation from potential intermittent exposures.

Table 6. Derivation of the acuteESLveg	
Study	Alberta's Ethylene/Crop Research Project Report III
Study population	Barley, field pea, canola, and tree seedlings
Exposure Method	Growth Chambers
Critical Effects	Vegetative effects and decrease in photosynthesis
POD (Sub-Threshold Concentration)	1,400 µg/m3 (1,200 ppb)
Exposure Duration	1.5, 3, 6, 12 h
$^{acute}ESL_{veg}$	**1,400 µg/m3 (1,200 ppb)**

3.3 Short-Term ESL and Values for Air Monitoring Evaluation

The acute evaluation resulted in the derivation of the following acute values:

- $^{acute}ESL_{veg}$ = 1,400 µg/m^3 (1200 ppb)
- acute ReV = 570,000 µg/m^3 (500,000 ppb)
- $^{acute}ESL$ = 170,000 µg/m^3 (150,000 ppb)
- $^{acute}ESL_{odor}$ = 310,000 µg/m^3 (270,000 ppb)

The short-term ESL for air permit reviews and air monitoring evaluations is the $^{acute}ESL_{veg}$ of 1,400 µg/m^3 (1,200 ppb) as it is lower than the $^{acute}ESL$ and the $^{acute}ESL_{odor}$ (Table1). The acute ReV and the $^{acute}ESL_{odor}$ may also be used for air monitoring evaluations. The $^{acute}ESL$ (HQ = 0.3) will not be used by the TS to evaluate air monitoring data.

Chapter 4 Chronic Evaluation

4.1 Noncarcinogenic Potential

4.1.1 Physical/Chemical Properties and Key Studies

Physical/chemical properties of ethylene are discussed in Chapter 3. Due to the unavailability of chronic inhalation exposure studies in humans, the TS selected well-conducted animal studies to develop the chronic ReV. A two-year inhalation study conducted by Hamm et al. (1984) was selected as a key study to determine the chronic ReV. In the study, Hamm et al. (1984) randomly divided 960 Fischer-344 rats into 4 groups of 120 animals for each sex and exposed them to 0, 300, 1,000, or 3,000 ppm of ethylene for 6 h/day, 5 days per week for 106 weeks. There were no reports of any chronic toxicity or oncogenicity at any of the concentrations tested. Comprehensive analysis of various tissues (e.g., kidney and nasal turbinates) indicated no signs of carcinogenic effects. While a variety of proliferative, degenerative, and inflammatory lesions were observed in both the control and treatment groups, the authors reported that these types of lesions are typical of the animal. A discussion on the high concentrations of ethylene is warranted based on previous findings that 3,000 ppm is the highest concentration that could be safely studied for long-term chronic studies (CIIT, 1980). Ethylene is

explosive when it reaches 3% or higher in air composition. However, for acute exposure experiments, investigators were able to use higher concentrations of ethylene safely even up to 50,000 ppm (Section 3.1.3.1). Based on safety issues, Hamm et al. (1984) reported 3,000 ppm as the NOAEL for long-term chronic studies. TS will therefore consider 3,000 ppm as a free-standing NOAEL.

A 90 day sub-chronic study reported by Rhudy et al. (1978) was selected as a supporting study to determine the chronic ReV. Rhudy et al. (1978) exposed Sprague-Dawley rats to various concentrations of ethylene (0, 300, 1,000, 3,000, or 10,000 ppm) for 6 h/day, 5 days/week for 14 weeks. The authors reported no toxic effects related to ethylene exposure on conducting a comprehensive microscopic analysis of tissue specimens. In addition, the authors also did not report any changes or abnormalities in hematology, clinical chemistry, and urinalysis. A free-standing NOAEL of 10,000 ppm was determined from the Rhudy et al. (1978) study.

4.1.2 MOA Analysis and Dose Metric

The MOA of ethylene is described in detail in Section 3.1.2. For the key and supporting studies, data on concentration of the parent chemical is used as the default dose metric.

4.1.3 POD for Key and Supporting Studies

The NOAEL reported in the Rhudy et al. (1978) study (10,000 ppm) was higher than the NOAEL reported in the Hamm et al. (1984) study (3,000 ppm). However, the TS selected the NOAEL (3,000 ppm) from the Hamm et al. (1984) study because it was a chronic, rather than a sub-chronic exposure study.

4.1.3.1 Default Exposure Duration Adjustments

The TS conducted an adjustment from the discontinuous animal exposure regimen to a continuous exposure regimen with the following equation to determine the POD_{ADJ}`. The POD_{ADJ} was determined to be 535.71 ppm (see below).

$$POD_{ADJ} = POD \times (D/24\ h) \times (F/7\ d)$$

where:
POD_{ADJ} = POD from animal studies adjusted to a continuous exposure scenario
POD = POD from animal studies based on discontinuous exposure scenario
D = Exposure duration, h per day
F = Exposure frequency, days per week

$$POD_{ADJ} = 3{,}000\ ppm \times (6/24) \times (5/7) = 535.71\ ppm$$

4.1.3.2 Default Dosimetry Adjustments

Similar to section 3.1.4.2, the TS considered ethylene as a Category 3 gas and the duration exposure adjustments from animals to humans was conducted to determine the human equivalent POD or POD_{HEC} with the following equation:

$$POD_{HEC} = POD_{ADJ} \times ((H_{b/g})_A / (H_{b/g})_H)$$
Where:

POD_{HEC} = Point of Departure at Human Equivalent Concentration
POD_{ADJ} = Adjusted Point of Departure
$H_{b/g}$ = Ratio of blood: gas partition coefficient
A = Animal
H = Human

The POD_{HEC} based on the Hamm et al. (19784) study:

$POD_{HEC} = POD_{ADJ} \times (H_{b/g})_A / (H_{b/g})_H$
$= 535.71 \text{ ppm} \times 1$
$= 535.71 \text{ ppm}$

4.1.4 Application of Uncertainty Factors to the POD_{HEC} based on MOA Analysis

TS applied appropriate UFs to derive a Chronic ReV in accordance with the ESL Guidelines (TCEQ 2006). The POD_{HEC} of 535.71 ppm is based on a 2-Year study conducted by Hamm et al. (1984). The following UFs are applied: A UF of 3 is applied to account for extrapolation from animals to humans (inter-species variability, UF_A), a UF of 10 is applied to account for intraspecies variability (UF_H), and a UF of 3 to account for deficiencies in the database (UF_A). The total UF was equal to 100 (3 x 10 x 3).

$ReV = POD_{HEC} / (UF_A \times UF_H \times UF_D)$
ReV = 535.71 ppm / (3 x 10 x 3);Rev = 535.71 ppm/100
ReV = 5.3571 ppm (5,300 ppb or 6,100 µg/m^3) (rounding up to two significant figure)

A UF_A of 3 was used because default dosimetric adjustments from animal-to-human exposure were conducted which account for toxicokinetic differences but not toxicodynamic differences. A UF_H of 10 was used to account for potentially sensitive subpopulations, and a UF_D of 3 was used because of the availability of well-conducted chronic and sub-chronic toxicity studies with a wide range of end points The confidence in the chronic database is medium.

4.1.5 Health-Based Chronic ReV and $^{chronic}ESL_{nonlinear(nc)}$

The chronic ReV of 6,100 µg/m^3 (5,300 ppb) rounded to two significant figures was used to calculate the $^{chronic}ESL_{nonlinear(nc)}$ by using the following formula and a hazard quotient (HQ) of 0.3 (Table 7):

$^{chronic}ESL_{nonlinear(nc)}$ = chronic ReV x HQ
= 5,300 ppb x 0.3 = 1,600 ppb (1,800 µg/m^3)

Table 7. Derivation of the Chronic ReV and $^{chronic}ESL_{nonlinear(nc)}$	
Study	Chronic toxicity and oncogenicity bioassay of inhaled ethylene in Fischer-344 rats
Study population	Fischer-344 rats
Study Quality	Medium
Exposure Method	Inhalation
Critical Effects	Hepatic damage
POD (original animal study)	3,000 ppm, NOAEL
Exposure Duration	6 h/day, 5 days/wk, 2 years
Extrapolation to continuous exposure (POD_{ADJ})	535.71 ppm
POD_{HEC}	535.71 ppm (gas with systemic effects based on default RGDR =1)
Total UFs	100
Interspecies UF	3
Intraspecies UF	10
LOAEL UF	Not Applicable
Subchronic to chronic UF	Not Applicable
Incomplete Database UF (Database Quality)	3 (Medium)
Chronic ReV (HQ = 1)	**6,100 µg/m^3 (5,300 ppb)**
$^{chronic}ESL_{nonlinear(nc)}$ (HQ = 0.3)	**1,800 µg/m^3 (1,600 ppb)**

4.2 Carcinogenic Potential

Concern over the toxicity of ethylene is due to the metabolic conversion of ethylene to EtO which has been designated as a carcinogen and a genotoxicant (Bolt and Filser 1987). However, the percentage conversion of ethylene to EtO is insignificant (See Section 3.12). According to the ACGIH report published in 2005, "the potential toxicity due to EtO formation from the metabolic conversion of ethylene to EtO will not likely pose a cancer risk based on the current knowledge of the significance of adducts". In conclusion, ethylene is a relatively non-toxic chemical and is assumed to have a threshold, non-linear MOA. ACGIH (2005) has designated ethylene as A4 (i.e., it is not classified as a human carcinogen).

