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HASKELL LABORATORY OF INDUSTRIAL TOXICOLOGY
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Enclosed is our report on the Preliminary Toxicity Tests on 15 compounds submitted as per your letter of July 30, 1947. This work was carried out on our project.

HASKELL LABORATORY OF
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Preliminary Toxicity Tests

Acute toxicity tests have been carried out on a group of compounds as per letter of July 30, 1947, to Dr. Foulger. The compounds and the details of the tests on each compound are as follows:

Sodium Nitrotriacetate

The compound was given in a water solution containing 0.25 grams/ml. in one series of M L D tests and 0.203 grams/ml. in a second series. All doses of sodium nitrotriacetate greater than 1500 mg/kg. killed the rats within 30 to 100 minutes. Prior to death the rats became weak, developed convulsions, and became cyanotic. At autopsy the lungs showed slight to severe congestion and edema. The mucosa of the stomach was slightly inflamed. One rat surviving 1500 mg/kg. was killed two days after treatment and did not show any gross or microscopic pathology.

Sodium Tartrate

The Sodium Tartrate solution used contained an equivalent of 0.25 grams of tartaric acid per ml. The M L D for Sodium Tartrate is around 7500 mg/kg. The rats that survived this and lower doses did not show any gross or microscopic pathology when sacrificed forty-eight hours after treatment.

Tartaric Acid

The M L D for Tartaric Acid is around 7500 mg/kg. Rats receiving doses of 5000 mg/kg. or less all survived and were killed 12 to 15 days after treatment. No gross or microscopic pathology was observed. One rat which died after a dose of 7590 mg/kg. showed edema and hemorrhages in the lung and acute inflammatory changes in

stomach with superficial loss of tissue from the stomach wall.

Methyltrimethylolmethane

The effect of this compound on the skin was tested in guinea pigs with the following results:

		<u>Reactions</u>			
	<u>No. G.P.</u>	<u>+</u>	<u>Sl+</u>	<u>Ysl+</u>	<u>Leg.</u>
Initial Patch	10			2	9
Final Patch	10			2	9

These tests indicate that methyltrimethylolmethane is not particularly irritant to the skin and does not produce sensitization in guinea pigs.

Rats were fed doses as high as 7590 mg/kg. and aside from some discomfort immediately following treatment, they did not show any untoward effects. The rats were killed 8 to 15 days after treatment and did not show any gross or microscopic damage to the internal organs. The gain in weight of these rats between treatment and the time they were sacrificed was normal.

Nitrogen Triacetic Acid

Rats survived single doses of this compound as high as 7590 mg/kg. Doses up to 2250 mg/kg. did not produce any apparent effect. Higher doses made the rats slightly uncomfortable following treatment, and doses of 7590 mg/kg produced considerable prostration and progressive loss in weight during the eight days following treatment. No gross or microscopic pathology was noted in the rats receiving 5000 mg/kg. or less nor in two rats receiving 7590 mg/kg. One rat receiving the latter dose showed minor changes in the liver at autopsy. The liver cells were slightly shrunken, and the nuclei were pyknotic.

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Isino Diacetic Acid Hydrochloride

Doses of this compound up to 2250 mg/kg. did not produce apparent effect. Higher doses made the animals uncomfortable, and one rat fed a dose of 5000 mg/kg. died 10 hours after treatment. The stomach was badly burned, and there were extensive hemorrhages in the mucosa. This chemical necrosis extended to tissues adjacent to the stomach, such as the liver and abdominal wall. Microscopically the liver, stomach, and kidneys were superficially disintegrated where there had been contact with the chemical. The rats that survived doses ranging from 2250 to 1000 mg/kg. gained weight normally. Higher doses inhibited the normal increase in weight. Rats that survived doses up to 3375 mg/kg. did not show any gross or microscopic pathology when sacrificed 12 to 15 days after treatment.

Skin Tests

The remaining nine compounds were tested for skin irritation or sensitization, and the results of the tests are presented in tabular form. Ten guinea pigs were used in each test, and the standard technique was followed in making the tests.

Compound	Reaction			Final Patch			Leg.
	+ SI*	VSI*	Leg.	+ SI*	VSI*	Leg.	
Bis(ethylene glycol) glutarate			10			10	
Bis(propylene glycol) glutarate			10			10	
Monyl Alcohol	1	1	0	1		0*	
Dinonyl Phthalate	1	0	0	1		0*	
Trinonyl Phosphate	3	7	0	2	4	1	2*

* 2 of 7 in group died during experiment.

Compound	Initial Patch			Reaction			Final Patch		
	+	±	-	+	±	-	+	±	-
Dicyanobutene				10					10
Adiponitrile				10					10
Tolualdehyde				10	1	4	0		0
Benzaldehyde				10			1		0

Summary and Conclusion

None of the compounds tested orally are highly toxic and some of them are relatively non-toxic. The data on K P D are summarized as follows:

<u>Compound</u>	<u>Approx. MFD in mg/Kilo</u>
Sodium Nitritotriacetate	2200
Sodium Tartrate	7500
Tartaric Acid	7500
Nethyltrimethylolmethane	7500
Nitrogen Triacetic Acid	More than 7500
Imino Diacetic Acid Hydrochloride	More than 5000

With the exception of sodium nitritotriacetate, death from these compounds resulted from an acute corrosive effect in the upper gastrointestinal tract. Sodium nitritotriacetate produced marked prostration and convulsions in the rats before death. At autopsy pulmonary edema was present. It is possible this difference in toxicity between this compound and nitrogen triacetic acid may be due to an alkalosis produced by excess sodium ion.

Dinonyl phthalate and trinonyl phosphate appear to be irritant to guinea pig skin but do not sensitize. Tolualdehyde appears to produce sensitization in guinea pigs.

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