ETHYLENE OXIDE

Identity

Name (parent)	Ethylene oxide
UN number	1040
CAS number	75-21-8
Intervention value (AGW in mg/m^3)	100
Structure	C_2H_4O

Occurrence

Chemical state (at 20 °C)	Gas
Physical appearances	Flammable gas with a sweet odor
Industrial products	Ethylene oxide is used to make other chemicals, especially ethylene glycol (which is used to make antifreeze and polyester). Further used in insecticides and to sterilize medical equipment and supplies.

Physicochemical properties

Molecular weight	44.1
Vapor pressure (mbar at 25 °C)	1500
Octanol/water partition coefficient (log Ko/w)	-0.3 [1]
Water solubility (in mg/L at 25 °C)	Completely soluble

Toxicokinetics (parent)

Uptake by inhalation	The average alveolar retention of ethylene oxide is 75% - 80% [2].
Uptake by skin absorption	Absorption of gas: *in vitro* study using human cadaver skin: percutaneous absorption was 1.3% and 46% under occlusion [3].
Uptake via gastrointestinal tract	unlikely to occur
Distribution	rapidly distributed throughout the body
Metabolism	Hydrolysis by epoxide hydrolase and conjugation by glutathione-*S*-transferase [4]
Excretion via lungs	Excretion of CO_2 and ethylene oxide. In rats, 12% of ^{14}C-ethylene oxide was exhaled as CO_2 and 1% as ethylene oxide [4].
Excretion via urine	Primary excretion route. In rats, 59% of ^{14}C-ethylene oxide was excreted in urine [4].
Excretion via feces	Minor excretion route. In rats, 4.5% of ^{14}C-ethylene oxide was excreted in feces [4].

Toxicodynamics

Toxicity	Neurotoxicity, irritation of the eyes, skin, and mucous membranes. Dermal contact with liquid ethylene oxide causes a freezing effect comparable to frostbites [4].
Classifications for carcinogenicity	Group 1, known human carcinogen [5].
Classifications for reprotoxicity	Embryo and fetal toxicity. Exposure increases the rate of miscarriages in female workers. Male and female reproductive systems are target organs for ethylene oxide, cited in ATSDR [4].
Classifications for sensitizing properties	Exposure to ethylene oxide can cause type I, type III and type IV hypersensitivity reactions [6].

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Biological monitoring

Biomarkers	**N-2-Hydroxyethylvaline (HOEtval)**	**N-acetyl-S-(2-hydroxyethyl)cysteine / hydroxyethylmercapturic acid (HEMA) in urine**
Molecular weight	**161.2**	207.25
Involved enzymatic metabolism	Glutathione-S-transferase	Gluthation-S-transferase
Biological material	Blood	Urine
Type of sample	Venous blood	Spot urine
Sampling strategy	Timing of blood sampling is not critical [7]	Several spot saples within a few hours after the accident
Excretion pattern	Hemoglobin adducts have the life-span of the erythrocytes (126 days)	Monophasic excretion HEMA in urine. Half-life HEMA in urine: < 5 h [8]
Materials	Vacutainer tubes, containing coagulant (heparin, sodium edentate). Syringes and needles sterilized by γ-radiation [7]	Polystyrene universal container
Transportation	Within 24 h at 4°C [7]	4°C [8]
Storage	-20°C	-20°C [8]
Stability	> 5 month at -20°C (After lysis of the erythrocytes) > 4 years at -20°C (after globin isolation) [9]	At -70°C for > 6 years [10]
Measurement principle	GC-MS	HPLC-APCI-MS-MS [10] LC-MS-MS [11]
Aliquot for 1 analysis	5 mL	1 mL [10] 2mL [11]
Limit of quantification	- 10 pmol HOEtVal / gr of Hb (detection limit) [9] - 19 pmol / gram globin (detection limit) (DFG) - Not possible to determine because quantification limit was well below the average background value in non-smokers, non-occupationally exposed people; 5 pmol / g globin was measurable without analytical difficulty [7]	LOD: 0.68 µg / L in a 1 mL urine sample (HPLC-APCI-MS-MS) [10] LOD: 0.5 µg / L urine (LC-MS-MS) [11]
Recommended adjustments	Adjustment for globin content of blood	Adjustment for creatinine
Preferred units for expression of results	µg/L	µg HEMA / g creatinine
Conversion factor	1 µg HOEtVal / L blood = 43.2 pmol / gr globin (DFG)	1 µg HEMA/ g creatinine = 0.55 µmol/mol creatinine 1 µg HEMA / L urine = $4.8 * 10^{-3}$ µmol /L urine
Biological exposure value US	BEL value: 6.8 nmol HOEtVal / g globin [12]	n/a
Biological exposure value Germany [13]	Ethylene oxide in air (mg/m^3) 0.92 1.83 3.66 Concentration HOEtVal (µg/L blood) 45 90 180	n/a
Background value	20 pmol / g globin (non-smokers) [7]	2.8 µg/ g creatinine (smokers, United

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		States) 1.1 µg/ g creatinine (non-smokers, United States) [10]
Possible confounders	Smoking, occupational exposure GST polymorphism [8]	Not specific for ethylene oxide, it is also a metabolite of other chemical such as vinyl chloride and ethylene dibromide. Smoking, occupational exposure GST polymorphism [8]
Remark	Other possibilities for biomonitoring are the determination of ethylene oxide in blood or end-exhaled air [2].	

References

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