

Summary Geraniol 2 Reports- Pet Products

Geraniol Spot Treatment for Fleas and Ticks vs. Frontline

STUDY: Controlled Efficacy Studies of Fulltec Geraniol X-Line Spot Treatment in Comparison with 1. Vitakraft Insectfuge, and 2. Frontline Spot -On for Dogs, Dr. Alois Muelhofer

List of Subjects of the Laboratory Tests:

TP = X-Line

RF1 = Vitakraft contre Tiques & Puces

RF2 = Frontline Spot on Chien XL

TP1 = Munsterlander, female, 2 years, 50 fleas, 4 ticks

TP2 = German Shepard, female, 9 years, 20 fleas, 12 ticks

TP3 = Poodle, white, male, 11 years, 50 fleas, 5 ticks

RF1-1 = Spitz, female, 8 years, 20 Fleas, 8 ticks

RF1-2 = German Shepard, white, female, 3 years, 30 fleas, 4 ticks

RF1-3 = Golden Retriever, male, 10 years, 50 fleas, 14 ticks

RF2-1 = Poodle, black, female, 6 years, 30 fleas, 2 ticks

RF2-2 = German Shepard, crossbreed, female, 2 years, 30 fleas, 8 ticks

RF2-3 = Rottweiler, short-haired, female, 4 years, 10 fleas, 13 ticks

These studies tend to confirm the same spectrum of efficacy as laboratory studies did: subjects treated with Fulltec Geraniol X-LINE or Fipronil were free of parasites at the first follow-up check, one day following the application of the products. They remained free of any infestation even after the 6th follow-up check, 5 weeks following application. It can therefore be concluded, that these products show excellent efficacy regarding the deletion as well as the prevention of parasites

Subjects treated with Vitakraft were free from any infestation only after the 2nd follow-up check after 1 week. However, a light infestation with fleas was noted during the 3rd follow-up check after 2 weeks, while from the 4th follow-up check after 3 weeks on, a massive infestation with fleas and ticks was detected. Consequently, the Vitakraft product showed, in contrast to X-LINE and Fipronil, a limited spontaneous efficacy and a significantly shorter protection period against re-infestation.

Fleas, Lice and Ticks on Dogs and Cats

STUDY: Controlled Study of Repellent Effects of Fulltec Geraniol SPOT ON-X-Line in Treatment of Dogs and Cats for Fleas, Lice and Ticks in Laboratory and Field Study, Dr. Alois Muelhofer, LHS Laboratories, Department of Entomology, Wiener Neustadt, Austria, Meg R. Kalb, Animal Home of the Society for the Protection of Animals, January 2002

Animal Subjects and insects

a) Cats – Without Infestation

V-K1 = Tabby cat, smooth, short-haired, male, 1 year old

V-K2 = British blue cat, dark grey, female, 4 years old

V-K3 = Tricoloured, smooth coat, male, 3 years old

V-K4 = Angora, tricoloured, female, 9 months old

b) Cats - Infested

V-K5 = Smooth coat, black, female, 5 years old, 13 fleas, 2 lice and 6 ticks

V-K6 = Half angora, greying, male, 8 weeks old, 23 fleas

V-K7 = Smooth coat, very thick, black, female, 5 years old, 5 lice and 8 ticks

V-K8 = Angora, silver-grey, male, 7 years old, 16 fleas and 5 ticks

c) Cats – reference without initial infestation

R-K1 = Half angora, white, very thick coat, female, 12 weeks old

R-K2 = Tabby cat, smooth-haired, male, 3 years old

e) Dogs – Without Infestation

V-H1 = German shepherd, long-haired, male, 8 years old

V-H2 = Boxer, short-haired, female, 9 months old

V-H3 = Rottweiler mongrel, female, 6 years old

V-H4 = Spitz, female, 8 years old

f) Dogs - Infested

V-H5 = Poodle, trimmed, male, 6 months old, 25 fleas, 5 lice

V-H6 = Mongrel, female, 4 years old, 18 fleas, 4 lice, 8 ticks

V-H7 = Munsterlander, male, 5 years old, 26 fleas, 6 ticks

V-H8 = Retriever, long-haired, female, 13 months old, 25 fleas 11 ticks

g) Dogs – Reference without initial infestation

R-H1 = Mongrel, female, 2 years old

R-H2 = Poodle, trimmed, male, 5 years old

Results:

Lab Tests: On average, SPOT ON-XA prevented renewed infestation of the testes with fleas for 47 days. In the case of untreated reference animals fleas always settled in their coats within 2 minutes. On average, SPOT ON-XA prevented renewed infestation of the animals with ticks for 38 days. In the case of untreated reference animals ticks always settled in their coats within 30 minutes. This experiment clearly shows that a single treatment of flea, lice and tick-infested cats and dogs with SPOT ON-XA completely evicts the parasites. More mobile species such as fleas are already evicted 3 hours after treatment, whereas the more immobile species like lice and ticks take up to 6 hours to leave the host animal or drop off it. The complete relief of testes from infestation 6 hours after treatment shows that, used properly, the product is 100% effective

Field Trial Results: The dogs PH13 to PH16, together with untreated animals serving as references, were taken for walks every day in a meadowland known to be contaminated with ticks. Whereas the reference animals showed 1 to 6 ticks after every daily walk, all 4 animals from the test series remained free of ticks until the 5th week, corresponding to

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an average REPELLENT PERIOD of about 30 days, after a single treatment of the animals with SPOT ON-XA. With all test animals the REPELLENT PERIOD against renewed infestation amounted to at least 30 days, With all 8 animals the EVICTION PERIOD was under 24 hours.

Skin Absorption in Pets

STUDY: Skin Penetration Test of Fulltec Geraniol X-Line Spot Pet According to OECD in Vitro Skin Absorption Test Draft New Guideline 428, Univ. Prof., Dr. Hüttinge University of Vienna, Department of Pharmaceutical Chemistry, Vienna, Austria. Austrian Research Centres Seibersdorf (ARCS), 2444 Seibersdorf, Austria December 13, 2003.

Results: A typical application to the human skin results in an uptake of active components via penetration, which is at least 37.500-fold to 50.000-fold lower than the one needed to observe any toxicological reaction. Due to this product safety it is to be expected, that even a skin exposure 10 - fold higher than a typical one will not cause any damage to health, because even in this very unlikely case the uptake of active components will be 3.750 - fold to 5.000 - fold lower than the corresponding *No Observed Effect Level* (NOEL).

Toxicity Reports

STUDY: Laboratory Study on the Toxicity of Fulltec Geraniol X-Line Spot Pet Treatment According to OECD Guidelines for dogs and cats, Dr. Alois Muelhofer, LHS Laboratories, Department of Entomology, Wiener Neustadt, Austria, February 2002.

**Results: ACUTE ORAL TOXICITY
ACCORDING TO OECD, SECTION 4, SUBSECTION 401**

As for the reason that the chemical composition was known by the institute and it could be expected, that the tested product X-Line will be meaningless acute toxic product it should be checked first with the limit test applying 20 g/kg bodyweight whether this dose can be survived by the tested animals for 14 days.

As all tested animals survived the 14 days observation period under normal increase of body weight and the histology for bacteria remained without result, that means that no substance related mortality happened according to the OECD, S.4, SS 401, a further check of the product for acute oral toxicity could be omitted

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The tested substance X-Line is, as expected, to be classified as acute non toxic substances.

**Investigation for:
ACUTE DERMAL TOXICITY
ACCORDING OECD, SECTION 4, SUBSECTION 402**

The tested product X-Line did not show any system related mortality being tested for acute dermal toxicity for the rabbits of the species New Zealand, which are known for being extremely sensitive. All tested animals survived the observation period of 14 days and did not show any toxic reactions against the tested substance, which have to be classified as acute dermal non toxic.

