

*Check lower dose of emetic.*

PROTOCOL

Client:

Imperial Chemical Industries.

Test:

Survival study of monkeys dosed with paraquat containing an emetic substance.

Test Materials:

Paraquat as the commercial formulation 'Gramoxone'.  
Emetic supplied by ICI (No. 50796)

Objectives:

To determine whether monkeys dosed with paraquat containing an emetic are induced to vomit sufficient of the dose to increase their chances of survival compared to a control group receiving paraquat only.

Test Species:

Male cynomolgus monkeys (m. Fascicularis) weight 3.5 - 5 kg.

Group Size:

Part I - 4 per treatment group.  
Part II - 2 animals.  
Part III- 10 per treatment group.

Experimentation:

Part I - Dose range finding study.

In a previous study of orally administered paraquat in monkeys, several animals vomited part of the dose at some time during the first 10 hours after dosing. In order to reduce the incidence of this it is proposed to include 5 g of 'Complan' with the dose to render it less unpalatable. Two animals previously dosed in this way survived an oral dose of 65 mg/kg paraquat.

In order to find a dose of paraquat in 'Complan' which will kill 75-100% of dosed animals, 4 monkeys will be dosed by oral gavage with 100 mg/kg paraquat in 40 ml of aqueous solution containing 5 g 'Complan' and observed over a 14 day period.

Depending upon the results of this test, the experiment may be repeated with further groups of 4 animals until a suitable dose of paraquat in 'Complan' is found. This dose will be used for the main experiment ( Part III ).

Blood samples (2 ml) will be taken from 2 animals dosed with 100 mg/kg paraquat in 'Complan' for measurements of plasma paraquat levels at 0, 1, 2, 3, 4, 6, 8 and 10 hours after dosing. The plasma from these samples will be sent to CTL for analysis.

### Part II - Test of emetic in monkeys

Two animals will be dosed by oral gavage with the emetic substance provided by CTL in 40 ml of water containing 5 g of 'Complan' to confirm that vomiting occurs within one hour of dosing.

### Part III- Survival study

Two groups of 10 monkeys will be dosed with paraquat in 40 ml of water containing 5 g 'Complan' by oral gavage. In addition, one group will receive the emetic in the oral dose. The animals will be observed over a 14 day period, no further treatment being given.

4 animals from each group will be bled at 0, 1, 2, 3, 4, 6, 8 and 10 hours after dosing for measurements of plasma paraquat levels.

Food will be withheld from all animals from 15 hours before dosing.

#### Observation:

Bodyweight will be recorded weekly from 2 weeks before dosing until death.

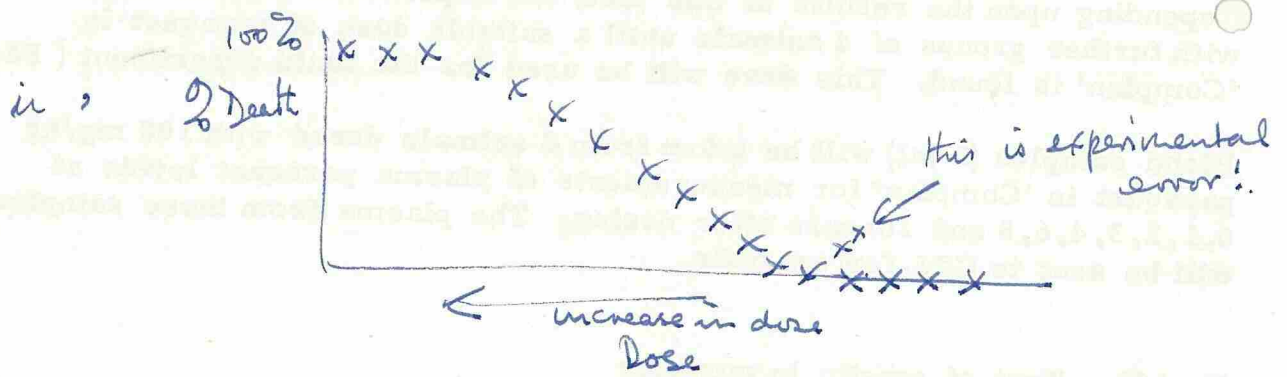
Food consumption will be recorded daily from 2 weeks before dosing until death.

Q. How soon after Gramoxone minus complan do monkeys vomit?  
If this 'experiment' is going to 'work' then the answer had better be greater than the time it takes for monkeys to vomit after the emetic.

(1) If this experiment is also being carried out in dogs please tell me where the money tree is.

(2) I bet if you give ~~the~~ decreasing amounts of paraquat to

animals at some point they will stop dying



Suggested addition to label of Gramoxone for suicides

'Please drink less'