Application of criteria in 3.8.1.1 and 3.8.1.6 when a substance can be classified into both the specific target organ toxicity (single exposure) hazard class, for non-lethal effects, and acute toxicity hazard class, for lethal effects

Information on substance

Data

Human experience:

Numerous separate instances of accidental exposure involving hundreds of people have been reported over a 30-year period. Severe neurotoxic effects (i.e., mild peripheral neuropathy to permanent paralysis) were observed after single exposures. Data considered robust and reliable.

Animal data:

Route	Species	LD_{50} value	Remark
Oral	Rat	1,160 mg/kg	• Liver – Advanced fibrosis was noted during necropsy as the cause of mortality. • Clinical observations: Ataxia was observed in animals at dose levels ≥ 200 mg/kg
Dermal	Rabbit	3,100 mg/kg	• Liver – Fibrosis was noted during necropsy as the cause of mortality. • No other effects on organs were noted during necropsy.

Answer

Acute oral toxicity; Category 4

Acute dermal toxicity; Category 5

Specific target organ toxicity – single exposure; Category 1 (nervous system)

Rationale

(a) Acute oral toxicity

Classification via application of criteria in GHS Table 3.1.1 is possible. The study used the preferred test species (i.e., rat) as noted in paragraph 3.1.2.3 and the Oral (rat) LD_{50} of 1160 is within the Category 4 range of 300 < ATE ≤ 2000 resulting in a Category 4 classification via the oral route.

(b) Acute dermal toxicity

Classification via application of criteria in GHS Table 3.1.1 is possible. The study used the preferred species (i.e., rat or rabbit) as noted in paragraph 3.1.2.3 and the Dermal (Rabbit) LD_{50} of 3100 is within the Category 5 range of 200 < ATE ≤ 5000 resulting in a Category 5 classification via the dermal route.

(c) Specific target organ toxicity – single exposure

The effects seen after human exposure (i.e., mild peripheral neuropathy to permanent paralysis) are non-lethal toxic effects on the central nervous system. Specifically, the Category 1 criteria "(a) reliable and good quality evidence from human cases or epidemiological studies" in Figure 3.8.1 support a Category 1 classification.

In this case, the acute oral and dermal toxicity classifications do not preclude classification into the STOT hazard class since they reflect the lethal effects on a separate target organ (i.e., liver was confirmed as the cause of death during necropsy) via a different mechanism than the non-lethal effects on the central nervous system.

(Reference document: ST/SG/AC.10/C.4/2020/14, example 2)