

DESCRIPTION OF THE ACUTE ORAL TOXICITY SOFTWARE PROGRAM

Under contract to the U.S. EPA, Westat (Rockville, MD) developed the Acute Oral Toxicity (Guideline 425) Statistical Program" (AOT425StatPgm) to perform the statistical calculations associated with the OECD GUIDELINE FOR THE TESTING OF CHEMICALS, Section 4: Health Effects Test No. 425, Acute Oral Toxicity: Up-and-Down Procedure (OECD TG 425). The program may also be used with the U.S. EPA guideline, "Acute Oral Toxicity: Up-and-Down Procedure". The AOT425StatPgm program recommends a dose level for each animal, determines when dosing should stop, and calculates point and interval estimates for the LD50.

In addition to developing the AOT425StatPgm, Westat performed quality assurance testing for the statistical program and developed a report called, "QA Testing for the AOT425StatPgm Program." This document presents the results of testing to assess and to document the quality of the calculations performed by the program.

Westat also provided a complete report, called "Simulation Results for the AOT425StatPgm Program", which presents graphs of estimated LD50s, confidence interval (CI) widths, and expected animal usage, all obtained by automated means. These simulations were carried out to gauge the performance of the program and to determine the statistical performance of the OECD TG 425 procedure under various conditions.¹ They examine both the Main Test and the Limit Test.

The Acute Oral Toxicity 425 Statistical program (AOT425StatPgm), the quality assurance report, and simulations report which were made available to the UDP Peer Review Panel (Panel) for the August 21, 2001 review are currently found on the Internet at: http://iccvam.niehs.nih.gov/methods/udpdocs/udprpt/udp_ciprop.htm.

The software program and accompanying documentation are currently being revised by the U.S. EPA in accordance with recommendations from the Panel and comments received from the public. Upon completion of these revisions, the software program and accompanying documentation will be available through the U.S. EPA, Office of Pesticide Programs website at: <http://www.epa.gov/pesticides/>.

¹ The simulations assumed that the long-term and short-term outcomes (death or survival) were the same. One thousand simulated tests were generated for each simulation scenario, which included specified test type (Limit or Main), limit dose (2000 or 5000 mg/kg), and other defining features of the dose-response profile and its evaluation (e.g., true LD50 and sigma; assumed LD50 and sigma).

