

**EFFICACY REVIEW  
HARTZ REFERENCE 121**

**DATE:** 09/08/05

**FILE SYMBOL:** 2596-RLU

**DP BARCODE:** D318907

**DECISION NUMBER:** 357507

**REGISTRANT:** Hartz Mountain Corporation

**GLP:** Yes

**CHEMICAL:** Chamber A:  
Permethrin (45.00%)  
Chamber B:  
Dinotefuran (14.85%)  
Pyridine (1.48%)

**PURPOSE:** Provide efficacy data for product registration.

**MRID:** 46552709. Young, D. (2005) In Vivo Adulticidal and Ovicidal Activity of a Flea and Tick Dermal Treatment Against the Cat Flea (*Ctenocephalides felis*) and the Brown Dog Tick (*Rhipicephalus sanguineus*) on Dogs: Final Amended Report. Project Number: HMNJ/04C/0301/2, 1715, HMNJ/04C/0301. Unpublished study prepared by Young Veterinary Research Services. 47 p.

46552710. Fourie, L. (2005) Efficacy of an Experimental Spot-on Formulation Administered Topically to Dogs (10 Pounds or Less of Body Weight) Infested with Fleas (*Ctenocephalides felis*) and Ticks (*Rhipicephalus sanguineus*). Project Number: 1727, CV/04/205. Unpublished study prepared by ClinVet International. 28 p.

46552711. Fourie, L. (2005) Efficacy of an Experimental Spot-on Formulation Administered Topically to Dogs (11 to 20 Pounds of Body Weight) Infested with Fleas (*Ctenocephalides felis*) and Ticks (*Dermacentor variabilis*). Project Number: 1729, CV/04/206. Unpublished study prepared by ClinVet International. 24 p.

46552712. Fourie, L. (2005) Efficacy of an Experimental Spot-on Formulation Administered Topically to Dogs (Over 55 Pounds of Body Weight) Infested with Fleas (*Ctenocephalides felis*) and Ticks (*Rhipicephalus sanguineus*). Project Number: 1730, CV/04/207. Unpublished study prepared by ClinVet International. 27 p.

46552713. Fourie, L. (2005) Effect of Shampooing on the Efficacy of an Experimental Spot-on Formulation Administered Topically to Dogs (21 to 55 Pounds of Body Weight) Infested with Fleas (*Ctenocephalides felis*) and Ticks (*Rhipicephalus sanguineus*). Project Number: 1728, CV/04/208. Unpublished study prepared by ClinVet International. 25 p.

46552714. Young, D. (2005) Water Immersion Impact on the In Vivo Adulticidal and Ovicidal Activity of a Flea and Tick Dermal Treatment Against the Cat Flea (*Ctenocephalides felis*) and the Brown Dog Tick (*Rhipicephalus sanguineus*) on Dogs. Project Number: HMNJ/04C/0302/1, 1734, HMNJ/04C/0302. Unpublished study prepared by Young Veterinary Research Services. 41 p.

46552715. Slone, R. (2005) Evaluation of the Efficacy of an Experimental Spot-on at 2, 6 and 12 Hours Following Topical Administration to Dogs Between ~21-55 Pounds of Body Weight Infested with the Cat Flea (*Ctenocephalides felis*) and the Brown Dog Tick (*Rhipicephalus sanguineus*). Project Number: 1736, PLRS/0434. Unpublished study prepared by Professional Laboratory and Research Services, Inc. 44 p.

46552716. Slone, R. (2005) Evaluation of an Experimental Spot-on Applied Topically to Dogs (Between ~21 and 55 Lbs of Body Weight) to Repel, Kill and Stop Blood-Feeding of Adult *Aedes aegypti* Mosquitoes. Project Number: 1737, 0436. Unpublished study prepared by Professional Laboratory and Research Services, Inc. 52 p.

46552717. Carroll, S. (2005) Laboratory Trial: Efficacy of a Topical Containing S-1638/Permethrin/Nylar as a Mosquito (*Culex pipiens quinquefasciatus*) Repellent and Adulticide in Domestic Dogs. Project Number: 1762, HMC/003. Unpublished study prepared by Carroll, Dr. Scott P. 19 p.

