Date of Approval: November 4, 2002

FREEDOM OF INFORMATION SUMMARY

Genesis™ Topical Spray

Solution of 0.015% triamcinolone acetonide

For control of pruritus
associated with allergic dermatitis in dogs

New Animal Drug Application

Sponsored by

RMS Laboratories, Inc.
1903 East First Street
Vidalia, Georgia 30474

FREEDOM OF INFORMATION SUMMARY
Genesis™ Topical Spray

I. General information

A. File Number:	NADA 141-210
B. Sponsor:	RMS Laboratories, Inc. 1903 East First Street Vidalia, Georgia 30474 Drug labeler code: 067292
B. Established Name:	Triamcinolone acetonide 0.015% topical spray
C. Proprietary Name:	Genesis™ Topical Spray
D. Dosage Form:	Solution
E. How Supplied:	16 ounce bottles with spray applicators
F. How Dispensed:	Prescription (Rx) – US Federal law restricts this drug to use by, or on the order of, a licensed veterinarian.
G. Amount of active ingredient:	Each mL contains 0.15 mg of triamcinolone acetonide
H. Route of Administration:	Topical
I. Species/Class:	Dogs
J. Recommended Dosage:	Apply sufficient pump sprays to uniformly and thoroughly wet the affected areas while avoiding run-off of excess product. Avoid getting the spray in dog's eyes. The recommended treatment schedule is twice daily for seven days, then once daily for seven days, then every other day for an additional 14 days (28 days total). To avoid overdosing the product, use Table 1 to determine the maximum number of pump sprays per treatment application. For mild pruritus or for small treatment surface areas, the number of pumps used should be less than this maximum amount.

Table 1. Maximum allowable dosage

Dog weight		Maximum number of pumps per single application [1]	Total maximum volume (mL) per 28-day treatment regimen
lb	kg		
11	5	4	101
22	10	7	176
33	15	11	277
44	20	15	378
55	25	19	478 (one 16-oz bottle)
66	30	22	554
77	35	26	655
88	40	30	756
99	45	33	832
110	50	37	932 (two 16-oz bottles)

[1] Using the recommended dosing regimen, there are 2 applications per day for the first week, one application per day for the second week, and one application every other day for the last 2 weeks of treatment.

K. Pharmacological Category: Glucocorticoid anti-inflammatory

L. Indications: Genesis Topical Spray is indicated for the control of pruritus associated with allergic dermatitis in dogs.

II. Effectiveness

A. Dosage characterization

1. General Dosing Information and Maximum Allowable Dosage

The general dosing instructions on the labeling ("Apply sufficient pump sprays to uniformly and thoroughly wet the affected areas while avoiding run-off of excess product") are intended to provide practical guidance for applying a topical solution. The instructions for tapering of the dose from twice daily to every-other-day follows standard practice for administering corticosteroids.

To avoid overdosing the product, precise calculations are provided in Table 1 to show the maximum allowable dosage for the 28-day treatment period. The maximum allowable dosage was set at 0.1 mg triamcinolone acetonide/kg/application based on literature references which show suppression of the hypothalamic-pituitary-adrenal axis (HPA) at ≥ 0.2 mg triamcinolone/kg/day (see Animal Safety, page 10).

The maximum dose for each weight group was calculated using the following general information: 1) each mL of Genesis Topical Spray provides 0.15 mg triamcinolone acetonide and 2) each pump spray delivers approximately 0.9 mL (0.135 mg) triamcinolone acetonide.

2. Inflammatory Response Study

Dr. Douglas J. DeBoer, Veterinary Medical Teaching Hospital, University of Wisconsin – Madison studied the effect of triamcinolone spray (0.015%) on decreasing cutaneous inflammatory response in an exploratory laboratory study in three dogs (2 females, 1 male).

An approximate 20x25 cm treatment area on the left and right lateral thorax of each dog was clipped free of hair. Twice daily on days 1-8, one side was treated with the triamcinolone spray and the other with the formulation's pharmacologically inactive vehicle (negative control). Both were sprayed in a manner to uniformly and thoroughly wet the defined treatment area just until the fluid started to run off. The investigator was not aware of which side had been treated with triamcinolone and which with the placebo.

Both treatment areas were re-clipped carefully after the day 5 treatments dried. One hour after the morning treatment on day 7, the dogs were sedated, grids were marked on both treatment areas and various concentrations of the following inflammatory stimuli were applied in duplicate on each side at specified grid locations: buffered saline diluent, compound 48/80 solution, mouse anti-canine IgE purified from ascites, substance P and morphine sulfate (all administered intradermally at 0.1 mL).

