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HUNTINGDON RESEARCH CENTRE,
HUNTINGDON, ENGLAND

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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 find an approximate LD 50 dose of a solution of Gramoxone containing 500 mg/l of emetic

Test species: Male cynomolgus monkeys (M. fascicularis)

Group size: 2 per treatment group

Experimentation: In a previous study of orally administered paraquat, 100 mg/kg produced plasma levels of approximately 16 µg/ml and resulted in the death of all the animals. The same dose of paraquat administered with 2 mg/kg emetic produced plasma levels of approximately 2 µg/ml and failed to cause any deaths.

In order to find a dose which will kill 50% of the animals, up to 10 monkeys will be dosed in groups of two. An initial dose of 500 mg/kg paraquat and 5 mg/kg emetic is proposed, subsequent dose levels depending upon the results.

The doses will be administered by oral gavage in 20 ml. of aqueous solution containing 10 g of 'Complan'.

Blood samples (2 ml) will be taken from all animals for measurements of plasma paraquat levels at 0, 1, 2, 3, 4, 6, 8 and 10 hours after dosing.

- 1) No Complan
- 2) Use dosing solution of 2x diluted Gramoxone (100 µg/ml) + 1 µg/ml emetic.

Observation:

The animals will be retained for up to 14 days following dosing. Bodyweight will be recorded weekly, and food consumption daily, from 2 weeks before dosing until the end of the observation period.