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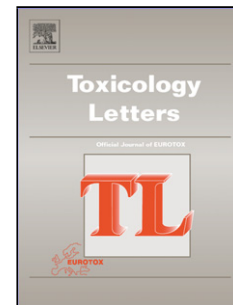
Title: A physiologically based toxicokinetic model for inhaled ethylene and ethylene oxide in mouse, rat, and human

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## **A physiologically based toxicokinetic model for inhaled ethylene and ethylene oxide in mouse, rat, and human**

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This paper is dedicated to the memory of György András Csanády, an excellent scientist, dear friend and wonderful colleague.

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### **Highlights**

A physiologically based toxicokinetic model was developed for mouse, rat, and human.

It predicts uptake and disposition of inhaled ethylene (ET) and ethylene oxide (EO). The model was extensively validated against published data in the three species. Adduct levels to hemoglobin and DNA were modeled for various exposures to ET or EO.

The model is applicable for assessing health risks from inhaled ET or EO.

### **Abstract**

The olefin ethylene (ET) is the largest volume organic chemical. Mammals metabolize ET to ethylene oxide (EO), another important industrial chemical. The epoxide alkylates hemoglobin (Hb) and DNA and has mutagenic and carcinogenic properties. In order to estimate the EO burden in mice, rats, and humans resulting from inhalation exposure to gaseous ET or EO, a physiological toxicokinetic model was developed. It consists of the compartments lung, richly perfused tissues, kidneys, muscle, fat, arterial blood, venous blood, and liver containing the sub-compartment endoplasmic reticulum. Modeled ET-metabolism is mediated by hepatic cytochrome P450 2E1, EO-metabolism by hepatic microsomal epoxide hydrolase or cytosolic glutathione S-transferase in various tissues. EO is also spontaneously hydrolysed or conjugated with glutathione. The model was validated on experimental data collected

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