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September 29, 1983

Dr. Allan T. Ford
Mail Code A1SE
Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63166

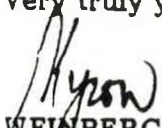
Dear Al:

As usual, I have a second issue to cover at the same time.

In "Fate of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) in the Environment: Summary and Decontamination Recommendations," the authors (Young, Thalken, Arnold, Cupello and Cockerham, 1976) discuss hepatic ultrastructure studies (cf. page 27 et seq.). The inference made by the authors of this report is that ingestion of TCDD do not cause structural or steric effects on the endoplasmic reticulum. I would appreciate it if you would review this against your knowledge of effects of TCDD on hepatocellular ultrastructure and intracellular organelles and tell me if you agree with the inference I have drawn. Can we conclude that TCDD has no effect on the endoplasmic reticulum? What other references support your conclusions? What is known about effects of TCDD on cellular organelles in the intact mammal?

I would appreciate your help in both of these areas.

Very truly yours,


WEINBERG CONSULTING GROUP Inc.
Myron S. Weinberg, Ph.D.

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March 6, 1984

Dr. Myron S. Weinberg
Weinberg Consulting Group, Inc.
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Dear Myron:

Al Ford has asked that I answer your letter of February 23, 1984 in which you ask a number of questions about Crosby's work and how it might influence your thinking about the amounts of TCDD which could reach the so-called human exposure level.

Crosby has written a number of papers on photochemistry of dioxins as have many other authors. I have just started to collect these and try to see what they mean.

The photochemistry of TCDD depends greatly on the kind of exposure. TCDD irradiated as a film on glass or as a suspension in water does not degrade after 2-weeks exposure. Likewise, it is not decomposed when applied to a 0.25 mm thick layer of soil on a glass plate and exposed to a sunlamp. However, it does degrade when dispersed or solubilized in water by means of a surfactant. TCDD undergoes extensive photodegradation when exposed in methanol or hydrocarbon solution.

In such solutions, all workers agree that the process follows "first order" kinetics. They really mean pseudo first order. In a true first order mechanism, the rate of decrease of the concentration of the component of interest, dioxin in this case, would depend only on its concentration c and a proportionality constant k .

$$\frac{-dc}{dt} = kc$$

The TCDD photodegradation involves abstraction of hydrogen or hydroxyl from the hydrocarbon or alcohol. Therefore, it is not a first order reaction in the strict sense. However, it appears to follow the first order rate equation given above. This is because the experiments are carried out in very dilute solution with the alcohol or hydrocarbon as the solvent. The solvent concentration is, therefore, many orders of magnitude greater than that of the TCDD. This means that even when all the TCDD has reacted, the solvent concentration is essentially unchanged and can be taken as constant. This type of reaction is a pseudo first order reaction.

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The rate constant k depends on the reaction conditions. In this case the light intensity and its wavelength, and the nature of the solvent are the most important variables. For example, the rate constant would be directly proportional to the light intensity. The rate constant is not significantly affected by temperature since this is a photochemical process. As you can see from all this, the rate constant is a constant only for a given fixed set of conditions.

The half-life for a first order reaction can be calculated from the equation:

$$\text{Half-life} = \frac{0.693}{k}$$

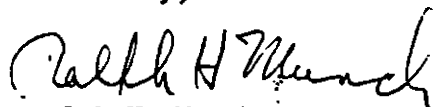
This is derived from the first order rate equation given above. Since, as stated above, the rate constant k applies only to a fixed set of conditions, the half-life also changes with conditions. For example, if light intensity is doubled so that k is increased by a factor of two, the half-life is cut in half. Any other change in reaction conditions will also affect the half-life.

You are particularly interested in a better understanding of the conditions which influence the amount of TCDD which could have reached the so-called human exposure or breathing level. One property which influences this is the vapor pressure. This is reported to be 1.5×10^{-9} millimeters at 25°C . The molecular weight of TCDD is 322. Using these two pieces of data for TCDD and the fact that 22.4 liters at 760 mm pressure is the volume of one gram mol of a gas, we can calculate that air saturated with TCDD would contain 8×10^{-14} grams per liter. A usual breathing rate is 12/min. A large breath would be 4 liters. For an 8-hour day, this would be 2.3×10^4 liters or 1.8×10^{-9} grams of TCDD per 8-hour day. Most people would agree that this is a very insignificant amount. If a significant amount is to be inhaled, the TCDD would have to be present as a finally dispersed solid or adsorbed on other solid particles. This would seem to indicate that actual contact with solids or liquids would be more likely to be important modes of exposure.

If a worker spraying Agent Orange or working in a chemical plant for 8 hours got 1 gram of Agent Orange or 1 gram of 2,4,5-T containing 1 part per million of TCDD in himself, he might contact 10^{-6} gram of TCDD or about a thousand times as much as he could from breathing TCDD saturated air for the same time.

I hope this all helps you. If you have further questions, please do not hesitate to write.

Sincerely,


Ralph H. Munch

/dkr

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