

DEC 3 1940

MEMO TO Allen Ford

This is the letter I called you about. Apparently this man is interested because of the Czechoslovakian accident a few years back.

Is it alright to answer his questions?

Bill Dwyer

FROM _____

G-321

300g/Kg
2700g = Allen found
0.011 ug/kg/day
toxic in 6 months
resulting in death
of 5 of 7 females

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Tentative dates,
dependent upon
funding
Revised Timing

1. ¹⁴C TCDD distribution, June 4, 1980 -
preliminary, in cynomolgus monkey July 31, 1980
15 ug/kg, individual animals
sacrificed at 2, 4 & 6 weeks, urine and
• blood metabolite identification, ¹⁴C kinetics
2. Acute Toxicokinetic study June 2, 1980
relate signs of toxicity with May 31, 1981
TCDD in blood, urine, feces & skin (1st group dosed
+ dosed at 50 ug/kg if no toxic signs @ 2 wks Sept. 5)
dosage: 2, 10, 25 ug/kg
- 3 Rhesus monkeys from Dow & WSEL/level
¹⁴C administered with dose 24 hour
sample collections will be made 10 times during
a 200 day recovery period. sacrifice at 200 days
blood enzyme & constituent measurements conducted
July 6, 1981, Dec 1983
3. CHRONIC Toxicity study 24 months 15 ♀ Rhesus
• To counter Allen's work at 50 & 500 ppt in diet
9 months dosing 0.5, 1.0, 10.0 ug/kg/month
by gavage. (500 ppt in 200g diet $\approx$ 0.5 ug/kg/month)
toxic in Allen's study
6 month pre dose observation
blood, urine, feces, tissue TCDD metabolite
and blood constituent & enzyme levels to
be determined through out dosing period.

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females bred with control mals after 6 months

questions

1. - Rhesus for pilot study with ^{14}C
~ \$3000

2 - use cynomolgus for pilot
for toxicokinetic study, would
not need to re dose 2 mg/kg

collect total
feces + urine for
initial period
- need quantitative
recovery.

3 Chronic study

- dose form - treat give daily
fruit
apple sauce
drink

- dosage

$\mu\text{g/kg}/\text{mo}$	$0.5 \mu\text{g/kg}/\text{mo}$	$= 500 \text{ ppt}$
$0.05 = 50 \text{ ppt}$		
$0.5 = 500$	(0.5 ppb)	
$5.0 = 5000$	(5.0 ppb)	

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7/16/80

John Ramsey (517) 636-0620

WANT good KINETIC DATA

Compare Rhesus with Rat data

Believes chronic study premature

Do not use cynomolgus in ^{14}C distribution

TOO EXTENSIVE tissue GC-MS - only major

CONCENTRATE on ^{14}C excretion & kinetics

Dow would support modified and substantially reduced effort

Dow has been in contact with WSA

Proposal originally submitted to Hoffman lab

9/8/80

- 1) good TCDD pharmacokinetic study to determine absorption / elimination study.

Dow study - 3 dose levels
reduce tissue analysis

- 2) Ramsey has contacted Mike Taylor (recommended combining 2 studies, use fewer monkeys & reduce time post exposure)

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Byron word review of Brehm analytical capabilities

8-10 TCDD standards

Fred Hileman at Dayton reference
for Brehm Lab capability

Dayton trace analysis group monitor

Dow / Dayton / Brehm Round robin for
analytical capability

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