

June 5, 1991

NOTE TO: George Ghali, Ph.D.
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I cannot concur with the RfD/Peer Review Committee document "Ocular Effects of Organophosphates". Although one important new study has been added (Misra et al. 1985), I find that the overall the report has not changed substantially since the earlier Jan. 31, 1991 draft. I had provided Dr. Dementi with some suggested language on the epidemiologic section and I find to my dismay that he has elected not to use any of it.

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SUGGESTED REPLACEMENT FOR SUMMARY STATEMENT

Many publications in the Japanese literature report findings in human populations of a visual disease syndrome (Saku disease) reportedly associated with exposure to organophosphate pesticides in agriculture. Typically, the syndrome is manifest as myopia with astigmatism, reduced visual acuity and narrowing of the visual field. Detailed examinations often show abnormal eye movements, abnormal pupils or pupillary responses, and optic neuritis. Most of the cases also exhibit one or more positive neurological findings such as sensorial neuropathy, dysmetria, or abnormal EEG.

Evidence for the intensity, duration and extent of exposure is generally lacking from these studies. The Saku district is a farming area where organophosphates are intensively used and homes are distributed among the fields where chemicals are sprayed. The most direct evidence of exposure comes from cholinesterase measurements on patients seen at the local hospital. Both adults and children show significantly reduced serum cholinesterase levels. In one report of 60 children tested, 55 percent had a reduction of serum cholinesterase (5). Another study of 51 adults reported that 80 percent had reduced cholinesterase levels (7). A review article noted that narrowing of the visual field was "correlated well with the reduction in cholinesterase level" but did not provide the statistical analysis that supported this finding (4). Reportedly, biopsy of the lateral rectus muscle of the eye in several patients revealed total inhibition of cholinesterase, but methods used, number tested, and associated symptomatology was not provided in the available literature that has been examined so far. Different reports have stated that treatment with atropine, an antidotal therapy for excessive acetylcholine buildup, and PAM (pralidoxime), a cholinesterase reactivator, has improved the vision of many patients (6, 8). This suggests that the visual impairment in many cases was originally due the anticholinergic effect from exposure to organophosphate insecticides. Details on how many patients received this treatment, how many recovered, or to what extent are not available in the literature so far reviewed.

Tamura and Mitsui (3) point out that myopia incidence over the 1957 to 1973 time period increased in primary school and junior high school children in a manner that was highly correlated with increasing use of organophosphates in the area. However, other explanations for the increase, such as changes in disease ascertainment or perhaps increased reading requirements for school children, could not be ruled out.