The International Agency for Research on Cancer (IARC) (1994) has classified ethylene as a Group 3, which indicates that it is a not classified as a human carcinogen. The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK Commission) has classified ethylene as a 3B (Deutsche Forschungsgemeinschaft 2004 in ACGIH 2005). The TS has determined that the data are inadequate for an assessment of human carcinogenic potential by the inhalation pathway.

4.3. Welfare-Based Chronic ESL

4.3.1. Development of Vegetation-Based Chronic ESL ($^{chronic}ESL_{veg}$)

Four key studies were identified to determine the $^{chronic}ESL_{veg}$. The first study was the Alberta Ethylene Research Project in which barley, field peas, and canola were exposed to various concentrations of ethylene for different durations (Alberta Canada Study). The second key study was conducted by Klassen and Bugbee (2002) in which they evaluated the sensitivity of wheat (*Triticum aestivum* L.) and rice (*Oryza sativa*) to various concentrations of ethylene. The third study was conducted by Reid and Watson (1985) who examined the sensitivity of oats (*Avena Sativa* L. cv. Random) and canola to chronic exposure to ethylene. In the fourth key study, Blankenship and colleagues (1993) conducted experiments to study the effects of continuous low levels of ethylene on growth and flowering of Eastern lily (*Lillium longiflorum* Thumb. Culitvar 'Nellie White').

4.3.1.1 The Alberta Canada Study

Archambault and Li (2001) wanted to determine the critical duration of exposure and long-term vegetative effects based on yield when plants are exposed to ethylene during a sensitive stage of growth. The Alberta Environment (2003) report includes various ethylene exposure scenarios and is discussed below. For short-term exposure scenarios (less than or equal to 12 h) please see Section 3.4. Two of the exposure scenarios are discussed below. For a detailed description of the treatments and exposure regimens, please see the Alberta's Ethylene Crop Research Project Report titled "Response of Barley, Field Peas, Canola, and Tree Seedlings to Ethylene Exposure (2001)".

Exposure Scenario 1:

In this scenario, Archambault and Li exposed barley plants to 50 ppb of ethylene for 0, 3, 6, 12, 18, and 24 days, and field peas to 50 ppb of ethylene for 0, 12, 16, 20, 24, and 28 days in growth chambers according to standard laboratory protocols. In the case of barley, the seed yield decreased by 41% when the plants were exposed to 50 ppb for 3 days and by 89% when the plants were exposed for 24 days. However, there were no effects on the above ground and root biomass, plant height, or tiller number after exposure to 50 ppb for 24 days. Field peas on the other hand were found to be relatively more insensitive to long-term exposures to ethylene. Exposure of field peas to 50 ppb of ethylene did not result in significant effects in plant height, number of pods, weight of pods, number of seeds, or seed yield. A threshold concentration of 50 ppb for long-term exposures was therefore determined from the studies on barley.

Exposure Scenario 2:

A second exposure protocol included a summary of long-term ethylene exposures in barley, field peas, and canola where barley plants were exposed to a range of ethylene concentrations (10 – 250 ppb). The investigators reported a 63% reduction in seed yield of barley when barley plants were exposed to 34 $\mu g/m^3$ (30 ppb) for 14 days. A threshold concentration of 34 $\mu g/m^3$ (30 ppb) for long-term exposures was therefore determined from the second set of exposure scenarios.

4.3.1.2 Klassen and Bugbee (2002)

Klassen and Bugbee (2002) evaluated the sensitivity of wheat (*Triticum aestivum* L.) and rice (*Oryza sativa*) to continuous ethylene levels ranging from 0 to 1,000 ppb in a growth chamber throughout the growing season. The authors reported anthesis (flowering stage) to be the most sensitive period for the crop plants. Exposures that stopped at the flowering stage were found to have lower reductions in yield. In this experiment, the authors reported that exposure to 50 ppb of ethylene reduced the yield by 36% in wheat and 63% in rice, respectively. In addition, plants that were exposed to 1000 ppb were found to be completely sterile. A threshold concentration of 50 ppb for long-term exposures was therefore determined from the studies on wheat and rice.

4.3.1.3 The Reid and Watson Study (1985)

Reid and Watson (1985) conducted a suite of experiments to determine the effect of various concentrations of ethylene on plant growth in oats (*Avena sativa* L. cv. Random) and canola (*Brassica campestris* L. cv. Candle) plants. Reid and Watson exposed oats for 100 days to 0, 8, 40, 81, and 173 $\mu g/m^3$ of ethylene and canola plants to 0, 12, 40, 173, and 690 $\mu g/m^3$ of ethylene for 87 days. At the 40 $\mu g/m^3$ concentration, the authors reported per plant floret number to decrease by 26% in oats and per plant seed yield to decrease by 57%. The authors therefore reported 40 $\mu g/m^3$ (34 ppb) to be the threshold concentration at which negative effects occur.

4.3.1.4 The Blankenship study (1993)

Blankenship and colleagues (1993) studied the effects of continuous, low levels of ethylene on growth and flowering of Easter lily (*Lililum longiflorum*) Thumb, cultivar 'Nellie White' by exposing Easter lilies to 0, 0.01, 0.05, or 0.1 µl/l (ppm) ethylene for 77 days. The authors reported that the Easter lilies continuously exposed to 50 ppb (0.05 µl/l) had greater than 50% decrease in dry weight in both shoots and inflorescences. In addition, both the 50 and 100 ppb exposure groups were unmarketable. The plants in the 10 ppb were reported to not be affected and were reported to be marketable. Therefore, the reported threshold concentration for long-term exposure for flowering plants is 50 ppb.

4.3.1.5 Determination of $^{chronic}ESL_{veg}$

Vegetation-based ESLs are set at the threshold concentration for adverse effects and are determined in accordance with ESL Guidelines (TCEQ 2006). Amongst all the key studies identified by the TS, the barley exposure studies (Exposure Scenario 2) reported the lowest threshold concentration of 34 $\mu g/m^3$ (30 ppb). The TS, therefore, determined the $^{chronic}ESL_{veg}$ to be 34 $\mu g/m^3$ (30 ppb).

Table 8. Derivation of the $^{chronic}ESL_{veg}$	
Study	Alberta's Ethylene/Crop Research Project Report III, 2001 (Exposure Scenario 2)
Study population	Barley
Exposure Method	Growth Chambers
Critical Effects	63% reduction in seed yield for barley
POD (Threshold Concentration)	34 µg/m^3 (30 ppb)
Exposure Duration	14 days
$^{chronic}ESL_{veg}$	34 µg/m^3 (30 ppb)

4.3.1.6 Other Vegetation-Based Studies Reviewed by TS

Among crop plants, vegetative effects of cotton (*Gossypium hirsutum*) and potato (*Solanum tuberosum*) have been studied on exposure to ethylene. Hall et al. (1957) reported extensive plant damage in cotton plants in the vicinity of a polyethylene manufacturing plant in Texas. The reported ambient concentrations of ethylene ranged from 0.04 to 30 ppm. In addition to reduction in yield, cotton plants exhibited leaf abscission, scattered seedling death, vine-like growth habit, and abscission of squares. In a growth chamber experiment, Heck et al. (1961) exposed cotton to constant levels of 40 or 100 ppb ethylene for 27 days. While no severe plant injury or death was reported, the authors reported a 25–50% reduction in yield (Heck et al. 1961). Cotton leaf and fruit abscission were also investigated by Hall et al. (1957). TS did not consider these studies as key studies because these studies were reported either in a review article or limited dose-response information was presented.

4.4 Long-Term ESL and Values for Air Monitoring Evaluation

The chronic evaluation resulted in the derivation of the following chronic values:

- $^{chronic}ESL_{veg}$ = 34 µg/m^3 (30 ppb)
- chronic ReV = 6,100 µg/m^3 (5,300 ppb)
- $^{chronic}ESL_{nonlinear(nc)}$ = 1,800 µg/m^3 (1,600 ppb)

The long-term ESL for air permit reviews and air monitoring evaluations is the $^{chronic}ESL_{veg}$ of 34 µg/m^3 (30 ppb). The chronic ReV of 6,100 µg/m^3 (5,300 ppb) may also be used in air monitoring evaluations (Table 1). The $^{chronic}ESL_{nonlinear(nc)}$ (HQ= 0.3) will not be used by the TS to evaluate air monitoring data.