At 20 minutes post-injection, skin reactions were scored (0-5 with saline as the 0 reference) and traced onto clear acetate for size measurements. Table 2 shows the subjective scoring results and reaction site area measurements for each type and concentration of intradermal stimulus.

Table 2. Skin reaction scores and reaction areas

Inflam-matory stimulus	Conc.	Skin reaction scores (Mean, n=3, 6 sites)			Reaction area (mm^2) (Mean, n=3, 6 sites)		
		Control	TAC Spray	% Change	Control	TAC Spray	% Change
Compound 48/80 (µg/mL)	10000	5.00	5.00	0	292	210	-28
	1000	4.67	3.83	-18	171	126	-26
	100	3.83	3.17	-17	154	94	-39
Anti-IgE (ng/ml)	1000	3.33	1.33	-60	116	63	-46
	500	3.33	1.67	-50	113	73	-35
	250	2.83	1.67	-41	95	72	-24
Substance P (µM)	1000	3.50	1.83	-48	136	81	-41
	100	3.00	1.67	-44	90	68	-25
	10	2.33	1.50	-36	83	66	-21
Morphine sulfate (µM)	1000	3.83	2.83	-26	125	96	-23
	100	2.67	2.33	-13	93	73	-21

Conclusion: Subjective and objective measurements of the gross skin reactions demonstrated a diminished inflammatory response in the skin at drug-treated sites as compared with placebo-treated sites.

3. Exploratory Field Study

Dr. Douglas J. DeBoer, Veterinary Medical Teaching Hospital, University of Wisconsin – Madison conducted an exploratory field study to assess the effectiveness of triamcinolone acetonide in a 0.015% formulation in dogs with inflammatory skin disease.

Seventeen dogs with a history of atopic dermatitis and/or pruritus were treated. There was no control group. The affected area was sprayed (until wet) twice daily for seven days, once daily for seven days, and once every other day for the remainder of the treatment period. Duration of treatment ranged from 17 to 364 days. Owners subjectively scored the response to therapy based on two five-point scales — one for overall effectiveness and one for comparison of effectiveness to other treatments used prior to the study.

Owners rated the triamcinolone spray "very effective" (i.e., producing 60-90% improvement) in 8/17 dogs (47%) and "moderately effective" (i.e., 30-60% improvement) in an additional four dogs (24%), thus demonstrating at least moderate effectiveness in 12/17 (71%) of the dogs (Table 3). Five dogs showed less than 30% improvement.

Table 3. Results of effectiveness assessments of triamcinolone acetonide spray (0.015%)

Score	Description	No. of animals receiving this score (n=17)
0	Not effective or minimally effective; improvement <10%	2
1	Somewhat effective; improvement 10-30%	3
2	Moderately effective; improvement 30-60%	4
3	Very effective; improvement 60-90%	8
4	Extremely effective; improvement >90%	0

Owners' impressions were favorable in the comparison of the effectiveness of the triamcinolone spray to previous treatments, with an average score of 2.4 suggesting that it worked as well as or better than other medications (Table 4).

Table 4. Results of product comparison assessments (triamcinolone acetonide spray vs. other medications)

Score	Description	No. of animals receiving this score (n=17)
0	Didn't work nearly as well	1
1	Worked almost as well	4
2	Worked equally as well	5
3	Worked somewhat better	1
4	Worked much better	6

The only adverse effect observed was increased appetite in one dog.

Conclusion: Owner ratings for overall effectiveness and product comparisons in this limited field study supported the findings of the laboratory study for the 0.015% triamcinolone acetonide formulation in dogs with inflammatory skin disease.

B. Substantial Evidence of Effectiveness

Clinical Evaluation of Genesis Topical Spray for the Control of Pruritus Associated with Allergic Dermatitis in Dogs

Type of study: Field Study

Investigator(s):

Investigator	Address
Douglas J. DeBoer, D.V.M., ACVD (Principal Investigator)	Veterinary Medical Teaching Hospital University of Wisconsin – Madison 2015 Linden Drive West Madison, WI 53706
Carlo Vitale, D.V.M., ACVD	San Francisco Veterinary Specialists 3619 California Street San Francisco, CA 94118
Karin Beale, D.V.M., ACVD	Gulf Coast Veterinary Specialists 1111 West Loop South, Suite 120 Houston, TX 77027
Rusty Muse, D.V.M., ACVD	Animal Dermatology Clinic 2965 Edinger Avenue Tustin, CA 92780
Reid Garfield, D.V.M., ACVD	Animal Dermatology Referral Clinic 4444 Trinity Mills, Suite 101 Dallas, TX 75287

General design of the investigation: Multi-center, double-blind, placebo-controlled field study.

