

confidence intervals are provided in the journal article. Using this regression, doses for LD₁, LD₂, LD₄, LD₈, LD₁₆, LD₃₂, and LD₆₄ were taken from the regression and used in the main study. The goal of the study was to estimate the LD₁ and extrapolate the LD_{0.1}. For the pilot study the actual doses and number of animals killed are not presented. The LD₁, LD₁₆, and LD₅₀ results only, by sex, were presented in a table in Haley *et al.* (1975) as predicted doses from the pilot study and calculated doses from the main study. The actual doses in the main study were chosen based on the results from the pilot study. The log of actual doses and percentage of animals killed are presented in a graph for each sex, except the value of the LD₂ for males which gave an aberrant response.

One of Gowan's key criticisms of Haley *et al.* (1975) was that no mortality data was presented from the pilot experiment and complete data from the main experiment is presented only in graphical form. Because the actual doses and animals killed at each dose are not cited, Gowan stated that the LD₅₀ results cannot be replicated or confirmed. EPA agrees with Gowan that the lack of tabulated mortality data is a serious flaw in this experiment. EPA attempted to recover the actual mortality data from the National Center for Toxicological Research, but the NCTR was not able to recover it. Gowan also raised other issues regarding Haley *et al.* (1975) which included the variations in main study mortality response, lack of information on the use of control data, and other questions or potential problems with the study methodology or design. The Agency addresses these issues in detail in the technical background document supporting this rulemaking.

5. Phosmet Oral Mouse Study (Gowan 2002)

Because of the uncertainties surrounding verification of results of the Haley study, EPA proposed conducting a new acute oral mouse LD₅₀ study using the Up-And-Down Method, as described in the Office of Prevention, Pesticides and Toxic Substances (OPPTS) new Harmonized Test Guideline 870.1100 for Acute Oral Toxicity. This guideline has been adopted by the Federal Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), the Organization for Economic Coordination and Development (OECD) and EPA's Science Advisory Panel (SAP). EPA's participation in ICCVAM is part of the Agency's commitment to support testing that reduces the use of animals.

Before EPA initiated the new test, Gowan decided to conduct its own acute toxicity study in mice. Based on its review of the existing toxicity data and the recommended test method, EPA provided Gowan with the recommended test method and comments on Gowan's draft test protocol. EPA recommended that Gowan test at multiple dose levels using the Up and Down Procedure (UDP) for acute oral toxicity. (See Docket for test method and comments provided to Gowan.)

Gowan completed its study of mouse responses to acute oral exposure to phosmet in December 2002. Their study planned to dose 20 female mice at 40 mg/kg, initially, with subsequent doses tested, if warranted. Twenty female mice were administered 40 mg/kg by oral gavage. After 14 days observation, there were no mortalities. Because no mortality occurred at 40 mg/kg, Gowan saw no need to conduct further tests. Thus, Gowan conducted a single dose study rather than an LD₅₀ test. Gowan believes the test results confirm that the oral LD₅₀ of phosmet exceeds 25 mg/kg listing criterion and that there is no basis for continuing to list phosmet as an Extremely Hazardous Substance.

The study results have been carefully reviewed by a cross-agency ad hoc committee whose consensus was that the Gowan study seemed to confirm the oral mouse LD₅₀ results from most of the previous literature studies, which showed LD₅₀s greater than EHS listing criterion of 25 mg/kg. EPA believes that the new test results support the conclusion that the acute oral LD₅₀ of phosmet exceeds 25 mg/kg and that phosmet should be removed from the EHS list. The Gowan study appears to be sound and conducted properly according to Good Laboratory Practices, although it is only for a single dose. The large number of mice (20) tested at a much higher concentration than the EHS List criterion supports the probability that the acute oral mouse LD₅₀ is greater than 25 mg/kg. In addition, Gowan had done a thorough chemical analysis of the phosmet material that was administered to the animals.

Normally EPA would not accept a single dose study for drawing conclusions about the LD₅₀ for a chemical. However, the Agency believes this study can be used in its analysis because of existing data indicating the approximate range of probable LD₅₀ values and data showing that phosmet has a steep dose-response curve. Although the new test did not follow new acute oral toxicity testing guidelines, the test results are consistent with the variability of individual animal

dose response seen in existing oral mouse LD₅₀ studies.

Phosmet is an organophosphate pesticide, with known lethal and toxic human health effects. However, after careful consideration of all of the toxicity data, EPA proposes that phosmet should be delisted from the EHS list for the following reasons: (1) The mouse oral LD₅₀ data that meet the criteria from the Haley *et al.* (1975) study have a number of deficiencies that increase the uncertainty around the results, such as lack of tabulated mortality data for either the pilot or the main study, lack of information on treatment of the control data, and considerable variability in the results at the LD₀₁–LD₀₈ doses, (2) the Haley LD₅₀ results are right at the limit of the oral toxicity listing criteria of 25 mg/kg, and (3) other acute mouse oral studies (including Gowan's December 2002 study conducted using Good Laboratory Practices) indicate the mouse oral LD₅₀ exceeds the 25 mg/kg listing criteria. EPA solicits comment on the proposed delisting decision and its rationale, and invites the public to submit or identify relevant peer-reviewed studies or data, of which the Agency may not be aware. EPA invites submission of any valid oral toxicity studies for phosmet that meet the listing criteria which are not already been reviewed by EPA. EPA's review of all currently available acute oral 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.

IV. Statutory and Executive Order Reviews

A. Executive Order 12866: Regulatory Planning and Review

Under Executive Order 12866 (58 FR 51735), the Agency must determine whether this regulatory action is "significant" and therefore subject to formal review by the Office of Management and Budget (OMB) and to the requirements of the Executive Order, which include assessing the costs and benefits anticipated as a result of the proposed regulatory action. The Order defines "significant regulatory action" as one that is likely to result in a rule that may: (1) Have an annual effect on the economy of \$100 million or more or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or state, local, or tribal governments or communities; (2) create a serious inconsistency or otherwise interfere with an action taken or planned by