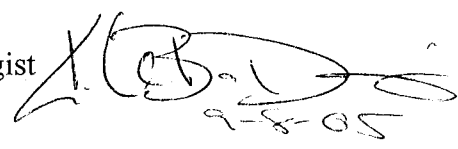
46552718. Carroll, S. (2005) Laboratory Trial: Efficacy of a Topical Containing S-1638/Permethrin/Nylar as a Mosquito (*Ochlerotatus triseriatus*) Repellent and Adulticide in Domestic Dogs. Project Number: 1763, HMC/004. Unpublished study prepared by Carroll, Dr. Scott P. 19 p.

46552719. Sloane, R. (2005) Evaluation of the Efficacy of an Experimental Spot-on Following Topical Administration to Dogs Between ~21-55 Pounds of Body Weight Infested with Adult Texas Lone Star Ticks (*Amblyomma americanum*) and the In Vitro Efficacy Against Deer Tick Nymphs (*Ixodes scapularis*). Project Number: 1751, PLRS/0442. Unpublished study prepared by: Professional Laboratory and Research Services, Inc.. 58 p.

46552720. Slone, R. (2005) Evaluation of the Efficacy of an Experimental Spot-on Following Topical Administration to Dogs Between ~21-55 Pounds of Body Weight Infested with Adult Gulf Coast Ticks (*Amblyomma maculatum*). Project Number: 1778, PLRS/0450. Unpublished study prepared by Professional Laboratory and Research Services, Inc. 36 p.

**TEAM REVIEWER:** Rita Kumar

**EFFICACY REVIEWER:** Kable Bo Davis, M.S., Entomologist



**SECONDARY**

**EFFICACY REVIEWER:** Joanne Edwards, M.S., Entomologist

#### **BACKGROUND:**

Hartz Reference 121 is intended for the treatment and prevention of ticks, fleas, and mosquitoes on dogs and puppies 7 weeks of age or older. The directions for use state that the material should be applied evenly “along the dog’s back, from the shoulder blades to the base of the tail.” Upon completion of application, the dog should be held in an upright position for two

minutes to prevent the loss of material. The product should be repeated monthly, and must never be used on other animals, including cats. Label claims include: "Controls fleas, ticks, and mosquitoes for up to one month", "Kills fleas, ticks, and mosquitoes within 24 hours", and "Kills fleas before they lay eggs".

#### **DATA REVIEW:**

The following data review is comprised of study objectives, and a summation of experimental results.

**46552709. Young, D. (2005) In Vivo Adulticidal and Ovicidal Activity of a Flea and Tick Dermal Treatment Against the Cat Flea (*Ctenocephalides felis*) and the Brown Dog Tick (*Rhipicephalus sanguineus*) on Dogs: Final Amended Report. Project Number: HMNJ/04C/0301/2, 1715, HMNJ/04C/0301. Unpublished study prepared by Young Veterinary Research Services. 47 p.**

Experiments were conducted to determine the efficacy of three different doses (2.3, 2.5, 2.8 ml TS#12404/1.0 ml TS#12396) of Hartz Reference 121 against cat fleas (*Ctenocephalides felis*) and brown dog ticks (*Rhipicephalus sanguineus*) infesting dogs weighing between 21 and 55 pounds. In addition, larvacidal flea efficacy was studied by observing the percentage of successful flea egg hatching and development.

#### **Reported Results:**

The percent mortality for adult fleas ranged from 96.8% to 100% for all three doses through day 30. The percent mortality for ticks ranged from 100% to 89.5% (day 30) for the low dose, 83.2% (day 2) to 96.4% for the middle dose, and 77.8% (day 2) to 95.0% for the high dose. The percentage hatch of fleas was decreased by 96.6% or better for all doses.

