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WASHINGTON, D. C. 20009

August 21, 1967

TO: Members of the Food, Drug, and Cosmetic Chemicals Committee

SUBJECT: Report of the Panel on Potentiation of the FDA Advisory Committee

Gentlemen:

At the June 13 meeting of the FDCC Committee, I was asked to obtain the subject report dated March 16, 1967 for your information.

Enclosed is a copy.

Sincerely yours,

Morgan M. Hoover

MMH:sjg

Enclosure

FOOD AND DRUG ADMINISTRATION

ADVISORY COMMITTEE ON PROTOCOLS FOR SAFETY EVALUATIONS

Report of the Panel on Potentiation on

Testing for Potentiation between Anticholinesterase Pesticides

March 16, 1967

Committee Members:

Norton Nelson, Chairman
Julius M. Coon
Leo Friedman
Robert E. Gosselin
Calvin M. Kunin
Ted A. Loomis
Philippe Shubik
James L. Whittenberger
James G. Wilson

Panel on Potentiation Members:

Julius M. Coon, Chairman
Kenneth P. DuBois (consultant)
John P. Frawley (consultant)
Robert E. Gosselin
Ted A. Loomis

FDA Liaison Representative to the Panel on Potentiation:

Joseph L. Svirbely

Executive Secretary:

Charles J. Kokoski

Report of the Panel on Potentiation on

Testing for Potentiation between Anticholinesterase Pesticides

In 1957, it was found that EPN exerted a marked potentiation of the toxicity of malathion under certain experimental conditions. Since that time numerous examples of important toxicological interactions have come to light, not only between other anticholinesterase pesticides, but also between these agents and other environmental chemicals, as well as drugs. There has been a continuing and growing concern about these toxicological interactions.

This panel was assigned the specific task of considering the usefulness of the FDA requirement (F.R. par. 120.35) that each new anticholinesterase pesticide be tested for toxicity in combination with each of the other anticholinesterase pesticides for which a tolerance has been set. In regard to this requirement and the design of the tests that have been run to meet it, this panel has two recommendations to make:

1. The present requirement as set forth in the Federal Regulations (par. 120.35) should be abandoned since it has failed to serve any useful purpose. This recommendation is based on two considerations.

Firstly, no single, practical experimental design has been developed by which it is possible to detect all cases of potentiation between pairs of anticholinesterase pesticides.

Secondly, even in cases where the current test procedure has shown the existence of potentiation, the results do not supply information pertinent to the safety evaluation of pesticide residues on agricultural commodities. None of the established potentiative pairs, when fed subacutely to experimental animals at or near the minimal effect levels, has shown

establish the optimal procedur for detecting anti-aliesterase activity. In the meantime, the panel urges the FDA to accumulate data that would contribute to our knowledge of the general toxicologic and physiologic significance of the aliesterases.

Dr. J. L. Svirbely (FDA Representative)
Dr. K. P. DuBois (consultant)
Dr. J. P. Frawley (consultant)
Dr. R. E. Gosselin
Dr. T. A. Loomis
Dr. J. M. Coon (chairman) ✓

March 16, 1967