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SUBJECT: Protocol Recommendations for Inhalation Testing of Phosphine

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This memo is in regards to inhalation testing requirements that you may have or institute for phosphine or its precursor forms, e.g., aluminum phosphide. In any inhalation study the portal-of-entry tissues (i.e. the upper and lower respiratory tract) would necessarily be suspect for effects. In recognition of this possibility, all chronic and subchronic inhalation studies of the National Toxicology Program examine the complete respiratory tract histopathologically, with the nasal turbinates being sectioned at least 3 levels (see Buckley et al., Fundam. Appl. Toxicol. 5, 341-352, 1985).

Consideration of portal-of-entry effects for inhalation of phosphine is especially relevant. Available information indicates that at least the lower respiratory tract is a target tissue for this compound. The Hazardous Substance Data Base (HSDB) notes that toxicity from inhalation exposure to this compound is characterized by both mucous membrane and pulmonary irritation with pulmonary edema being a life-threatening sequelae of higher level exposures. Besides my concern for the completeness of any inhalation study to maximize the information to be gleaned from the study both for present and future questions, such information has special use in other EPA evaluations such as the Reference Concentration (RfC) where information on portal-of-entry tissues is required for derivation of the RfC (see Interim Methods for Development of Inhalation Reference Concentrations, U.S. EPA, 1990.)

My recommendation, therefore, is to incorporate requirements for a thorough histopathologic analysis of the respiratory tract tissues into the protocol of any inhalation study for this compound.

cc: M. Greenberg
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RfC File: Phosphine (CASRN 7803-51-2, TIP No. 0706)