1. **Purpose.** The purpose of this study was to demonstrate the effectiveness of Genesis Topical Spray (0.015% triamcinolone acetonide) in controlling pruritus associated with allergic dermatitis in dogs under field conditions.

2. **Test animals.** A total of 110 client-owned dogs were enrolled. The 105 that completed the study included 42 males and 63 females of 38 different breeds, age 1-14 years (mean 6.1 years), weighing 3.7-52.7 kg. Of these, 54 received Genesis Topical Spray and 51 received a placebo.

3. **Control group.** The control group received a placebo (product vehicle).

4. **Diagnosis.** Following exclusion of skin disease due to bacterial, fungal, and parasitic infection, diagnosis was based on the investigator's subjective assessment of the magnitude and nature of pruritus, erythema, and papular-pustular eruption, with a required minimum overall score (minimum of 3 on a 0-5 scale) for eligibility. Concurrent medications permitted included: allergen immunotherapy if initiated at least 6 months prior to entry, antimicrobial shampoos or rinses and thyroid supplementation. Non-permitted concurrent medications included: corticosteroids, antihistamines, fatty acid supplements, antifungal drugs and initiation of hypoallergenic diet within 3 months of study entry. The dogs enrolled presented with a range of allergic skin diseases, as show below:

   atopy and presumed atopy (83)
   unspecified allergic dermatitis (10)
   flea allergy and atopy (6)
   flea allergy (4)
   flea and food allergy (1)
   atopy and food allergy (1)

5. **Dosage form.** The test article was Genesis Topical Spray, an aqueous 0.015% solution of triamcinolone acetonide of a formulation intended for marketing. The control article was the aqueous vehicle for Genesis Topical Spray, containing no pharmacologically active ingredient.

6. **Route of administration.** Both products were administered topically, using a spray applicator. The owners were advised to wear gloves when applying the products.

7. **Dosage.** Using a plastic spray bottle applicator, each product was administered as a sufficient number of pump sprays to uniformly and thoroughly wet the affected areas, twice daily for 7 days, then once daily for 7 days, and then every other day for an additional 14 days (28 days total).

8. **Test duration.** January 22, 1999 to August 7, 2000.

9. Pertinent parameters measured

a. Investigator assessment of dermatitis-related clinical signs (pruritus, erythema, papular-pustular eruption and overall evaluation) prior to initial treatment and on day 28.

b. Client assessment of dermatitis-related clinical signs (itchiness, redness/inflammation, rash and overall effectiveness) prior to initial treatment and on day 28.

c. Observations for adverse reactions.

d. Hematology and blood chemistry analyses prior to initial treatment and on day 28.

10. Results

Treatment success was defined as clinical improvement (relief of pruritus) as determined by comparison of the investigator's overall clinical evaluation at the beginning and end of the 28-day treatment period. Success was defined for the individual animal as an improvement of two or more grades in the overall clinical score. Based on this definition, 64.8% (35/54) of the test cases were considered treatment successes compared to 23.5% (12/51) of the controls.

Based on this reduction of two or more grades in the overall evaluation by the investigator, a significantly greater percentage of the test cases were considered treatment successes ($p<0.05$), compared with the controls (Table 5).

Table 5. Percent of cases considered treatment successes.

Treatment	Percent Success [1]
Genesis Topical Spray	35/54 = 64.8% *
Placebo	12/51 = 23.5%

[1] Success = reduction in the level of severity by two or more grades in the investigator's overall evaluation from the pre-treatment to the post-treatment evaluation period.
* Significantly different from placebo at $p < 0.05$

Dogs treated with Genesis Topical Spray were, on the average, significantly less affected ($p<0.05$) after the 28-day treatment period than the control group for the following variables: the investigator's evaluations of pruritus, erythema and eruption, the investigator's overall evaluation and the owner's overall evaluation (Table 6).

Table 6. Mean post-treatment scores assigned by investigator or owner

Clinical Sign	Genesis Topical Spray (n=54)	Placebo (n=51)
Pruritus	1.5*[1]	2.8
Erythema	1.3*[1]	2.4
Eruption	0.4*[1]	1.6
Investigator Overall	1.7*	3.2
Owner Overall	2.3*	1.2

The evaluation scale for Pruritus, Erythema, Eruption, and Investigator Overall ranged from 0 = not affected to 5 = most severely affected. The evaluation scale for Owner Overall ranged from 0 = not effective to 3 = very effective.
[1] n=52 in the group treated with Genesis Topical Spray.
* Significantly different from placebo, $p < 0.05$.