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資料　12

米陸軍健康増進・予防医学センター
野生生物に対するエチレンの毒性評価
2008 年４月

U.S. Army Center for Health Promotion and Preventive Medicine
JANUARY 2006

Wildlife Toxicity Assessment for Ethylene

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USACHPPM

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Prepared by
Health Effects Research Program
Environmental Health Risk Assessment Program

USACHPPM Document No: 37-EJ1138-01Q
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Readiness Thru Health

Wildlife Toxicity Assessment for Ethylene

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Table of Contents

Department of the Army
U.S. Army Center for Health Promotion and Preventive Medicine

Wildlife Toxicity Assessment for Ethylene

CAS No. 74-85-1 **January 2006**

1. Introduction

Ethylene is a colorless gas that is produced by the petrochemical industry in vast quantities throughout the world. As summarized by the International Agency for Research on Cancer (IARC), the compound serves as the "building block" for the production of polyethylene, as well as other important chemicals and intermediates such as ethylene oxide, ethylene dichloride, ethylbenzene, ethylene glycol, ethanol and vinyl acetate monomer among others (IARC 1994). In medicine, the compound has been used as an anaesthetic when mixed with air. However, the use of this formulation has been largely discontinued because of the explosive nature of the ethylene-oxygen mixture. The compound is released to the environment as a product of burning vegetation, a by-product of petroleum refining, through production by steam cracking of hydrocarbon feedstocks, incomplete combustion of fossil fuels, in automobile and diesel exhausts and by sewage treatment plants (HSDB 2001). Ethylene is also produced and emitted by all plants and hence is present naturally in the environment. Human beings and other mammals also produce the compound endogenously.

This Wildlife Toxicity Assessment summarizes current knowledge of the toxicological impacts of ethylene on wildlife. Evaluating the toxicity of ethylene is intended to contribute to the derivation of toxicity reference values (TRVs) that could serve as screening-level benchmarks for wildlife in the vicinity of contaminated sites. The protocol for the performance of this assessment is documented in the U.S. Army Center for Health Promotion and Preventive Medicine Technical Guide 254, *Standard Practice for Wildlife Toxicity Reference Values* (USACHPPM 2000).

2. Toxicity Profile

2.1 Literature Review

Relevant biomedical, toxicological, and ecological databases were electronically searched April 20, 2001 and May 2, 2001, using Dialog to identify primary reports of studies and reviews on the toxicology of ethylene. Separate searches were carried out linking the compound to mammals, birds, and reptiles and amphibians (combined). In general, a two-tiered approach was used in which all citations were first evaluated as titles and “key words in context.” All available abstracts of those articles that were selected

in the first tier as possibly relevant to TRV development were then evaluated for relevancy and retention for evaluation in the second tier. For ethylene, 9 articles were marked for retrieval from 538 initial hits, a disparity arising because the initial sweep captured a substantial number of reports of studies that featured the use of "ethylene" as part of the name of a large number of other compounds. These were eliminated in Tier 2 of the selection process. Details of the search strategies and the results of each are documented in Appendix A.

In addition to Dialog searching, a number of U.S. Army reports were identified in the Defense Technical Information Center (DTIC). Secondary references and sources of information on ethylene included the National Library of Medicine's Hazardous Substances Databank (HSDB 2001) and IARC monographs (IARC 1979, 1994).

2.2 Environmental Fate and Transport

Ethylene is a ubiquitous component of the atmosphere, with concentrations reaching 5 $\mu g/m^3$ at remote sites. However, its concentration can range greater than 1000 $\mu g/m^3$ in urban centers, largely as a result of vehicle exhaust emissions. Ethylene is produced for a variety of uses in large quantities; about 47 billion pounds were produced in 1995 (Chemical and Engineering News 1996). Industrial release of ethylene to the air is substantial throughout the developed world. IARC (1994) reports an estimated total industrial release of 17,400 tons of ethylene in the United States in 1991. A report from the American Petroleum Institute (Suriano 2003) in support of the EPA Toxic Release Inventory indicates that 1.7 billion pounds of ethylene was released by petroleum refineries in 2000.

Volatilization of soil-borne ethylene is likely, based on the compound's high vapor pressure of 5.2×10^4 and a Henry's Law constant of 2.3×10^{-1} atm-m^3/mole at 25°C (HSDB 2001). As listed in Table 1, these and other physical-chemical characteristics also favor volatilization of ethylene from the surface of marine and freshwater systems. However, although sparingly soluble in water, the compound has been detected in oceans, lakes, and rivers in and around the United States. For example, concentrations of ethylene up to 35 nL/L were measured in water samples taken in the Mississippi delta.

Table 1. Summary of Physical-Chemical Properties of Ethylene

CAS No.	74-85-1
Molecular weight	28.05
Color	Colorless

Table 1. Summary of Physical-Chemical Properties of Ethylene

Physical state	Gas
Melting point	-169°C
Boiling point	-103.7°C
Odor	Sweet
Solubility	131 mg/L in water at 20-25 °C slightly soluble in benzene, ethanol, acetone, soluble in diethyl ether
Partition coefficients:	
Log K_{ow}	1.13
Log K_{oc}	2.0–2.5
Vapor pressure at 25 °C	5.2×10^4 mm Hg
Vapor Density	0.978 (air = 1)
Henry's Law constant at 25 °C	2.3×10^{-1} atm.m^3/mole
Conversion factors	1 ppm = 1.15 mg/m^3 1 mg/m^3 = 0.87 ppm

Sources: HSDB (2001), IARC (1994)

A number of mechanisms have been suggested for how the chemical is degraded in the environment. For example, the compound can degrade rapidly in the atmosphere as it reacts with photochemically-produced hydroxyl radicals. This process has a half-life of about 1.9 days. Nitrate radicals and ozone will also cause ethylene degradation, however at a lower rate. Ethylene can also be broken down as a result of microbial action as determined by pure culture research, however, it is expected to oxidize to ethylene oxide which is no metabolized further and may accumulate in the environment (HSDB 2001).

Given the volatility of ethylene, it is unlikely that it would persist in the environment long enough to allow for significant exposures to terrestrial wildlife. In the event that exposure would occur, the most likely route would be inhalation followed possibly by the dermal route. Importantly, ethylene is readily converted to ethylene oxide, which is somewhat more stable and could pose some risk to wildlife.

2.3 Summary of Mammalian Toxicity

2.3.1 Mammalian Toxicity - Oral

Given the gaseous nature of ethylene at ambient temperatures and pressures, there are no data on the toxicological effects of ethylene when administered via the oral route.

2.3.1.1 Studies Relevant for Mammalian TRV Development for Ingestion Exposures

Not applicable.

2.3.2 Mammalian Inhalation Toxicity

2.3.2.1 Mammalian Inhalation Toxicity – Acute

Due to the fact that ethylene serves as a rapid onset anesthetic, humans and animals have been exposed to relatively high concentrations without notable long-term adverse effects. For example, rats exposed to ethylene at concentrations of up to 500,000 ppm for 5 hours are reported to have suffered no long-term adverse effects (HSDB 2001). The apparent tolerance to high concentrations of ethylene in animals and humans has precluded the identification of a reliable compound-specific median lethal concentration (LC_{50}). However, it appears that concentrations of ethylene necessary to induce effective anesthesia come close to inducing hypoxia as the proportion of oxygen in the ethylene-air mixture is reduced.

Although there are few if any toxicological consequences of exposure to ethylene via inhalation, the ability of the compound to react with biological macromolecules has been demonstrated. For example, Eide et al. (1995) exposed male Sprague-Dawley rats to ethylene (one of a range of alkenes under investigation) at 300 ppm for 12 hours/day on three separate days. Exposure took place in a conically-shaped steel chamber with a glass door and walls. At termination, aliquots of blood and samples of lung, brain, liver, kidney, and peripheral fat were measured for ethylene. The formation of DNA adducts in liver and lymphocytes were monitored using the ^{32}P-postlabelling technique detected using gas chromatography/mass spectrometry. N-(2-hydroxyalkyl) valine adducts of hemoglobin and 7-alkylguanine adducts of DNA were detected consistently in these experiments, including N-(2-hydroxyethyl) valine and 7-ethylguanine when ethylene was used as the test compound.

2.3.2.2 Mammalian Inhalation Toxicity – Subchronic

An experiment by Vergnes and Pritts (1994) used a subacute dosing regime to examine ethylene's ability to induce the formation of micronuclei in the bone marrow of male F344 rats and B6C3F1 mice. Ten animals/group were exposed to 0, 40, 1000, and 3000 ppm ethylene, 6 hours/day, 5 days/week for 4 weeks, with bone marrow collected 24 hours after the last exposure. Exposure took place in a steel inhalation chamber with glass windows. Examination of cell smears revealed little if any formation of micronuclei or polychromatic nuclei in ethylene-exposed groups, although the incidence of these features was significantly increased in the cells of animals receiving 200 ppm ethylene oxide, a major carcinogenic metabolite of ethylene. This finding appears uncharacteristic in view of the likelihood that ethylene oxide is a metabolite of ethylene. However, the contradiction may have been explained by Walker et al. (2000) who used a similar experimental protocol to show that while both ethylene and ethylene oxide induce the formation of N-(2-hydroxyethyl) valine in hemoglobin and N7-(2-hydroxyethyl)guanine in DNA, only ethylene oxide had the ability to increase the frequency of

Hprt mutants in splenic T cells. The authors presented evidence to show that the cytochrome P4502E1-mediated conversion of ethylene to ethylene oxide saturates at levels that are insufficient to trigger the toxic responses that are typical of ethylene oxide exposure.

