6-1-93

JUN 1 1993

Reviewed by: J. Thomas McClintock, Ph.D., Microbiologist
Science Analysis Branch
Health Effects Division (H7509C)

DATE EVALUATION REPORT

STUDY TYPE: Acute Intraperitoneal Toxicity

MRID NO.: None Assigned CASWELL NO.: None Assigned

TEST MATERIAL: Cydia pomonella (the codling moth) granulosis virus (CpGV)

SYNONYMS: Cyd-X

STUDY NO.: S3210

SPONSOR: Espro Inc.
Oakland Center
8990 Route 108
Columbia, MD 21045

TESTING FACILITIES: Cosmopolitan Safety Evaluations, Inc.
P. O. Box 71
Lafayette, NJ 07848

TITLE OF REPORT: Acute Intraperitoneal Toxicity/Pathogenicity Study in Mice

AUTHOR: G. Rosenfield

REPORT ISSUED: August 12, 1991

CONCLUSION: An intraperitoneal injection of approximately $1x10^7$ CpGV granules (**NOT** "...polyhedral inclusions bodies per test animal...") did not produce any apparent signs of overt systemic toxicity following a 21 day test period. The study author states that an objective of this study was "...to estimate the clearance of the MPCA." Although samples were sent to the sponsor, presumably for analysis, this data was NOT included in the report. Although microbial clearance is not a requirement for the intraperitoneal study, these data, if available, should be submitted to the Agency. Alternatively, the required cell culture data could be used to provide a reasonable assurance of lack of infectivity and/or replication in mammalian cells.

CLASSIFICATION: Supplemental.

STUDY DESIGN: A. Test Article. SAB presumes that the test article consisted of $1x10^7$ granules (0.01 ml)/animal of CpGV (Lot No. 052591) and **NOT** "...polyhedral inclusion bodies per test animal..."

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B. Test Animal. Healthy young adult mice (AAI Mice, NIH) with weights ranging from 19.1 to 21.0 gm were used.

C. Methods. Twenty-nine male and 29 female mice were divided into 3 test groups which consisted of a control group (3 male and 3 female-no injection), a treated group (14 male and 14 female-0.01 ml of CpGV/animal), and a vehicle control group (12 male and 12 female-0.5 ml sterile normal saline). Body weights were recorded prior to dosing and on Day 3, Day 7, Day 14, and Day 21 and at death. Upon termination of the study all animals were sacrificed and the following organs examined: heart, lungs, spleen, liver, adrenals, kidneys, urinary bladder, stomach, small and large intestines, and reproductive organs. Body fluid and tissue were harvested for quantification of the microbial test article. Urine and feces were also collected for microbial quantification.

RESULTS: All treated and control group mice gained weight and survived to the scheduled sacrifice date. There was no evidence of treatment-related signs following administration of the test material and throughout the course of the study. No significant changes were observed in any mice upon necropsy.

DISCUSSION: An intraperitoneal injection of approximately $1x10^7$ granules (0.01 ml)/animal of CpGV did not produce any apparent signs of overt systemic toxicity following a 21 day test period. As stated by the author an objective of this study was "...to estimate the clearance of the MPCA." Although samples were sent to the sponsor, presumably for analysis, this data was NOT included in the report. Although microbial clearance is not a requirement for the intraperitoneal study, these data, if available, should be submitted to the Agency. Alternatively, the required cell culture data could be used to provide a reasonable assurance of lack of infectivity and/or replication in mammalian cells.