(7-20-83)

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Registration Standard Bacillus thuringiensis

Subject: Acute Oral LD_{50} Toxicity/Infectivity Study of Teknar in the Rat

Test Compound: Bacillus thuringiensis var. israelensis; Teknar product (B.t.i.)

MRID Number: 142733

Test Facility: Sandoz Research Institute,
Dept. of Preclinical Safety Assessment
East Hanover, NJ

Study Number: T-1866

Testing Period: June 22 to July 20, 1983

Purity of Test Material:

2.3×10^{10} B.t.i. spores 1 gram; 557 AA u/mg, liquid formulation .

Batch Number: Lot #21751

Materials and Methods:

Forty Taconic (Tac: N(50) FBR) rats were divided into two groups of 10 males and 10 females each.

Teknar (2.3×10^{10} spores/gram) was diluted 1:4 w/v prior to dosing orally. Group I animals received no B.t.i., while group II animals were administered one dose of 5000 mg/kg orally as a suspension in distilled water at a volume of 20 mL/kg.

Prior to dosing, animals were acclimated to laboratory conditions for a 2-week period and were fasted for approximately 18 hours. Study animals were observed daily for toxic signs, and body weights were recorded prior to dosing 8, 15, 21, and 28 days postdosing. All animals were fasted for necropsies, which were performed on day 29 postdosing.

At necropsy, all study animals were given a thorough gross pathological examination. The terminal body weights were recorded at sacrifice, as well as the liver, kidneys, and brain weights from each study animal.

All gross lesions, samples of the stomach, small intestine, large intestine, mesenteric lymph node, lung, kidneys, liver, and spleen were collected and fixed in buffered formalin. The stomach and G.I. tract were removed last to avoid contamination with spores.

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Microscopic examinations were limited to eight gram stained tissue sections and two blood smears from each sacrificed animal. gram stained tissues examined for gram + organisms were gross lesions, lung, small and large intestine, mesenteric lymph nodes, kidneys, liver, and spleen.

Results:

No mortalities. No gross lesions related to Teknar administrations. There was no evidence that Teknar had any effect on rat body or organ weights.

No gram + organisms were found on the eighth tissue secretions or blood smears from any test animals. No Gram + bacteria were found in any of the gross lesions examined.

The tester states that a few gram + bacteria were found within the intestinal and/or stomach contents, but this observation would be expected in most of the control, as well as the test rats. They further state that the bacteria found were the surface of the gut lumen, and therefore did not represent any stage of initiation of an infective pathological process.

Conclusions:

This study shows that Bacillus thuringiensis administered in massive doses by the gastrointestinal tract to rats did not affect the rats; no clinical signs of toxicity or illness were observed, and no test-related effects were noted when the animals were examined for gross pathological effects, or when pertinent selected tissues, including blood, were examined microscopically.

The tester should have plated saline washing of stomach and intestinal contents on to surface blood agar and also plate cultured blood samples in attempts to recover virable B.t.i. negative cells; these procedures are not critical, however, they should be performed in microbid infective pathology studies.

The tester should also have included plans to begin animal temperature monitoring upon observing signs of rapid breathing. piloerection, or general clinical signs of developing stress in rats.

LD_{50} = > 5 grams/kg Tox. Category III

Classification: Core Minimum Data