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**COMMITTEE OF EXPERTS ON THE TRANSPORT OF
DANGEROUS GOODS AND ON THE GLOBALLY
HARMONIZED SYSTEM OF CLASSIFICATION
AND LABELLING OF CHEMICALS****Sub-Committee of Experts on the
Transport of Dangerous Goods**
(Twenty-first session, 1-10 July 2002,
agenda item 8 (c))**LISTING AND CLASSIFICATION****Miscellaneous amendment proposals (Parts 2 and 3)****Definition for acute oral toxicity (Division 6.1)****Transmitted by the expert from the United States of America**

1. The current acute oral toxicity definition in the Model Regulations is based on the requirements in the Organisation for Economic Co-operation and Development (OECD) Test Guideline (TG) 401. The OECD has agreed to three test methods that will replace the current TG 401. The experts from the United Kingdom, Germany and the United States of America took the lead in the development of the three alternative tests that OECD has now adopted and published the OECD Guidelines for the Testing of Chemicals. The expert from the United States of America is proposing to amend the acute oral toxicity definition to take into account the phase out of OECD TG 401 and the publication of the new TGs.

Background

2. A procedure for calculating the oral LD₅₀ was first described by Trevan in 1927. This procedure has been used as a benchmark for comparing the toxicity of chemicals. The original method used 50 animals or more. In 1981, the OECD adopted TG 401 for determining acute oral toxicity and to estimate LD₅₀ values. In 1987, the test guideline was revised to reduce the minimum number of animals used in the traditional acute oral toxicity test from 30 to 20 animals. The current definition for *LD₅₀ for acute oral toxicity* in paragraph 2.6.2.1.1 is based on OECD TG 401. In a continuing attempt to improve the estimate of acute oral toxicity while reducing the number of animals used per test, three alternative TGs have been developed and implemented to replace TG 401. The three TGs are the Fixed Dose Procedure (FDP, TG 420), the Acute Toxic Class Method (ATCM, TG 423), and the Up-and-Down Procedure (UDP, TG 425).

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3. OECD countries, through the OECD Chemical Committee of delegates responsible for national chemical policies and safety procedures in their own countries, have agreed to abolish TG 401 which has been widely criticized as inhumane to animals. The OECD manual of internationally accepted TGs, which sets guidelines for the testing of chemicals and chemical products world-wide, will delete OECD TG 401, also known as the LD₅₀ Draize test, after a phase-out period of one year at which time the test will be rejected by the regulatory community. TGs 420, 423 and 425, will be phased in over the coming year in order to give industry, test laboratories and the regulated community sufficient time to become familiar with the new methods. The OECD website on the Test Guidelines Programme (<http://www.oecd.org/ehs/test>) provides detailed information on the alternative methods and the deletion of TG 401 as well as a information on the phase out and phase in time frames.

4. In order to reflect the new OECD TGs for obtaining acute oral toxicity data it is necessary to amend the definition for LD₅₀ for acute oral toxicity in the Model Regulations.

Proposal

5. It is proposed that the current definition for acute oral toxicity in paragraph 2.6.2.1.1 be replaced with the following text:

"LD₅₀ (median lethal dose) for acute oral toxicity is the statistically derived single dose of a substance that can be expected to cause death within 14 days in 50 per cent of young adult albino rats when administered by the oral route. The LD₅₀ value is expressed in terms of mass of test substance per mass of test animal (mg/kg)."
