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THE BIOLOGICAL LABORATORIES
HARVARD UNIVERSITY

MEMORANDUM DATE:

TO:

FROM: M. Meselson

I enclose four items
related to your interest
in the use of 2,4,5-T.

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April 1974

The aim of our research over the past four years has been the development of analytical methods for detecting TCDD in environmental samples.[1,2,3] Due to the extraordinary toxicity of TCDD, we have sought to achieve a sensitivity on the order of one part per trillion (ppt) for monitoring this compound. We have developed a procedure consisting of digestion in alcoholic base, extraction with sulfuric acid, alumina chromatography and analysis by high resolution time-averaged mass spectrometry. Our present limit of detection of TCDD is about one picogram (pg) or 10^{-12} grams, permitting the detection of TCDD corresponding to a concentration of about 1 ppt in a one gram sample.

High resolution time-averaged mass spectrometry is a particularly suitable means of detecting TCDD at low levels because of its excellent sensitivity and specificity. High specificity is obtained by using a mass resolution of about one part in ten thousand. This mass accuracy combined with the observed isotopic isomer ratios (naturally occurring chlorine contains 75.53% ^{35}Cl and 24.47% ^{37}Cl) establishes the molecular formula. Analysis of fragmentation can be used to confirm the structure. A combined recovery and quantitation standard is provided by the addition of ^{37}Cl TCDD prior to analysis.

We have analyzed samples of fish and shrimp from South Vietnam, collected in rivers and estuaries draining areas heavily sprayed with the herbicide n-butyl 2,4,5-trichlorophenoxyacetate. These samples contain up to several hundred ppt of TCDD. No TCDD above the sensitivity limit of about 3 ppt was found in control samples.

Our results suggest that TCDD may be quite stable in the environment and that it may accumulate in food chains, although further research is needed to quantify these statements. Nevertheless, it becomes of interest to consider what accumulated dose to an individual (expressed as ppt of his body weight) could result from a given average concentration of TCDD in the diet. As an example, we consider life-long exposure for a 50 year old person consuming fivetimes his weight in food each year. The accumulated dose will depend on the biological half-life of TCDD and the average concentration in the diet as shown in the table.

Unfortunately, neither the biological half-life nor the range of present dietary concentrations is known. However, limited experiments suggest that the biological half-life for lethality is not less than two years in monkeys.[2,4] Also, pilot studies by EPA indicate that levels of about 1-40 ppt of TCDD appear in fat and liver of sheep and cattle grazed on land treated with 2,4,5-T containing 0.04 ppm TCDD.[5] Thus, for exposed populations dietary levels in the range in the table cannot reasonably be ruled out. Depending on the biological half-life, this could result in accumulated doses of the order of 10 ppt or more of TCDD as a result of the use of 2,4,5-T containing 0.1 ppm TCDD.

From the existing toxicological data, it is not possible to say that such accumulated doses are or are not hazardous. Short term doses of a few hundred ppt and a few thousand ppt have been found toxic to the immune systems of guinea pigs and mice, respectively,[6] and are lethal to guinea pigs.[7] Whether long term chronic exposure leading to the same total dose would have

similar effects is not known. Neither is it known whether still lower doses would depress the activity of the immune system or otherwise be toxic. Certainly the cell mediated immune system is of particular interest because of its ubiquitous role in combating infection and surpressing neoplasms, but this knowledge itself provides no clear guide to action. However, it does seem to us that serious risk from the continued use of 2,4,5-T is not outside of the realm of reasonable possibility and that further study is needed before safety limits can be more narrowly defined.

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HALF-LIFE (years)	TCDD IN DIET (ppt) 0.01	0.1	1.0
2	.14	1.4	14
10	.7	7	70
50	1.8	18	180
∞	2.5	25	250

TABLE

Accumulated dose of TCDD as a function of biological half-life and TCDD concentration in the diet. Accumulated dose is given for a 50 year old individual as ppt of his body weight, assuming continuous exposure to TCDD at the dietary concentration given in the table.