UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

29 MAY 1991

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OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: SACB Review of Supplemental Information Submitted by the Mycogen Corporation to Support the Registration of MYX7275 (MVP Bioinsecticide) (HED Project No. 1-1254; I.D. No. 053219-G; Supplemental Information to MRID No. 411997-01; Caswell No. 066)

TO: Phil Hutton/Willie Nelson (PM-18)
Registration Division (H7505C)

FROM: J. Thomas McClintock, Ph.D., Microbiologist
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

JTM 5/24/91

THROUGH: Reto Engler, Ph.D., Chief
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

ACTION REQUESTED: In a recent review (see 3/25/91 memorandum from J. T. McClintock to P. Hutton/W. Nelson) SACB expressed specific concerns pertaining to the methodology used to ensure complete kill of Pseudomonas fluorescens, the host bacterium which encapsulates the Bacillus thuringiensis delta-endotoxin. SACB concluded that given the set of defined parameters there would be a reasonable probability that all cells would be killed. However, no data was provided on the effectiveness of the killing/fixation procedure using a pH of [redacted] To ensure the final pH and [redacted] and validation that all cells would be equally exposed to the components during the killing/fixation process, SACB requested information on the protocol and quality control/assurance procedure. In response to these issues the Mycogen Corporation has submitted additional information in support of the registration of MYX7275.

REVIEW OF DATA/INFORMATION SUBMITTED:

Manufacturing Process: 1). Confirmation of Cell Kill After Fixation-Previous Data. In a previous submission data was provided which demonstrated incomplete cell kill using the killing/fixation procedure outlined by Mycogen (Application for EUP for MYX7275; MRID No. 40897401; Table 1; for specific details see 3/25/91 memorandum from J. T. McClintock to P. Hutton/W. Nelson). Based on this set of data Mycogen concluded that the [redacted]

MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

QUALITY CONTROL PROCEDURE INFORMATION IS NOT INCLUDED

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factor." Unfortunately, this statement was misleading since the data did not support the conclusion(s). Mycogen has responded by stating that the [redacted]

SACB Conclusion. If one assumes that the [redacted] an attempt should have been made to identify the contaminates as an entirely different bacterium or as either a viable (non-engineered) or nonviable Pseudomonas fluorescens (genetically engineered). This approach would seem logical given the fact that in order for a [redacted]

2). Confirmation of Cell Kill After Fixation-New Data. The parameters [redacted] for the killing/fixation procedure, as described by Mycogen, would be sufficient to assume reasonable probability that all cells would be killed. In lieu of the fact that no data was provided on the effectiveness of cell kill using a pH of [redacted] SACB recommended that the correct pH range be limited to [redacted] Due to the large volumes associated with the large-scale fermentors Mycogen stated specific problems with the pH range proposed by SACB. Consequently, Mycogen has submitted data, [redacted] SACB is assuming that this experiment was not replicated and that the results are based on one experiment.

[redacted]

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SACB CONCLUSION: Based on these results SACB would conclude that the parameters [redacted] described for the killing/fixation procedure are adequate to assure that there will be a reasonable probability that all cells will be killed. Of utmost importance is that Mycogen demonstrate that the parameters described above are sufficient for complete cell kill at the large-scale level (i.e. during manufacture of batches under the conditions of registration, provided a registration is granted). In addition, SACB requested protocols and quality control/assurance procedure to ensure the final pH and [redacted] and validation that all cells will be equally exposed to these components during the killing/fixation procedure.