The Chemical Industry Institute of Toxicology (CIIT) has carried out two full-scale studies on the toxicology of ethylene, one of which was reported by Rhudy et al. (1978). The protocol featured the exposure of 15 "albino" rats/sex/group to 0, 300, 1000, 3000, or 10,000 ppm ethylene, 6 hours/day, 5 days/week for 13 weeks. Ethylene was delivered in unspecified inhalation chambers. During the study clinical signs, mortality, body weights, and food consumption were monitored daily; clinical chemistry, hematological, and urinalysis parameters were monitored in controls and high dose groups on days 6, 45 and 83; and full necropsies and histopathological evaluations were carried out on all survivors at termination. However, there were no compound-related differences in treatment groups compared to controls in any of the parameters under evaluation.

2.3.3.4 Mammalian Inhalation Toxicity – Chronic

The second CIIT study extended the duration to 24 months for 120 F344 rats/sex/group exposed to 0, 300, 1000, or 3000 ppm ethylene (Hamm et al. 1984). Exposure took place in four glass and stainless-steel chambers. Animals were euthanized on an interim basis after 6, 12, and 18 months, with these subjects and all survivors monitored for survival, clinical signs, ophthalmologic characteristics, hematology, clinical chemistry, and urinalysis. A full suite of histopathological examinations were carried out in control and high dose groups although, in these as in all other parameters under investigation, there appears to have been no compound-related effects.

2.3.3.5 Studies Relevant for Mammalian TRV Development for Inhalation Exposures

The use of high concentrations of ethylene as an anesthetic, with full recovery of faculties on cessation of exposure, is consistent with the negative toxicological results outlined in Sections 2.3.3.1–2.3.3.4. Taken together, these findings point to the benign nature of the compound in biological systems and argue against the likelihood that a viable TRV for ethylene can emerge from the overall toxicological information on the compound. However, the formation of 2-hydroxyethyl derivatives of hemoglobin and guanine shows that ethylene has biochemical activity, most likely mediated through its ethylene oxide intermediate. The disparity between the benign effects of ethylene and the more severe effects of ethylene oxide in toxicological tests has been addressed by Walker et al. (2000) and in a review by Bolt (1998) who estimated that exposure concentrations of 1000 ppm ethylene would be equivalent to about 7.5 ppm ethylene oxide. By implication, this concentration would probably be below the threshold at which any toxicological impacts (of ethylene oxide) would become apparent.

2.3.4 Mammalian Inhalation Toxicity – Other

Aveyard and Collins (1997) used Organization for Economic Cooperation and Development (OECD) guideline 421 to test the effects of ethylene on fertility, pregnancy, maternal and suckling behavior, and F1 growth and development in rats (strain unstated) exposed to ethylene. They reported that 10 parental animals/group were exposed head only to 0, 200, 1000, or 5000 ppm ethylene, 6 hours/day from 2 weeks prior to mating until gestation day (GD) 20 (males) or day 4 post-partum (females). No animals died during treatment, and no compound-related effects were evident on weight gain, food consumption, fertility, fecundity, litter characteristics, or on pathology or histopathology in either generation.

2.3.5 Mammalian Dermal Toxicity

No data are available.

2.4 Summary of Avian Toxicology

No toxicological data for the effects of ethylene on avian species was located. Ecotoxicological research on the effects of this compound on birds is recommended.

2.5 Amphibian Toxicology

No toxicological data for the effects of ethylene on amphibian species was located. Ecotoxicological research on the effects of this compound on amphibians is recommended.

2.6 Reptilian Toxicology

No toxicological data for the effects of ethylene on reptiles was located. Ecotoxicological research on the effects of this compound on reptiles is recommended.

3. RECOMMENDED TOXICITY REFERENCE VALUES

3.1 Toxicity Reference Values for Mammals

3.1.1 TRVs for Ingestion Exposures for the Class Mammalia

At this time it is not possible to derive a TRV for oral route of exposure for ethylene due to the lack of toxicity data and the gaseous nature of the compound which renders an oral exposure unlikely.

3.1.2 TRVs for Inhalation Exposures for the Class Mammalia

With the use of ethylene in high concentrations as an anesthetic, there is no evidence of toxicological effects occurring at levels that would be likely in the environment. It is, however, evident

that there are toxicological effects through its ethylene oxide intermediate. However, the effects were molecular in nature and were not linked to more toxicologically relevant endpoints such as tumor formation, morbidity or death. As a result, a TRV could not be derived for ethylene at this time.

4. IMPORTANT RESEARCH NEEDS

The limited availability of data on the toxicity of ethylene to wildlife species precludes the development of a TRV. Hence, more studies of the compound and its derivatives are recommended. The toxicity and biochemical activity of ethylene and ethylene oxide warrant attention to explain the relationship between these compounds. Also, chronic toxicity studies on non-mammalian wildlife such as birds, reptiles and amphibians are particularly warranted.

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APPENDIX A

LITERATURE REVIEW

Separate searches in DIALOG (three in all) were carried out on ethylene on April 20, 2001, and on May 2, 2001.

In the first search the following files were scanned:

File 155 MEDLINE, File 156 TOXLINE, File 5 BIOSIS, File 10 AGRICOLA, File 203 AGRIS, File 399 Chemical Abstracts, File 77 Conference Papers Index, File 35 Dissertation Abstracts, File 40 ENVIRONLINE, File 68 Environmental Bibliography, File 76 Life Sciences Collection, File 41 Pollution Abstracts, File 185 Zoological Record, File 6 NTIS, File 50 CAB, File 144 PASCAL, File 34 SCISEARCH, and File 434 SCISEARCH.

The search strategy for **Amphibians & Reptiles**:

- Chemical name, CAS numbers
- AND (amphibi? or frog or frogs or salamander? or newt or newts or toad? or reptil? or crocodil? or alligator? or caiman? snake? or lizard? or turtle? or tortoise? or terrapin?)
- AND (reproduc? or diet or dietary or systemic or development? or histolog? or growth or neurological or behav? or mortal? or lethal? or surviv? or (drinking()water))
- NOT glycol
- RD (reduce duplicates)
- NOT dibromide
- NOT dichloride
- NOT (human? or culture? or subcutaneous or vitro or gene or inject? or tumo? or inhalation or carcin? or cancer?)

The search strategy for **Birds:**

- Chemical name, CAS numbers
- AND chicken? or duck or duckling? or ducks or mallard? or quail? or (japanese()quail?) or coturnix or (gallus()domesticus) or platyrhyn? or anas or aves or avian or bird? or (song()bird?) or bobwhite? or (water()bird) or (water()fowl)
- AND (reproduc? or diet or dietary or systemic or development? or histolog? or growth or neurological or behav? or mortal? or lethal? or surviv? or (drinking()water))

- NOT (human? or culture? or subcutaneous or vitro or gene or inject? or tumo? or inhalation or carcin? or cancer?)
- RD (reduce duplicates)
- NOT dibromide or dichloride
- NOT dibromide
- NOT dichloride

The search strategy for **Laboratory Mammals:**

- Chemical name, CAS numbers
- AND (rat or rats or mice or mouse or hamster? or (guinea()pig?) or rabbit? or monkey?)
- AND (reproduc? or diet or dietary or systemic or development? or histolog? or growth or neurological or behav? or mortal? or lethal? or surviv? or (drinking()water))
- NOT (human? or culture? or subcutaneous or vitro or gene or inject? or tumo? or inhalation or carcin? or cancer?)/ti,de
- NOT (meeting()poster)
- NOT (meeting()abstract)
- NOT (conference()proceeding?)
- RD (reduce duplicates)
- NOT (patient? or cohort? or worker? or child? or infant? or women or men or occupational)
- NOT (glycols or polymer or poly or tetraacetic or tetraacetate or dichlorides)
- NOT EDTA
- NOT (dimethanesulphonate? or dimethanesulfonate? or diamine? or EDS)
- AND LA=English

The search strategy for **Wild Mammals:**

- Chemical name, CAS numbers
- And (didelphidae or opossum? or soricidae or shrew? Or talpidae or armadillo? or dasypodidae or ochotonidae or leporidae) or canidae or ursidae or procyonidae or mustelidae or felidae or cat or cats or dog or dogs or bear or bears or weasel? or skunk? or marten or martens or badger? or ferret? or

mink? Or aplodontidae or beaver? or sciuridae or geomyidae or heteromyidae or castoridae or equidae or suidae or dicotylidae or cervidae or antilocapridae or bovidae arvicolinae or mycocastoridae or dipodidae or erethizontidae or sigmodon? or (harvest()mice) or (harvest()mouse) or microtus or peromyscus or reithrodontomys or onychomys or vole or voles or lemming?