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**46552710. Fourie, L. (2005) Efficacy of an Experimental Spot-on Formulation Administered Topically to Dogs (10 Pounds or Less of Body Weight) Infested with Fleas (*Ctenocephalides felis*) and Ticks (*Rhipicephalus sanguineus*). Project Number: 1727, CV/04/205. Unpublished study prepared by ClinVet International. 28 p.**

Experiments were conducted to determine the efficacy of three different doses of Hartz Reference 121 against cat fleas (*Ctenocephalides felis*) and brown dog ticks (*Rhipicephalus sanguineus*) infesting dogs weighing ten pounds or less. In addition, larvacidal flea efficacy was studied by observing the percentage of successful flea egg hatching and development.

#### **Reported Results:**

The percent mortality for adult fleas ranged from 93.0% to 100% for all three doses. The

percent mortality for ticks was at 96.0% or better for all doses after day 9. The day two results were below 70.0% for all three doses. The percentage hatch of fleas was reduced by 92.1% or better for all doses.

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**46552711. Fourie, L. (2005) Efficacy of an Experimental Spot-on Formulation Administered Topically to Dogs (11 to 20 Pounds of Body Weight) Infested with Fleas (*Ctenocephalides felis*) and Ticks (*Dermacentor variabilis*). Project Number: 1729, CV/04/206. Unpublished study prepared by ClinVet International. 24 p.**

Experiments were conducted to determine the efficacy of three different doses of Hartz Reference 121 against cat fleas (*Ctenocephalides felis*) and American dog ticks (*Dermacentor variabilis*) infesting dogs weighing between 11 and 20 pounds. In addition, larvacidal flea efficacy was studied by observing the percentage of successful flea egg hatching and development.

**Reported Results:**

The percent mortality for adult fleas ranged from 88.7% (day 30, low dose) to 99.9% for all three doses. The percent mortality for ticks ranged from 66.9% (day 2) to 94.5% for the low dose, 76.7% (day 2) to 97.5% for the middle dose, and 86.6% (day 2) to 97.6% for the high dose. The percentage of successful flea egg hatching was reduced by 100% for all doses.

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**46552712. Fourie, L. (2005) Efficacy of an Experimental Spot-on Formulation Administered Topically to Dogs (Over 55 Pounds of Body Weight) Infested with Fleas (*Ctenocephalides felis*) and Ticks (*Rhipicephalus sanguineus*). Project Number: 1730, CV/04/207. Unpublished study prepared by ClinVet International. 27 p.**

Experiments were conducted to determine the efficacy of three different doses of Hartz Reference 121 against cat fleas (*Ctenocephalides felis*) and brown dog ticks (*Rhipicephalus sanguineus*) infesting dogs weighing over 55 pounds. In addition, larvacidal flea efficacy was studied by observing the percentage of successful flea egg hatching and development.

**Reported Results:**

The percent mortality for adult fleas was at 92.0% or better for all doses, with the exception of the low dose at day two with the percent mortality of 88.4%. The percent mortality for ticks ranged from 46.6% (day 2) to 98.4% for the low dose, 42.5% (day 2) to 96.8% for the middle dose, and 25.8% (day 2) to 98.9% for the high dose. The percent mortality was at 96.8% or better for all doses starting with day 16. The percentage of successful flea egg hatching was reduced by 99.2% or better for all doses.

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**46552713. Fourie, L. (2005) Effect of Shampooing on the Efficacy of an Experimental Spot-on Formulation Administered Topically to Dogs (21 to 55 Pounds of Body Weight) Infested with Fleas (*Ctenocephalides felis*) and Ticks (*Rhipicephalus sanguineus*). Project Number: 1728, CV/04/208. Unpublished study prepared by ClinVet International. 25 p.**

Experiments were conducted to determine the effect of shampooing on the efficacy of Hartz Reference 121 against cat fleas (*Ctenocephalides felis*) and brown dog ticks (*Rhipicephalus sanguineus*) infesting dogs weighing between 21 and 55 pounds. In addition, larvicidal flea efficacy was studied by observing the percentage of successful flea egg hatching and development.

