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CENTRAL RESEARCH AND DEVELOPMENT DEPARTMENT

August 25, 1982

PERSONAL AND CONFIDENTIAL

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AMMONIUM PERFLUOROOCTANOATE (C-8)
IN HUMAN BLOOD

In reference to your July 29, 1982, letter to R. J. Zipfel (Retention of Ammonium Perfluorooctanoate [C-8] in Blood of Teflon® Workers) I would like to make several important suggestions. Acquisition and interpretation of C-8 blood concentrations in workers is very important in understanding how the human body handles C-8 and how accurately our animal models at Haskell correlate to the human situation. To better interpret these data, consider the following modifications:

- The 0.006 ppm blood level is termed a "rate" of accumulation when it would be more appropriate to call it an "average concentration" over the average of 91 days of employment. The average blood level of 0.006 ppm/day x 91 days gives the plateau, or steady-state, concentration (0.546 ppm) that more closely represents the dynamic aspects of exposure and elimination.
- The calculations assume a volume of distribution (Vd) equal to the blood compartment only (5.5 liters). Since C-8 is water soluble and binds protein, the Vd would actually be closer to the volume of total body water (approximately 42 liters/70 kg man).

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- To more accurately assess the retention of C-8 in the body as well as predict blood levels anticipated with continued low-level exposure, formulas commonly used to estimate drug-therapy regimen can be employed.

Assumptions:

- The blood level, C_p , is at a plateau (steady-state) concentration (i.e., absorption and elimination approximately equal).
- The volume of distribution, V_d , is in total body water, or 42 liters.
- The daily dose (D/T) is 0.081 mg/day.
- The elimination half-life, $t_{1/2}$, is estimated from a literature report on one individual. The value is 655 days, but could vary considerably.

Then from Goodman and Gilman (1970):

$$C_p = \frac{f \cdot 1.44 \cdot t_{1/2}}{V_d} \left(\frac{D}{T} \right)$$

- where f = fraction absorbed
- solving for f ,

$$f = \frac{C_p \cdot V_d \cdot T}{1.44 \cdot t_{1/2} \cdot D} = \frac{0.546 \text{ mg/l} \cdot 42\text{l} \cdot 1 \text{ day}}{1.44 \cdot t_{1/2} \cdot 0.081 \text{ mg/l}}$$

- then:

$t_{1/2}$ (days)	f	% Absorbed
30	6.55	655
197	1.00	100
360	0.55	55
655	0.30	30

- Thus, depending on the actual $t_{1/2}$, we can estimate only that greater than 30% of atmospheric C-8 is absorbed. This is in general agreement with your estimate, but until we know the actual $t_{1/2}$ we will not be able to accurately calculate fractional absorption.

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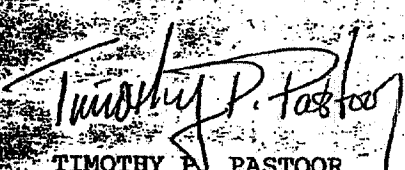
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- Regarding these calculations and in response to your suggestions in the July 29 memorandum,

- More human data is necessary from two sources:

1. current employees for determination of plateau (steady-state) concentrations
2. employees no longer exposed to C-8 for determination of the blood $t_{1/2}$ and the urinary excretion rate.

- We have performed radiochemical and biochemical analysis of the distribution and effects of C-8.


TIMOTHY P. PASTOOR
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