- AND (reproduc? or diet or dietary or systemic or development? or histolog? or growth or neurological or behav? or mortal? or lethal? or surviv? or (drinking()water))
- NOT (human? or culture? or subcutaneous or vitro or gene or inject? or tumo? or inhalation or carcin? or cancer?)/ti,de
- NOT (meeting()poster?)
- NOT (meeting()abstract?)
- NOT (conference()proceedings?)
- NOT (patient? or cohort? or worker? or child? or infant? or women? or men? or occupational?)
- RD (reduce duplicates)
- NOT steriliz?
- NOT oxide

When the search retrieved an appreciable number of hits, *keywords in context* were reviewed to minimize costs before any abstracts were downloaded (Tier 1). However, when only a limited number of studies were identified by the search, the abstracts were downloaded at the time of the search (Tier 2).

The second search examined the same files as the first but used the following structure:

For **Laboratory Animals**

- CAS Number
- AND (rat or rats or mice or mouse or hamster? or (guinea()pig?) or rabbit? or monkey?)
- AND (reproduc? or diet or dietary or systemic or development? or histolog? or growth or neurological or behav? or mortal? or lethal? or surviv? or (drinking()water))
- RD (reduce duplicates)

The third search examined the following databases

File 155 Medline, File 156 Toxline, File 535 Thomas Register Online, File 76 Life Sciences Collection, File 185 Zoological Record Online, File 5 Biosis Reviews.

For **Birds**

- CAS Number

- AND (chicken? or duck or duckling? or ducks or mallard? or quail? or (japanese()quail?) or coturnix or (gallus()domesticus) or platyrhyn? or anas or aves or avian or bird? or (song()bird?) or bobwhite? or (water()bird) or (water()fowl))

- RD (Reduce Duplicates)

For **Wild Mammals**

- CAS Number

- AND (didelphidae or opossum? or soricidae or shrew? Or talpidae or armadillo? or dasypodidae or ochotonidae or leporidae) or canidae or ursidae or procyonidae or mustelidae or felidae or cat or cats or dog or dogs or bear or bears or weasel? or skunk? or marten or martens or badger? or ferret? or mink? Or aplodontidae or beaver? or sciuridae or geomyidae or heteromyidae or castoridae or equidae or suidae or dicotylidae or cervidae or antilocapridae or bovidae arvicolinae or mycocastoridae or dipodidae or erethizontidae or sigmodon? or (harvest()mice) or (harvest()mouse) or microtus or peromyscus or reithrodontomys or onychomys or vole or voles or lemming?)

- RD (Reduce Duplicates)

For **Amphibians/Reptiles**

- CAS. Number

- AND (amphibi? or frog or frogs or salamander? or newt or newts or toad? or reptil? or crocodil? or alligator? or caiman? snake? or lizard? or turtle? or tortoise? or terrapin?)

- RD (reduce duplicates)

As noted in Section 2.1, 538 hits on ethylene were obtained in the initial searches, of which 9 were selected for retrieval.

資料　１３

国立労働生活研究所：スウェーデン労働基準の科学的基礎 13.
（抜粋）エチレンのコンセンサス・レポート
１９９６年１２月

National Institute for Working Life
December 11, 1996

Scientific Basis for Swedish Occupational Standards

XVIII

Consensus Report for Ethene

Consensus Report for Ethene

December 11, 1996

Physical and chemical data. Occurrence

CAS No:	74-85-1
Systematic name:	ethylene
Synonyms:	acetene, elayl, olefiant gas
Formula:	$CH_2=CH_2$
Molecular weight:	28.05
Density:	0.98 (air = 1)
Boiling point:	- 104 °C
Vapor pressure:	4270 kPa (0 °C)
Melting point:	- 169 °C
Explosion threshold:	2.75 vol % in air (100 kPa; 20 °C)
Distribution coefficient:	log P_{OW} = 1.13 (octanol/water)
Conversion factors:	1 ppm = 1.15 mg/m^3
	1 mg/m^3 = 0.87 ppm

Ethene at room temperature is a colorless gas with a sweet odor and taste. The reported odor threshold is 290 ppm (333.5 mg/m^3) (1, 26). The gas dissolves readily in water, acetone, ethanol and benzene. Ethene is stable under normal pressure and temperature conditions, but may polymerize at higher pressure and temperature.

Ethene is used primarily in the production of polyethylene and ethylene oxide / ethylene glycol. It is also used as a raw material in the production of other chemical substances. Ethene is used to accelerate the ripening of fruit. (It is formed naturally by ripening fruit.)

There are virtually no data on occupational exposure to ethene in connection with production of the substance. It is usually produced in closed systems. In one study (17) it is estimated that during the years 1941 to 1947 the exposure level for ethene around production of ethylene oxide was about 600 mg/m^3. Measurements of occupational exposure to ethene in warehouses where the gas is used to control the ripening of bananas showed air concentrations ranging from 0.02 to 3.85 mg/m^3, with a mean value of 0.35 mg/m^3 (28). In a study of firemen, it was found that they were exposed to ethene in some phases of fighting fires (20).

Uptake, biotransformation, excretion

Six volunteers were exposed to 0, 5 or 50 ppm ethene (0, 5.75 or 57.5 mg/m^3) for two hours. Most (94.4%) of the inhaled ethene was immediately exhaled. Calculations based on clearance of uptake and metabolic clearance indicated that alveolar retention at steady state was 2% and the biological half time was 0.65 hours (12). From theoretical calculations of gas uptake in the lungs, it can be concluded that the low uptake of ethene is due to its low solubility in blood.

Ethene can be detected in exhaled air of unexposed persons. Women exhale more ethene at the time of ovulation. The biochemical origin of this endogenously produced ethene has not been explained, but four theories have been proposed: lipid peroxidation, enzyme-catalyzed oxidative breakdown of methionine, oxidation of hemoglobin, and metabolism in intestinal bacteria (18).

Two hemoglobin adducts, N-(2-hydroxyethyl)histidine (HOEtHis) and N-(2-hydroxyethyl)valine (HOEtVal), have been used as dose measures for formation of ethylene oxide from ethene.

Exposure to ethene at concentrations of 10 to 20 ppb (11.5 to 23 μg/m^3) has been associated with an increase of adducts (HOEtVal) amounting to 4 – 8 pmol/g Hb at steady state (29). Fruit store workers exposed to 0.02 to 3.35 ppm ethene (0.023 to 3.85 mg/m^3) had adduct (HOEtVal) levels of 22 to 65 pmol/g Hb; levels in unexposed controls were 12 to 27 pmol/g Hb (28). The adduct level due to endogenous ethylene alone is estimated to be about 12 pmol/g Hb (12).

It has been estimated from adduct data that about 2 to 3% of inhaled ethene is metabolized to ethylene oxide (14, 28). Exposure to 1 ppm ethene (1.15 mg/m^3) for 40 hours/week is calculated to increase the adduct level by 100 to 120 pmol/g Hb (9).

Mice were exposed to 17 ppm (22.3 mg/m^3) ^{14}C-labeled ethene for one hour. Four hours later radioactivity was found primarily in kidneys and liver, with lesser amounts in testes and brain. A 48-hour urine sample contained S-(2-hydroxyethyl)cysteine, indicating that the ethene had been metabolized to ethylene oxide (8). Fischer-344 rats that were exposed to 10,000 ppm (11,500 mg/m^3) radioactively labeled ethene for 5 hours eliminated most of the radioactivity as exhaled ethene, while smaller amounts were excreted in urine and feces or exhaled as CO_2. Minor amounts of radioactivity were found in blood, liver, intestines and kidneys. The amounts of radioactivity in urine and CO_2 were higher in animals that had been pre-treated with Aroclor (a commercial PCB mixture), which indicates that ethene metabolism can be stimulated by substances that induce the mixed function oxidase system (15).

When Sprague-Dawley rats were exposed to between 0.1 and 80 ppm (0.12 and 92 mg/m^3) ethene, they eliminated 24% of available ethene by biotransformation and 76% by exhalation of unchanged ethene. The alveolar retention at steady state was 3.5% and the biological half time was 4.7 minutes (12). Metabolism was saturated at concentrations above 80 ppm (92 mg/m^3), with a maximum metabolism rate (V_{max}) of 0.24 mg/hour x kg body weight (11).

