

body exposure, possibility of other routes of exposure, specific emulsion components and their toxicity. The phosmet used in the experiment was manufactured in the Union of Soviet Socialist Republics (USSR) by a research institute using an unknown method. With the number of unanswered key questions regarding the experimental protocol, EPA has determined that the results in this paper are insufficient to provide the basis for the continued listing of phosmet on the EHS list.

EPA evaluated more than 20 other inhalation studies of technical grade phosmet ($\geq 94\%$ phosmet) and other phosmet formulations, such as wettable powders and emulsions. The testing exposure routes included vapor, particulates and aerosols. Only three of these inhalation studies produced any mortality. The LC_{50} data from these three studies were not in the range of the LC_{50} value in the Russian study and did not meet the primary toxicity listing criteria of ≤ 0.5 mg/L. Of these three studies, results of one study with mortality were not considered appropriate to use because the phosmet formulation contained methylene chloride, a toxic component. Another study conducted in 1994, exposed rats to aerosols from an emulsion containing 27.5% phosmet and 8.4% naphthalenes. The aerosols were respirable-sized having a mass median aerodynamic diameter (MMAD) of 1.5–2.2 microns (μm). This study resulted in a LC_{50} of 1.19 mg/L for male rats and 0.845 mg/L for females. A third study conducted in 1995 reported a LC_{50} of 1.6 mg/L for rats and exposed the animals to a 70% phosmet particulates having a MMAD of 1.61 to 2.38 microns (μm).

Given the uncertainties with the inhalation toxicity data from (Danilenko, 1969) and based on the Agency's review of all the acute inhalation toxicity data for phosmet, EPA believes that there are no inhalation data meeting the primary listing criteria for phosmet of sufficient reliability or quality to support the listing of phosmet as an EHS chemical. As a result, EPA has decided to remove this inhalation value from consideration for the purpose of listing phosmet as an EHS. EPA solicits comments on the validity of the available inhalation toxicity studies to support listing of phosmet as an EHS based on the listing criteria for inhalation toxicity. EPA invites submission of any valid acute inhalation toxicity studies not already made available to EPA. EPA's review of all currently available acute inhalation toxicity studies can be found in the February 2003 Technical Background Document: Proposed Rule to Delist

Phosmet from the EHS List available in the public docket.

2. Phosmet Acute Dermal Toxicity

EPA undertook review of existing acute dermal toxicity data for phosmet. EPA could find no dermal toxicity data that met the primary dermal listing criteria of $LD_{50} \leq 50$ mg/kg. The lowest test results for technical phosmet indicated that the dermal LD_{50} is greater than 3160 mg/kg.

3. Phosmet Acute Oral Toxicity

Gowan submitted several acute rat oral studies in 1996, for technical grade phosmet and phosmet powder and emulsion formulations. None of the rat LD_{50} values from these studies met the EHS listing criteria, even when the percentage of inert ingredients in the formulation was taken into account. The lowest reported rat oral LD_{50} for technical grade phosmet (96.1%) is 113 mg/kg, which does not exceed the primary oral listing criteria of 25 mg/kg. The lowest reported rat oral LD_{50} for a phosmet formulation of 70% dust is 147 mg/kg (73.5 mg/kg based on active ingredient). Even when adjusted for the percentage active ingredient, this dose still does not exceed the criteria of 25 mg/kg.

Subsequently, EPA retrieved LD_{50} values from six mouse oral studies on technical grade phosmet from toxicity databases and the literature. Gowan was able to supply five of the mouse studies, which had been conducted by Stauffer Chemical Company. EPA also reviewed oral acute toxicity data available from OPP. Review of the six acute mouse oral studies indicates that mice are more sensitive than rats to phosmet. One mouse study conducted by Stauffer Chemical Company in 1971 reported a phosmet technical LD_{50} of 23.3 mg/kg for mice for technical grade phosmet, percentage unspecified. Another study conducted by researchers at NCTR (Haley *et al.*, 1975) reported LD_{50} results of 23.1 and 24.9 mg/kg for males and female mice, respectively for 99.5% phosmet. Other acute oral studies of technical grade phosmet with mice had LD_{50} results varying from 36.9 to 51 mg/kg. For a phosmet powder formulation, the lowest reported oral LD_{50} was 79.4 mg/kg in mice for 50% phosmet wettable powder. These studies are discussed in more detail in the February 2003 Technical Background Document: Proposed Rule to Delist Phosmet from the EHS List, available in the public docket.

The oral mouse LD_{50} of 23.3 mg/kg for phosmet technical resulted from testing a material called Imidan-EDC. Phosmet is also known by the name "Imidan."

Gowan stated that EDC (ethylene dichloride or dichloroethane), was a solvent used in the initial synthesis step of a discontinued process and that the impurity profile is not known. Gowan was not sure whether this product was ever registered for commercial use by Stauffer, who was the previous pesticide registrant with EPA. Gowan never utilized the EDC process and currently uses a benzene process to manufacture technical phosmet, the product currently registered with EPA. According to Gowan, Stauffer also licensed the phosmet-benzene process as a registrant with EPA. The Stauffer researchers determined the mouse oral LD_{50} for Imidan-Benzene to be 43 mg/kg. The greater toxicity observed for technical phosmet synthesized via the EDC route presumably may have been due to impurities resulting from the starting material, incomplete synthesis, degradation or other syntheses method-specific factors. Gowan believes that the "Imidan-EDC" phosmet is an inappropriate test substance. Because of these uncertainties, EPA does not believe the Imidan-EDC results are representative for the phosmet manufactured and registered with EPA by either Stauffer Chemical (former pesticide registrant) or Gowan Company (current pesticide registrant). Therefore, EPA removed these values from consideration for EHS listing purposes.

4. Phosmet Oral Mouse Study (Haley *et al.*, 1975)

Only one other study (Haley *et al.*, 1975) reported results with an $LD_{50} \leq 25$ mg/kg. This study examined the acute oral toxicity of five organophosphate pesticides (including Imidan or phosmet) in a total of three experiments: a range finding experiment, a pilot experiment, and a main experiment designed to estimate an LD_1 value and extrapolate an $LD_{0.1}$ value. LD_{50} values for phosmet were reported from the pilot study as 25.2 and 23.1 mg/kg for males and females, respectively and from the main study as 23.1 and 24.9 mg/kg for males and females, respectively. The study was conducted by the National Center for Toxicological Research (FDA), Arkansas. After reviewing this information, Gowan made several arguments why the information in the Haley study was insufficient to support the listing of phosmet as an EHS.

Haley *et al.* (1975) conducted two dose response experiments, a pilot study (100 mice) and a main study (660 mice). A linear regression was developed from the pilot results. The LD_{50} and its confidence intervals, and the slope of the regression and its