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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, Cp, is at a plateau (steady-state) concentration (i.e., absorption and elimination approximately equal).
  - The volume of distribution, Vd, 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):

$$Cp = \frac{f \bullet 1.44 \bullet t\ 1/2}{Vd} \left(\frac{D}{T}\right)$$

  - where f = fraction absorbed
  - solving for f,

$$f = \frac{Cp \bullet Vd \bullet T}{1.44 \bullet t\ 1/2 \bullet D} = \frac{0.546\ mg/l \bullet 42\ell \bullet 1\ day}{1.44 \bullet t\ 1/2 \bullet 0.081\ mg/\ell}$$

  - 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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- 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.

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TPP:sgl