When Sprague-Dawley rats were exposed for 21 hours to ethene levels exceeding 1000 ppm (1150 mg/m^3) the amount of ethene absorbed per unit of time was constant (2). When Fischer-344 rats were exposed to 600 ppm (690 mg/m^3) ethene, the blood level of ethylene oxide rose rapidly during the first five to ten minutes and then dropped to a level that remained constant during the remainder of the 60-minute exposure. The level of cytochrome P-450 in liver declined steadily during the experiment (22). This was taken to indicate that during metabolism of ethene the phenobarbital-induced form of cytochrome P-450 is destroyed by transformation of the cytochrome heme to an abnormal porphyrin (23).

Sprague-Dawley rats were exposed to 300 ppm (345 mg/m^3) ethene 12 hours/day for three consecutive days: the concentration of ethene was low in all examined organs 12 hours after the last exposure. However, the levels of hemoglobin adducts and of 7-alkylguanine in lymphocytes and liver were elevated, indicating the formation of ethylene oxide (10).

Hemoglobin adduct (HOEtVal) levels of about 100 pmol/g Hb have been measured in several strains of rats, mice and hamsters after exposure to ethene (18). Calculations based on animal data indicate that uptake of 1 mg ethene per kg body weight corresponds to a tissue dose of ethylene oxide amounting to 0.03 mg x hour/kg body weight. This value agrees with the one calculated for human uptake (32).

Toxic effects

Ethene is not irritating to eyes or skin (4). People exposed to a concentration of 37.5% in air for 15 minutes experienced some memory disturbance, and 50% in air results in loss of consciousness due to oxygen deprivation (4).

Mice repeatedly exposed to concentrations resulting in loss of consciousness showed no histopathological changes in kidneys, adrenal glands, heart or lungs (24). The concentration was described as ”atmosphere in which the partial pressure of oxygen was 20 per cent and ethylene 90 per cent.”

Fischer-344 rats exposed to 10,000 ppm (11,500 mg/m^3) ethene for 5 hours showed no toxic effects (15). Nor were toxic effects observed in Sprague-Dawley rats with ethene exposures up to 10,000 ppm (11,500 mg/m^3) 6 hours/day, 5 days/week in a 90-day study (25), or in Fischer-344 rats with exposures up to 3000 ppm (3450 mg/m^3) in a two-year study (16). This absence of toxicity may be due to saturation of ethene metabolism (18).

Rats pre-treated with Aroclor and 24 hours later exposed to ethene concentrations of 10,000, 30,000 or 57,000 ppm (11,500, 34,500 or 65,550 mg/m^3) for 4 hours had dose-dependent effects on liver, indicated by elevated serum levels of sorbitol dehydrogenase and alanin-α-ketoglutarate transaminase and by the histological observation of centrilobular necrosis (5, 6, 15).

Mutagenicity, carcinogenicity, teratogenicity

Ethene caused no mutations in tests with *Salmonella typhimurium* (TA 100), either with or without metabolic activation (34). Ethene induced no micronuclei in the bone marrow of

rats and mice exposed to up to 3000 ppm (3450 mg/m^3) 6 hours/day, 5 days/week for four weeks (33).

The DNA adduct 7-(2-hydroxyethyl)guanine (7-HOEtGua) was found in levels of 2 to 6 nmol/g DNA in lymphocytes from untreated Sprague-Dawley rats (13) and in DNA from several different tissues from Fischer-344 rats and B6C3F1 mice (35). After mice were exposed for eight hours to 11 ppm (12.9 mg/m^3) radioactively labeled ethene, 7-alkylation of guanine could be demonstrated in DNA from liver, spleen and testes: 0.17 nmol/g DNA was measured in liver; 0.098 in spleen and 0.068 nmol/g DNA in testes, which was less that 10% above the background level (27).

Groups of Fischer-344 rats (120 of each sex) were exposed to 0, 300, 1000 or 3000 ppm (0, 345, 1150 or 3450 mg/m^3) ethene 6 hours/day, 5 days/week for up to 24 months. Rats were sacrificed and examined after 6, 12, 18 and 24 months. There was no difference in survival between exposed rats and controls. Histological comparisons of the high-dose group and the controls revealed no indications of any exposure-related toxicity and no elevated incidence of tumors (16).

Groups of Sprague-Dawley rats (both sexes) were exposed to 0 or 10,000 ppm ethene (0 or 11,500 mg/m^3) 8 hours/day, 5 days/week for three weeks. One week later the animals were given polychlorinated biphenyls (unspecified), 10 mg/kg body weight, by gavage twice a week for 8 weeks. The animals were then sacrificed and examined for ”ATPase-deficient foci.” There was no difference between the ethene-exposed animals and controls. (When ethylene oxide was used as a positive control, there was a pronounced increase of foci.) (7)

According to the IARC (18), it is not possible to determine whether ethene is carcinogenic to either man or experimental animals (”inadequate evidence”) and ethene has therefore been placed in Group 3: ”unclassifiable as to its carcinogenicity to humans.” As for the metabolite ethylene oxide, in the judgement of the IARC (19) there is ”limited evidence” that it is carcinogenic to humans and ”sufficient evidence” that it is carcinogenic to experimental animals, and in the overall assessment ethylene oxide is therefore placed in Group 1: ”carcinogenic to humans.”

In a theoretical presentation (29, 30, 31) it is postulated that ethene might cause cancer via activation to ethylene oxide which then binds to DNA, and that the consequent risk of cancer in Sweden due to ethene in city air would be equivalent to 30 cases per year (at an average exposure of 1.8 mg/m^3).

One study reports 6 miscarriages among 15 pregnant women who were working in a petrochemical industry. This rate was higher than that for 1,549 women who were living in the surrounding area. The main product was ethene (350,000 tons/year), but the women were also exposed to other substances including ethylene oxide, vinyl chloride and phthalates. No exposure data are given, but measured ethene concentrations in air outside the plant were on average 10 to 15 ppb (2).

Dose-response / dose-effect relationships

There are no data that can be used as a basis for calculating a dose-effect or dose-response relationship for human exposure to ethene. Occupational exposures of 0.023 to 3.5 mg/m^3 have resulted in elevated formation of hemoglobin adducts (28). Data from animal studies are summarized in Table 1.

Table 1. Effects of ethene inhalation on experimental animals.

mg/m^3	Duration	Species	Effects	Ref.
12.9	8 hours	Mouse	7-alkylation of guanine in DNA	27
92	6 hours	Rat	Saturation of ethene metabolism	11
3450	28 days	Mouse	No increase in micronuclei	33
3450	2 years	Rat	No toxic effects	16
11,500	5 hours	Rat	No toxic effects	15
11,500	90 days	Rat	No toxic effects	25
11,500	24 hours	Rat (pre-treated with Aroclor)	Liver effects	5, 6

Conclusions

Judging from available data on toxicity to humans, the critical effect of exposure to ethene is its effect on the central nervous system. (Ethene has been used as an anesthetic.) From animal data it can be observed that, if the animals have been enzyme-induced, effects on the liver may be the critical ones.

It has been debated whether exposure to ethene can give rise to toxic effects and/or cancer caused by the metabolite ethylene oxide. In its 1981 report, the Criteria Group stated that the critical effects of exposure to ethylene oxide were the mutagenic, cytogenetic and carcinogenic effects, and that cytogenetic effects of ethylene oxide were seen at occupational exposures of about 2 mg/m^3 (21).

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資料　１４

馬鈴しょ萌芽抑制効果に対するエチレン濃度限界に関する試験

（平成 20 年秋～21 年夏、酪農学園大学）

１．目的

加工用馬鈴しょの貯蔵中の萌芽を抑制し、国産馬鈴しょの周年供給体制を確立することを目的とし、エチレンによる芽の生長抑制効果と加工適性維持のための限界エチレン処理濃度を求めるために、代表的な 2 品種を用いて貯蔵試験を行った。

２．試験方法

１）供試材料

平成 20 年、帯広市川西産「きたひめ」、「スノーデン」を用いた。

２）エチレンの供給方法および濃度

ガス置換デシケータを利用したエチレン供給貯蔵基礎実験装置（参考資料１）を用いて 10 月 28 日から貯蔵試験を開始した。

３）貯蔵方法

無処理区も同様の貯蔵容器（デシケータ）を用いた（参考資料１を参照）。

貯蔵温度は 8℃とし、エチレン濃度はこれまでの試験において 4ppm で十分な効果が得られることが明らかになっているため、その 5 倍濃度の処理区として 20ppm と設定し、無処理区として 0ppm 区を設定した。

４)測定項目

貯蔵環境の温度、湿度、エチレン濃度については、貯蔵期間中継続して測定した。品質については、10月28日、12月26日、2月16日、3月20日、4月24日、5月29日、7月3日に測定した。

