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REPORT

ON

A SINGLE-DOSE ORAL TOXICITY STUDY OF H 72 6146 A
IN MALE AND FEMALE BEAGLE DOGS

October 31, 1974

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Report on a
single-dose oral toxicity study of H 72 6146 A
in male and female Beagle dogs

Summary:

In this single-dose oral toxicity study of H 72 6146 A, a dosage of up to 125 mg per kg body weight resulted in intolerance reactions, such as vomiting, in the animals.

Method:

Compound H 72 6146 A was given orally by means of a stomach tube to groups of 1 male/1 female pure-bred Beagle dogs, weighing 12.0 - 20.5 kg (mean body weight 15.35 kg). The animals received the compound as an oily suspension in several dosages. The dogs were fasted sixteen hours prior to treatment. The dogs were kept individually in boxes. Five to six hours after treatment the dogs were fed again (mixed feed Erka 8500, mfr.: Robert Koch oHG, Hamm). Food and tap water were provided ad libitum.

During the first 8 hours after treatment the dogs were observed constantly in order to record possible toxic reactions. During the subsequent 2-week follow-up period the dogs were weighed weekly and their behaviour was assessed several times a day.

Results:

Dose mg/kg	Concentration of suspension in %	No. of lethally intoxicated dogs/ No. of dogs per dosage group
125	3,125	0 out of 2
500	25	0 out of 2
1 000	25	0 out of 2
2 000	25	0 out of 2
4 000	25	0 out of 2

The individual findings are given in the following.

125 mg H 72 6146 A per kg body weight:

The male dog vomited 5 minutes after treatment. Two hours treatment the behaviour of this animal was normal again. The female dog showed no externally perceptible signs of intoxication after treatment, its behaviour was normal.

500 mg H 72 6146 A per kg body weight:

Both dogs vomited 10 minutes after treatment. Afterwards the behaviour of the animals was normal again.

1000 mg H 72 6146 A per kg body weight:

Ten minutes after treatment the female dog showed an increased salivation and vomited. The male dog also vomited 10 minutes after treatment. Afterwards the behaviour of both animals was normal again.

2000 mg H 72 6146 A per kg body weight:

Ten minutes after treatment both animals showed increased salivation and vomited. Afterwards the behaviour of both animals was normal again.

4000 mg H 72 6146 A per kg body weight:

Five minutes after treatment both animals vomited strongly. Thirty minutes later both animals vomited a second time. Afterwards the behaviour of the male dog was normal again, whereas the female dog showed slightly increased salivation and periodically coughed markedly up to 24 hours after treatment.

Dr Ho

October 31, 1974

Pharmaceutical Research/Toxicology
of
HOECHST AG

signed:

Dr Hollander

Dr Weigand

Enclosure

Composition of feed

ALL-MASH FOR DOGS — NO. 8500

(powdery-granular mixed feed)

(Producer: R.Koch OHG, 19 Nordstr., Hamm/Westphalia,
Federal Republic of Germany)

Content of relevant ingredients

22.4 % crude protein
5.8 % crude fat
2.6 % calcium
1.8 % phosphorus

Composition

28.50 % hydrolyzed starch
26.00 % animal protein foods
24.00 % by-products of milling
6.00 % oil cake
4.15 % mineral foods
3.50 % by-products of corn oil extraction
2.65 % cereals
2.00 % whey powder
1.50 % fats
1.20 % vitamin premix
0.50 % trace element premix

This mixed feed contains an addition of ethoxyquin
and vitamins.