

Interoffice Correspondence



Subject FC-143
Rat Toxicity Study
Request A67821
March 20, 1978

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Samples of serum from the rats surviving the IRDC 90-day sub-acute rat toxicity study (reference 137-089) were received for analysis of FC-143.

<u>RAT</u>	<u>SURVIVAL</u>	<u>DOSE (ppm)</u>	<u>143 in serum (ppm)</u>
Male	5/5	0	0
Male	5/5	10	21
Male	5/5	30	34
Male	5/5	100	36
Male	5/5	300	38
Male	5/5	1000	49
Female	5/5	0	0
Female	5/5	10	not measured
Female	5/5	30	0.15
Female	4/5	100	not measured
Female	4/5	300	0.25
Female	5/5	1000	0.65

Samples of whole blood from the rats surviving the IBT 28-day oral toxicity study (reference 8532-10654) were analyzed for FC-143.

<u>RAT</u>	<u>DOSE</u>	<u>143 in whole blood (ppm)</u>
Male	0	0
Male	1000	100
Male	3000	not measured
Female	0	not measured
Female	1000	1.5
Female	3000	not measured

DISCUSSION

Needless to say, it is most surprising to see a male rat accumulate and retain FC-143 at a level approximately 100 times greater than a female rat. To confirm the difference between the male and female, serum from the 1000 ppm dosage level was analyzed for total fluorine content.

<u>RAT</u>	<u>TOTAL FLUORINE (ppm)</u> ¹
Male - 1000 ppm	61
Female - 1000 ppm	2.5

¹ A new sampling technique (not yet fully calibrated) was used. In past analysis, approximately 1 g of serum solids was analyzed; with this new technique, only 0.02 g serum solids was used.

It should be kept in mind that due to the limited sample size and to reduce analysis time, all values are the result of a single determination. Sufficient sample remains for further characterization if desired.

Based on the above studies and the abstract to Professor Singer's latest publication, I believe the following study should be initiated at once.

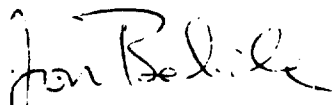
Proposed Study

<u>GROUP</u>	<u>NUMBER OF RATS</u>		<u>DOSAGE LEVEL</u>
	<u>Male</u>	<u>Female</u>	
1	4	4	1000 ppm
2	4	4	1000 ppm

Group 1 - at the termination of the 10-day study period, the serum should be collected and submitted as Group 1 - male; Group 1 - female.

Group 2 - at the end of the 10-day feeding study, the rats would be switched to control food (0 ppm FC-143) for an additional 10 days. At the end of this additional 10 days (total study time = 20 days) the serum would be collected and submitted as Group 2 - male; Group 2 - female.

The purpose of this experiment is to verify the difference between male and female rats in the accumulation of FC-143 and for the first time, Group 2 will show whether FC-143 is cleared from the serum with time.


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