(1)恒温室内温湿度

恒温室内温度、湿度をデーターロガーを用いて測定した。

(2)貯蔵容器（デシケータ）内エチレン濃度、二酸化炭素濃度

ガスタイトシリンジにより貯蔵容器の上下2箇所から容器内ガスを採取し、ガスクロマトグラフを用いてエチレン濃度および二酸化炭素濃度を測定した。

(3)試料質量、水分含量

電子天秤を用いて試料質量を測定し、質量減少率を求めた。水分含量は70℃24時間恒温乾燥法により求めた。

(4)芽の長さ

5㎜以下、5㎜以上の芽の塊茎当たりの個数、塊茎毎の最長芽の長さ、塊茎当たりの芽の質量を測定した。

(5)糖含量

HPLCを用いてショ糖、ブドウ糖、果糖含量を測定した。

(6)硬度

レオメータを用い、直径2㎜の円筒状プランジャを50㎜/sの速度で貫入させて荷重を測定した。

(7)ポテトチップカラー

試料を約1㎜の厚さにスライスし、180℃のサラダオイルで約120秒間フライし、その色をアグトロンメーターを用いて測定した。

３．結果

図 1～2 に貯蔵中エチレン濃度の推移を示す。

「きたひめ」「スノーデン」の初期のエチレン処理区において、急激な濃度の上昇があったが、これはコンプレッサの不調により空気の供給が停止したためである。また、このとき無処理区においてもエチレンが一時的に検出された。これ以外ではいずれもほぼ設定どおりに制御することができた。貯蔵開始当初は 1 時間換気、5 時間休止のサイクルで換気及びエチレンの供給を行っていたが、特に、エチレン区において CO_2 濃度の上昇が見られたため、2 時間換気、4 時間換気に変更することにより CO_2 濃度は 0.1%以下に抑えることができ、以後このサイクルで行った。

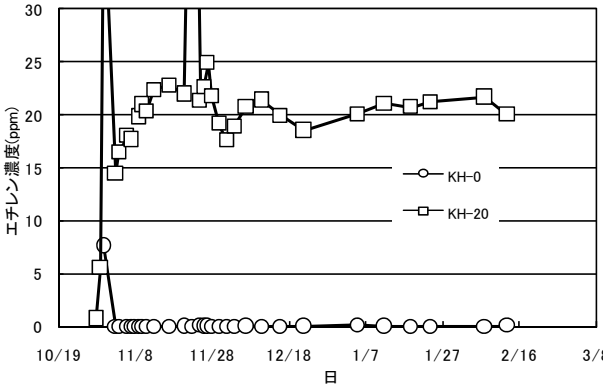

図1 貯蔵中エチレン濃度の推移(きたひめ)

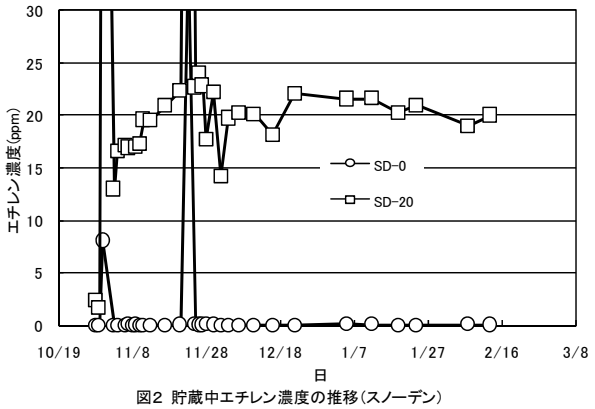

図2 貯蔵中エチレン濃度の推移(スノーデン)

図 3～4 に、塊茎毎の最長芽の長さの平均値の推移を示す。

いずれの品種においても 2 月 16 日の時点で萌芽が見られ、特に、無処理区において芽の伸長が大きかった。

貯蔵終了時点でいずれの品種においてもエチレン処理区では芽の長さが 20㎜ 以下に抑制された。

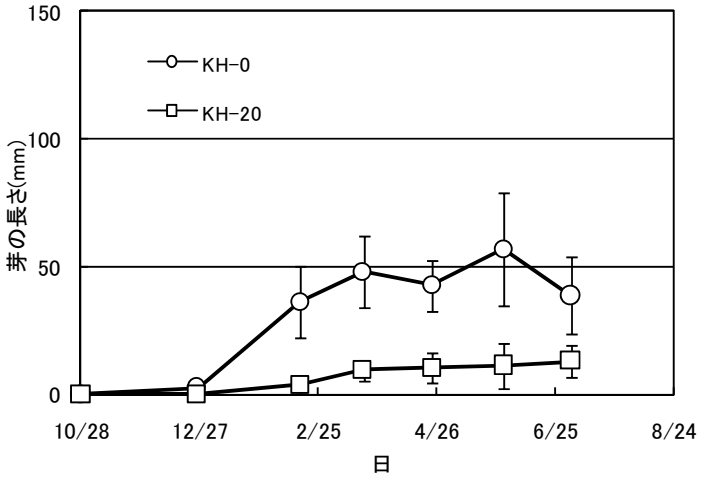

図3 最長芽の長さの推移(きたひめ)

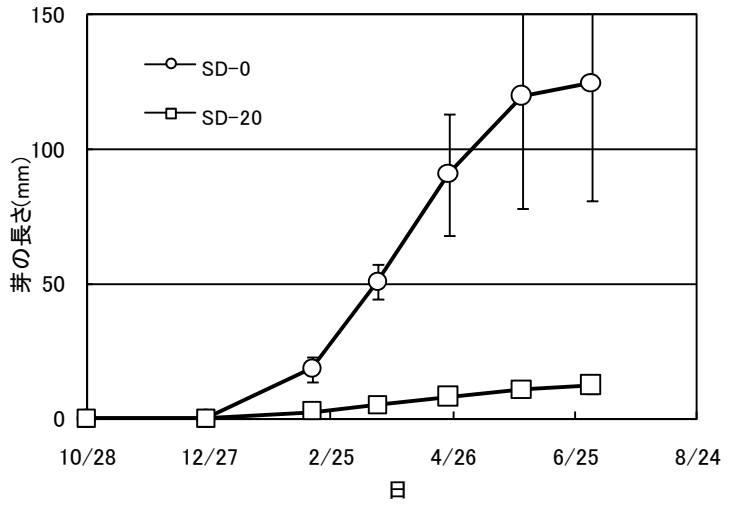

図4 最長芽の長さの推移(スノーデン)

図 5～6 に、還元糖含量の推移を示す。

いずれの品種も貯蔵初期に還元糖が増加し、その後低下する傾向にあり、貯蔵末期に再び増加する傾向もみられた。

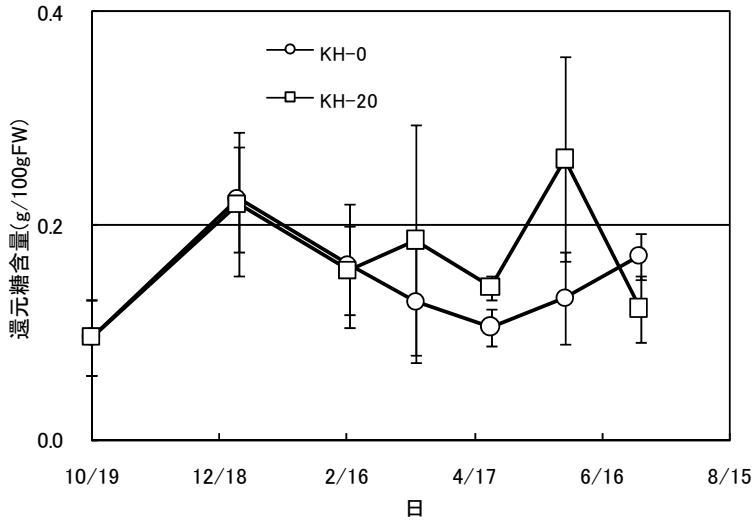

図5 還元糖含量の推移(きたひめ)

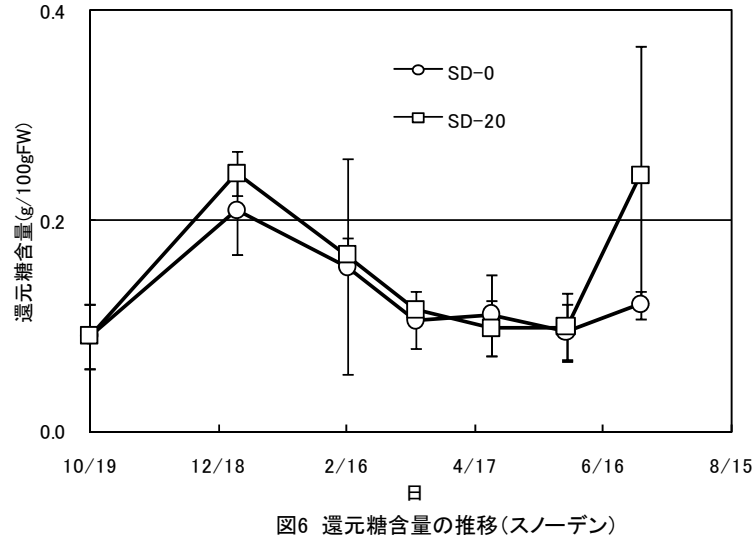

図6 還元糖含量の推移(スノーデン)

