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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

JAN 27 1977

SUBJECT: PP#6F1705/6H5111 - Bay NTN 9306, propos. for tolerances in cotton products; addendum to TB review of 1/6/76

007042

FROM: D. L. Ritter
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TO: L. Zink, SRS/RD WH-567
and
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I had indicated soon after the subject review was issued (comments of 2/12/76) that for the permanent tolerances a hen neurotoxicity study should be submitted.

I have now determined that this study was included in the original submission but that my comments did not appear in my review. For the record, the study is here addressed.

Hen Neurotoxicity Study (Bayer A.G. 5115)

Methods:

Groups of ten white leghorn hens each were gavaged once with test material at 25, 50, 60, 75 or 100 mg/kg; a sixth group of five hens received 250 mg/kg. Birds were observed till death or for 28 days for delayed toxicity. The LD_{50} for these hens was calculated to be 68 mg/kg with death occurring no later than day 8.

An additional group of six hens each received 375 mg/kg of TOCP orally in a single case as a positive control and were observed for 21 days.

At termination the animals were infused intracardially with 10% formalin and all nervous tissues were fixed for examination by at least six different staining methods:

1. Hematoxin an eosin (H.E.)
2. Luxol Fast Blue: Cresyl Fast Violet according to Kluver-Barrera
3. Method for preparing degenerating nerve fibres (only t. Fochiedici)
4. Modification of the Bodian staining method for neurofibrils according to Weinstiner (only thoracic and lumbar marrow)
5. Method described by Lapham for preparing myelin and glia fibres
6. Luxol Fast Blue-PAS-hemalaun according to Margolis and Pickett

Results:

NTN-9306 hens: Signs of poisoning persisted up to eleven days and included impairment of general health (not further characterized) and leg weakness. Nothing indicative of nervous system histopathological changes were noted in those tissues examined. Ataxia and paralysis were not seen.

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ABOCP-treated hens: 1/6 hens died at day 17. General health was seen to be affected up to day three with apparent recovery. Signs of neurotoxicity developed, at about day 10, consisting of unsteady gait, ataxia and lameness; finally total paresis of the legs appeared in all surviving animals. Nervous system degenerative changes were noted in all TOCP-treated animals; none was noted in the NTN-9306 treated animals.

Conclusions:

Bay NTN-9306 was not a delayed neurotoxin nor a demyelinating agent in this test at single oral ingestion levels up to 250 mg/kg in the acult hen. TOCP showed all the typical signs and histopathological findings of such an agent.

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