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PROPOSED ADDITIONAL TOXICITY STUDIES ON LEAD
REASONS FOR SUPPORT

Further animal studies are being proposed by Haskell Laboratory in order to set "effect" levels for other organ systems than that concerned with the formation of hemoglobin. When an effect level is established, it is then possible to see by how much it differs from the mean lead level of the general public. If the levels are widely separated, then the general public has a considerable safety factor; if, however, the levels are not very different, the public may have little or no margin of safety. At present we have not found the effect level for several organ systems and therefore cannot say what the margin of safety for these systems may be.

It can be argued that we already have a "built-in" margin of safety in the large amounts of lead being fed at the two higher dosage levels, but this argument can be misleading since the rats do not appear to absorb lead very readily. If instead of lead input the blood lead levels are studied, the following relationship is found.

Blood Lead Levels - Rats
(at 18 months)

Dose ppm	Lead µg/100 ml	
	Males	Females
0	10.0	10.0
0	0.0	0.0
10	10.0	10.0
50	10.0	10.0
100	20.0	10.0
500	50.0	60.0

From this table it can be seen that feeding 500 ppm of lead acetate results in a blood lead of about 50 micrograms lead per 100 milliliters. This level is found in the general population and while perhaps considered cause for concern, it is not considered cause for alarm. Yet at this blood lead level in rats there are changes in the microscopic appearance of the kidney and interference with hemoglobin synthesis. Similar findings are reported in the dogs. This finding of effects on important organs in animals at blood lead levels that are found in the general population makes the proposed additional studies most important. These studies will determine whether reproduction, for instance, is affected at a level only slightly above 50 micrograms lead per 100 milliliters blood or whether it is only affected at much higher levels.

The studies of delta-amino-levulinic acid (DALA) are directed at the same point. The animal studies would suggest that we might expect to find an abnormal excretion of DALA in some members of the general public with somewhat higher than average blood lead levels. The purpose of the study outlined in Point 3 of Dr. Clayton's letter is to see whether such persons can be found and the degree of correlation between their blood lead levels and the excretion of DALA.

Both from the viewpoint of being able to prepare a well-rounded scientific paper and the very practical consideration of evaluating the risk to the general population from present levels of lead, I recommend that the Organic Chemicals Department underwrites the proposed studies.

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