CSR

Final Report

Study Title	NS 3573: Maximum Tolerated Dose (MTD) Oral (Gavage Administration) Toxicity Study in the Monkey
Author	A Mould
Sponsor	NeuroSearch A/S 93 Pederstrupvej DK-2750 Ballerup Denmark
Study Monitor	Dr J Lichtenberg
Test Facility	Covance Laboratories Ltd Otley Road, Harrogate North Yorkshire HG3 1PY ENGLAND
Covance Study Number	1253/143
Covance Report Number	1253/143-D6154
Report Issued	June 2000
Page Number	1 of 49

1647

RESULTS

Clinical signs (Appendix 1)

After being dosed at 400 mg/kg/day during the MTD phase of the study, the m
vomited approximately 15 minutes after dosing on Day 6. On Day 7, both anim
were observed to be circling immediately after dosing and this persisted
approximately 5 minutes. In addition, at approximately the same time, the female
salivating and licking the cage.

After being dosed at 800 mg/kg/day on Day 8, both animals were observed to be h
flicking within a few minutes of being dosed. In addition, the female was circling
licking the cage. All observations persisted for approximately 5 minutes.

Both animals dosed at 250 mg/kg/day during the additional single dose phase vor
approximately 8 and 2 hours after dosing, for the male and female respectively. V
the same animals were dosed two days later at 1000 mg/kg/day, the only observ
in the female was salivation, which was present approximately 1 hour after do
The male vomited approximately 15 minutes after dosing. In addition, approxim
2 hours after dosing, the male was seen to be staggering and fell off its perch
subdued, shaking slightly, squinting and hunched.

Salivation was present in the female dosed at 500 mg/kg/day within a few minu
dosing. In addition, both animals vomited approximately 8 hours after dosing.

Body weight (Figures 1 to 4, Appendix 2)

There were no apparent effects on body weight during the study.

Food consumption (Appendix 3)

There were no treatment-related effects on food consumption during the perio