**Reported Results:**

Adult flea counts on dogs shampooed was reduced 92.5%, 100%, 82.7%, 85.8%, and 73.7% at days 2, 9, 16, 23, and 30. Tick counts on dogs shampooed were reduced 18.5% at day 2, and 90.0% or better on all other days. The percentage of successful flea egg hatching was reduced by 99.9% or better for each day.

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**46552714. Young, D. (2005) Water Immersion Impact on the In Vivo Adulticidal and Ovicidal Activity of a Flea and Tick Dermal Treatment Against the Cat Flea (*Ctenocephalides felis*) and the Brown Dog Tick (*Rhipicephalus sanguineus*) on Dogs. Project Number: HMNJ/04C/0302/1, 1734, HMNJ/04C/0302. Unpublished study prepared by Young Veterinary Research Services. 41 p.**

Experiments were conducted to determine the effect of water immersion on the efficacy of Hartz Reference 121 against cat fleas (*Ctenocephalides felis*) and brown dog ticks (*Rhipicephalus sanguineus*) infesting dogs weighing between 21 and 55 pounds. In addition, larvicidal flea efficacy was studied by observing the percentage of successful flea egg hatching and development.

**Reported Results:**

The percent mortality for adult fleas on dogs immersed in water was 93.7% or better for all days. The percent mortality for ticks on dogs immersed in water was 95.8% or better for all days, with the exception of 47.9% on day 2. The percentage of successful flea egg hatching was reduced by 100%, 100%, 75.9%, 98.5%, and 41.5% at days 5, 12, 19, 26, and 33.

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**46552715. Slone, R. (2005) Evaluation of the Efficacy of an Experimental Spot-on at 2, 6 and 12 Hours Following Topical Administration to Dogs Between ~21-55 Pounds of Body Weight Infested with the Cat Flea (*Ctenocephalides felis*) and the Brown Dog Tick (*Rhipicephalus sanguineus*). Project Number: 1736, PLRS/0434. Unpublished study**

**prepared by Professional Laboratory and Research Services, Inc. 44 p.**

Experiments were conducted to determine the efficacy of Hartz Reference 121 against cat fleas (*Ctenocephalides felis*) and brown dog ticks (*Rhipicephalus sanguineus*) infesting dogs weighing between 21 and 55 pounds at 2, 6, and 12 hours after application.

Reported Results:

The percent mortality after two hours was 59.0% for fleas and 30.3% for ticks. The percent mortality after six hours was 95.9% for fleas and 61.3% for ticks. The percent mortality after twelve hours was 100% for fleas and 74.2% for ticks.

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**46552719. Sloane, R. (2005) Evaluation of the Efficacy of an Experimental Spot-on Following Topical Administration to Dogs Between ~21-55 Pounds of Body Weight Infested with Adult Texas Lone Star Ticks (*Amblyomma americanum*) and the In Vitro Efficacy Against Deer Tick Nymphs (*Ixodes scapularis*). Project Number: 1751, PLRS/0442. Unpublished study prepared by: Professional Laboratory and Research Services, Inc. 58 p.**

Experiments were conducted to determine the efficacy of Hartz Reference 121 against Texas Lone Star ticks (*Amblyomma americanum*) infesting dogs weighing between 21 and 55 pounds. Additional experiments were conducted to determine the in vitro efficacy of Hartz Reference 121 against deer tick nymphs (*Ixodes scapularis*).

Reported Results:

The percent mortality for Texas Lone Star ticks ranged from 57.0% to 81.0%. The percent mortality for deer ticks was greater than 96.0% after both 24 and 48 hour exposures.

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**46552720. Slone, R. (2005) Evaluation of the Efficacy of an Experimental Spot-on Following Topical Administration to Dogs Between ~21-55 Pounds of Body Weight Infested with Adult Gulf Coast Ticks (*Amblyomma maculatum*). Project Number: 1778, PLRS/0450. Unpublished study prepared by Professional Laboratory and Research Services, Inc. 36 p.**

Experiments were conducted to determine the efficacy of Hartz Reference 121 against adult Gulf Coast ticks (*Amblyomma maculatum*) infesting dogs weighing between 21 and 55 pounds.