図 7～8 に、ポテトチップカラーの推移を示す。

還元糖含量の推移を反映し、貯蔵初期にポテトチップカラーが低下し、その後回復する傾向にあるが、「きたひめ」は低下の度合いが小さい。

また、貯蔵末期に低下する傾向にあった。いずれも 20ppm のエチレン処理においてもポテトチップカラーの大きな低下はなく、5 月下旬頃までは原料としての利用に耐える加工適性を保っていた。

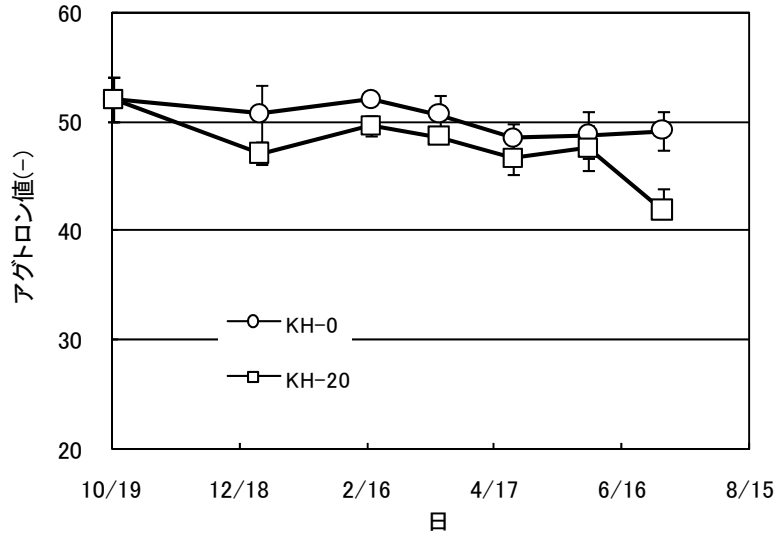

図7 チップカラーの推移(きたひめ)

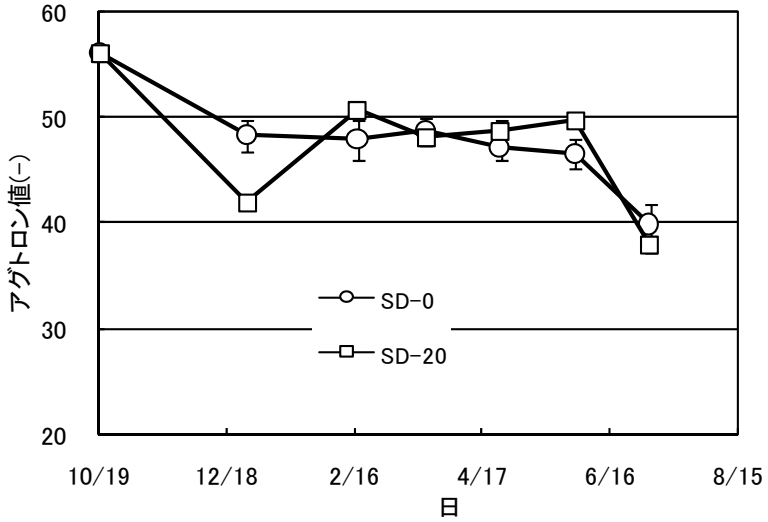

図8 チップカラーの推移(スノーデン)

４．要　約

エチレンによる芽の生長抑制効果と加工適性維持のための限界エチレン処理濃度を求めるために代表的な 2 品種を用いて貯蔵試験を行った。

エチレン濃度 20ppm で貯蔵を行った場合においても、芽の伸長は抑えられ、ポテトチップカラーの顕著な低下はなかった。

資料　１５

エチレン処理による馬鈴しょの残留性に関する試験

（平成 20 年秋～21 年夏、酪農学園大学、十勝農業試験場）

１．目　的

エチレン処理した馬鈴しょの中のエチレン残留量が通常の食品中に含まれるエチレン量を超えることがないこと等を裏付けるために、エチレン処理した馬鈴しょの長期貯蔵後のエチレン処理区と無処理区の塊茎中のエチレン濃度を調査する。

２．試験方法

○.酪農学園大学

１）供試品種：「きたひめ」、「スノーデン」、「トヨシロ」

２）試験期間：平成 20 年秋～21 年夏

３）エチレン：無処理区 0ppm、処理区は 4ppm、20ppm

４）試験実施：4 月 24 日、5 月 30 日

５）その他は参考試料 2 に示す。

○JA 士幌町（試験実施、試験担当は十勝農業試験場）

１）供試品種：「きたひめ」、「スノーデン」、「トヨシロ」

２）試験期間：平成 20 年秋～21 年夏

３）エチレン：無処理区 0ppm、処理区は 8ppm

４）試験実施：4 月 23 日、6 月 25 日

５）その他は参考資料 3 に示す。

○カルビーポテト（株）（参考）

１）供試品種：「スノーデン」

２）試験期間：平成 20 年秋～21 年夏

３）エチレン：無処理 0ppm、処理区 4ppm

４）試験実施：4 月 20 日

５）その他は種略

３．エチレン濃度の分析方法

酪農学園大学および JA 士幌町（十勝農試）でエチレン処理した馬鈴しょ 2 塊茎とスペーサーをラミネートフィルム袋に入れてヒートシールして密閉した（写真 1)。

フィルムにゴムパッチを貼付し注射針を刺し、真空ポンプにて内部の空気を完全に排気し（写真 2､3)、馬鈴しょ重量 300g に対し 1,000mL の空気を再度入れて封入した（写真 4)。

封入後、24 時間経過した時点（写真 5）で内部の空気をガスタイトシリンジでサンプリングしてガスクロマトグラフ（写真 6）にてエチレン濃度を測定した。

写真１．ビニールパック

写真 2．真空ポンプによる脱気

写真 3.真空状態

写真 4．一定量の空気を入れる

写真 5．空気を入れて 24 時間保管

写真 6．ガスクロ

４．結　果

表 1 に示す。

酪農学園大学において処理した馬鈴しょは、芽をすべて取り除いたのちに残留性試験を行ったが、その他の機関において処理したものについては、芽が付いたままの状態で試験に供試した。

酪農学園大学において処理した馬鈴しょでは、4 月 24 日の「きたひめ」20ppm 処理区においてのみエチレンが検出された。

JA 士幌町において処理した馬鈴しょでは、4 月 23 日の試料では無処理区においてのみエチレンが検出された。6 月 25 日においては、「トヨシロ」の無処理区を除いてエチレンが検出されたが、その他は無処理区の方が濃度が高かった。

カルビーポテト（株）において処理した馬鈴しょは、いずれもエチレンは検出されなかった。

本試験に用いた方法では、内生エチレンと処理に使用したエチレンの区別は出来ないが、ほとんどの場合エチレンが検出されないか、検出されても無処理区より濃度は低く、残留性は無いと判断できる。

表１　エチレン残留性試験結果

処理機関	試験期日	出庫後時間	品種	処理条件	質量 g	空気量 mL	エチレン濃度 ppm
酪農学園	4月24日	5時間後	きたひめ	0ppm	327.6	1092	-
				4ppm	304.4	1015	-
				20ppm	441.5	1472	0.084
			スノーデン	0ppm	309.9	1033	-
				4ppm	347.6	1159	-
				20ppm	315.8	1053	-
			トヨシロ	0ppm	308.3	1028	-
				4ppm	322.3	1074	-
酪農学園	5月30日	24時間後	きたひめ	0ppm	335.2	1117	-
				4ppm	318.9	1063	-
				20ppm	315.7	1052	-
			スノーデン	0ppm	372.6	1242	-
				4ppm	347.9	1160	-
				20ppm	402.1	1340	-
			トヨシロ	0ppm	330.8	1103	-
				4ppm	281.6	939	-

処理機関	試験期日	出庫後時間	品種	処理条件	質量 g	空気量 mL	エチレン濃度 ppm
士幌農協	4月23日	22時間後	きたひめ	0ppm	316.4	1055	0.094
				8ppm	222.2	741	-
			スノーデン	0ppm	365.5	1218	0.044
				8ppm	257.2	857	-
			トヨシロ	0ppm	313.9	1046	0.075
				8ppm	315.7	1052	-
士幌農協	6月25日	22時間後	きたひめ	0ppm	228.3	761	0.0897
				8ppm	250.4	835	0.0547
			スノーデン	0ppm	274.7	916	0.4877
				8ppm	255.6	852	0.0432
			トヨシロ	0ppm	269.4	898	-
				8ppm	243.1	810	0.0759

処理機関	試験期日	出庫後時間	品種	処理条件	質量 g	空気量 mL	エチレン濃度 ppm
カルビーポテト	4月28日	20時間後	スノーデン	0ppm	300.0	1000	-
				0ppm	318.8	1063	-
				0ppm	350.4	1168	-
				4ppm	313.1	1044	-
				4ppm	322.3	1074	-
				4ppm	335.0	1117	-