V. TOXICITY DETERMINATIONS

A. Procedures for toxicity determinations 1/2/

Recommended standardized operating procedures for acute subcutaneous toxicity determinations

1. Introduction

Three categories of agents were defined on the basis of their toxicity:

(i) super-toxic lethal chemicals;

(ii) other lethal chemicals;

(iii) other harmful chemicals.

Lethality limits in terms of LD_{50} for subcutaneous administration were established to separate three toxic categories at 0.5 mg/kg and 10 mg/kg.

2. Principles of the test method

The test substance is administered to a group of animals in doses corresponding exactly to the category limits (0.5 or 10 mg/kg respectively). If in an actual test the death rate was greater than 50 per cent, then the material would fall into the higher toxicity category; if it was lower than 50 per cent the material would fall into the lower toxicity category.

3. Description of the test procedure

3.1 Experimental animal Healthy young adult male albino rats of Wistar strain weighing 200 ± 20 g should be used. The animals should be acclimatized to the laboratory conditions for at least five days prior to the test. The temperature of the animal room before and during the test should be 22 ± 3° C and the relative humidity should be 50-70 per cent. With artificial lighting, the sequence should be 12 hours light, 12 hours dark. Conventional laboratory diets may be used for feeding with an unlimited supply of drinking water. The animals should be group-caged but the number of animals per cage should not interfere with proper observation of each animal. Prior to the test, the animals are randomized and divided into groups; 20 animals in each group.

3.2 Test substance Each test substance should be appropriately identified (chemical composition, origin, batch number, purity, solubility, stability, etc.) and stored under conditions ensuring its stability. The stability of the substance under the test conditions should also be known. A solution of the test substance should be prepared just before the test. Solutions with concentrations of 0.5 mg/ml and 10 mg/ml should be prepared. The preferable solvent is 0.85 per cent saline. Where the solubility of the

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1/ It was understood that these recommended standardized operating procedures (CD/CW/WP.30) for toxicity determinations might be supplemented or modified and/or, if necessary, reviewed.

2/ A view was expressed that appropriate methods for testing of non-lethal harmful chemicals need to be addressed at a later stage.