Reported Results:

The percent mortality for Gulf Coast ticks when exposed to Hartz Reference 121 was 85%, 97%, 82%, 94%, and 95% on days 2, 9, 16, 23, and 30.

**46552716. Slone, R. (2005) Evaluation of an Experimental Spot-on Applied Topically to Dogs (Between ~21 and 55 Lbs of Body Weight) to Repel, Kill and Stop Blood-Feeding of Adult *Aedes aegypti* Mosquitoes. Project Number: 1737, 0436. Unpublished study prepared by Professional Laboratory and Research Services, Inc. 52 p.**

Experiments were conducted to determine the repellent efficacy, mortality, and effect of blood feeding of adult *Aedes aegypti* mosquitoes when exposed to dogs (21 to 55 lbs) treated with Hartz Reference 121.

**Reported Results:**

Hartz Reference 121 was not found to be efficacious at repelling *Aedes aegypti* mosquitoes. The percent mortality for those mosquitoes exposed to treated dogs was 90% or better for all days tested. Hartz Reference 121 reduced the number of blood feeding mosquitoes on treated dogs by 87%, 93%, 89%, 86%, 84%, 90% on treatment days 1, 7, 14, 21, 28, and 36.

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**46552717. Carroll, S. (2005) Laboratory Trial: Efficacy of a Topical Containing S-1638/Permethrin/Nylar as a Mosquito (*Culex pipiens quinquefasciatus*) Repellent and Adulticide in Domestic Dogs. Project Number: 1762, HMC/003. Unpublished study prepared by Carroll, Dr. Scott P. 19 p.**

Experiments were conducted to determine the repellent efficacy, mortality, and effect of blood feeding of adult *Culex pipiens quinquefasciatus* mosquitoes when exposed to dogs (21 to 55 lbs) treated with Hartz Reference 121.

**Reported Results:**

The number of mosquito landings on treated dogs as compared to those untreated was 72.5%, 82.0%, 77.0%, 88.3%, and 81.6% on days 1, 8, 15, 22, and 29. The number of recorded dead mosquitoes exposed to dogs treated with Hartz Reference 121 as compared to untreated dogs was 75.9%, 86.2%, 81.1%, 49.6%, and 75.6% on days 1, 8, 15, 22, and 29. No bites were recorded on treated dogs on any of the exposure dates, and no blood feeding was observed.

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**46552718. Carroll, S. (2005) Laboratory Trial: Efficacy of a Topical Containing S-1638/Permethrin/Nylar as a Mosquito (*Ochlerotatus triseriatus*) Repellent and Adulticide in Domestic Dogs. Project Number: 1763, HMC/004. Unpublished study prepared by Carroll, Dr. Scott P. 19 p.**

Experiments were conducted to determine the repellent efficacy, mortality, and effect of blood feeding of adult *Ochlerotatus triseriatus* mosquitoes when exposed to dogs (21 to 55 lbs) treated with Hartz Reference 121.

## Reported Results:

The number of mosquito landings on treated dogs as compared to those untreated was 53.1%, 35.9%, 32.4%, 63.4%, and 68.4% on days 1, 8, 15, 22, and 30. The number of recorded dead mosquitoes exposed to dogs treated with Hartz Reference 121 as compared to untreated dogs was 96.1% or better on all days. Hartz Reference 121 reduced the number of blood feeding mosquitoes on treated dogs by 97.9% or better on all days.

## RECOMMENDATIONS:

The submitted data supports the use of Hartz Reference 121 on dogs and puppies for the treatment and prevention of fleas, ticks and mosquitoes. The following recommendations apply:

1. The submitted data supports the “kill” of ticks. It does not however show that it repels them. Rephrase the claim “Repels and kills ticks” to read, “kills ticks”.
2. Within the DIRECTION FOR USE portion of the label, rephrase the statements “Repeat every month. Do not reapply for 30 days.” to read, “Repeat every month, or as needed. Do not reapply for 30 days.”
3. All label claims mentioning “puppies” must clarify puppies over the age of seven weeks.
4. The following claim is not supported by the data and must be deleted from the label:  
-“Kills fleas before they lay eggs”