**Investigation for:
ACUTE TOXICITY AFTER INHALATION ACCORDING OECD, SECTION 4,
SUBSECTION 403**

All tested animals have survived the inhalative application of the tested product X-Line without any sign of intoxication symptoms and have survived the following observation period under normal increase of body weight. The dissection with subsequently following macro - and microscopic investigation of the interior organs remained without result. The tested substance to be classified as non acute toxic after inhalation.

**Investigation for:
LOCAL COMPATIBILITY PATCH TEST ON THE RABBIT
ACCORDING OECD, SECTION 4, SUBSECTION 404**

The tested substance X-Line did not cause with the tested animals New Zealand albino even on freshly shaved parts of the skin any whatever formed primary irritations and have to be classified therefore as local very good compatible. The generation of Pustules and Pruritis did not occur in all cases and also the second growth of the pelt (fur) on the treated areas did not show any abnormalities in comparison to the second growth of untreated control shavings.

**Investigation for:
LOCAL COMPATIBILITY PATCH TEST ON MAN
ACCORDING TO FEDERAL REGISTER VOL.38, No. 187, § 1500.41 dated
27.9.1973**

T
he patch test on living rabbit skin was expected to mirror the test series for local compatibility with the patch test on man, with 60 voluntary test persons, remained without result. The tested substance has confirmed the results of good local compatibility on the skin.

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Investigation for:

**MUCOUS MEMBRANE COMPATIBILITY ON THE RABBIT EYE
ACCORDING TO J.H. DRAIZE, APPRAISAL OF THE SAFETY IN FOOD,
DRUGS AND COSMETICS, ASS. OF FOOD AND DRUG OFFICIALS OF THE
U.S.p.p. 49- 52 (1959)**

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The conjunctival reaction against the applied tested substance X-Line, which have been injected into the right eye (conjunctive membrane pouch) of the tested animals was expressed in hardly perceptible reddish colour of the mucous membrane which disappeared after 24 hours observation period completely. The rigid evaluation according to DRAIZE justifies however for the tested substance a classification as mucous membrane irritating on the rabbit eye.

Investigation for:

**a) CHRONIC ORAL TOXICITY WITH REPEATED DOSAGE FOR 150 DAYS
b) CHRONIC INHALATIVE TOXICITY WITH REPEATED DOSAGE FOR 72
DAYS**

BOTH INVESTIGATIONS ACCORDING OECD, SECTION 4, SUBSECTION 452

All tested animals have survived the daily dosage of 3 ml/kg body weight of the testing substance for a trial period of 150 days using a oesophagus probang (probe) without interference of the increase of the body weight in comparison to untreated control groups and did not show after dissection which was performed 14 days after the end of the trial period any macroscopic abnormalities of the interior organs stomach – colon tract and liver. Also the checks for intoxication symptoms without lethal process (bristling of fur, sedation) remained negative.

X-Line to be classified as chronic oral non toxic for a dosage period of 150 days.

Trial guidelines according OECD S.4, SS.452 the evaluations have been performed in addition according to the Good Laboratory Practice guidelines following the methods of the MELLON INSTITUTE OF INDUSTRIAL RESEARCH, PITTSBURGH, PENNSYLVANIA, USA, for Range – Finding Toxicity.

For this purpose the tested animals in the investigation program of the tested substance X-Line have been exposed over a period of 72 days to a saturated flowing air stream. All animals have survived this exposition and did not show after dissection 14 days after the respective end of the trial any histologic changes and abnormalities with oesophagus and lungs. The total amount of exposition of tested substance was 681 g/kg body weight for 72 days, that as a consequence the chronic lethal dose for rats has to be adjusted much higher as the border line of 4g/kg body weight which has to be survived as stated in the regulations in order to classify a product as chronic inhalative non toxic.

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Investigation for:

OECOTOXICITY WITH GOLDORFENTEST

ACCORDING OECD GUIDE LINE 203, DIN 38412, PART 15

Result: The LC 50 = Concentration where 50 % of the applied fish have been killed during the trial period was obtained as follows: X-LINE 328,6 mg/Liter

The tested substance have therefore to be classified as Non-fish toxic.