The hematology and blood chemistry variables measured on day 28 were not significantly different between the test and the control groups ($p>0.05$) with the following exceptions: The group treated with Genesis Topical Spray had significantly fewer lymphocytes and eosinophils and a significantly greater serum albumin concentration than the control group ($p<0.05$).

11. Statistical analysis

The percentage of successes based on the investigator's overall evaluation was analyzed with a Mantel-Haenszel test that was stratified by investigator. The investigator's evaluation of pruritus, erythema and eruption, the investigator's overall evaluation and the owner's overall evaluation after the 28-day treatment period were analyzed with an analysis of covariance. The value of the dependent variable prior to treatment was included as a covariate. This hematology and blood chemistry results were also analyzed with an analysis of covariance.

12. Conclusions

Triamcinolone topical spray (0.015%) is effective for controlling pruritus associated with allergic skin disease in the dog.

13. Adverse reactions

Clinical observations were reported in both treatment groups as shown in Table 7 and were generally mild and self-limiting. There were 8 reports involving a reaction to the spray (discomfort, sneezing, watery eyes). These were attributed to both treatment

groups because the product vehicle was used as the control and could have contributed to these reactions.

Table 7. Adverse reactions

Adverse reaction	No. Dogs (all participants included)	
	Genesis Topical Spray (n=57)	Control (n=53)
Polydipsia	3 (5.3%)	3 (5.7%)
Polyuria	3 (5.3%)	0
Vomiting	1 (1.8%)	2 (3.8%)
Anorexia	1 (1.8%)	1 (1.9%)
Polyphagia	1 (1.8%)	0
Lethargy	1 (1.8%)	1 (1.9%)
Scaling	2 (3.6%)	1 (1.9%)
Diarrhea/loose stool	0	2 (3.8%)
Traumatic dermatitis	0	1 (1.9%)
Shedding	1 (1.8%)	0
Aversion/discomfort to spray	4 (3.6%)*	
Sneezing after spray	3 (2.7%)*	
Eyes watered after spray	1 (0.9%)*	

*These are grouped together since the vehicle was used as the placebo.

One dog was inadvertently treated with approximately 8 times the maximum allowable dosage of triamcinolone for the first week of the study. The owner reported that the dog licked some of the medication off its skin. The only reported adverse effects were polyuria and polydipsia present primarily during the first week during the twice daily treatment period. The signs decreased during the once daily treatment period and were resolved during the every other day treatment period.

V. Animal safety

A. Study to Determine Comparative Percutaneous Absorption of RMS Laboratories' Triamcinolone Acetonide Non-aerosol Pump to that of a Cream Formulation of Triamcinolone Acetonide

Type of study: Laboratory study

Investigator(s): Larry R. Cruthers, Ph.D.
Professional Laboratory and Research Services, Inc.
1251 NC 32 North
Corapeake, North Carolina 27926

General design of the investigation: A controlled study to evaluate the effects of topically applied triamcinolone on the hypothalamic-pituitary-adrenal axis (HPA) in dogs under laboratory conditions.

1. **Purpose.** The purposes of this study were 1) to determine if triamcinolone acetonide is absorbed percutaneously when applied via a topical spray and cream and 2) to evaluate the extent of absorption (based on plasma cortisol concentrations).

2. **Test animals.** Six mongrel female dogs weighing 10.8-19.7 kg and free of exogenous corticosteroids for approximately four weeks were used in the study. Two were treated with the triamcinolone spray, two with triamcinolone cream and two with a placebo.

3. **Control group.** Positive control—Vetalog® cream
   Negative control—spray vehicle

4. **Dosage form.** The test article was an aqueous solution of triamcinolone acetonide (0.015%). The positive control was Vetalog® cream (triamcinolone acetonide 0.1%). The negative control was the aqueous vehicle for the test article, containing no pharmacologically active ingredient.

5. **Route of administration.** All three products were administered topically in an approximate 15x25 cm treatment area between the shoulders, which was clipped free of hair. This location prevented the dogs from licking the treatment area.

6. **Dosage.** Each dog was treated once daily at approximately the same time for five consecutive days (days 0-4). Approximately 100 mL of the triamcinolone spray was topically applied to the delineated treatment area on each dog in Group A over the course of approximately one hour each day. The vehicle control was applied in the same manner and quantity to each dog in Group C. A total of 15 mL Vetalog® cream was manually applied to dogs in Group B each day. These quantities of product delivered 15 mg triamcinolone daily to Groups A and B.

7. **Test duration.** June 27, 1994 to August 19, 1994

8. **Pertinent parameters measured**

   a. Plasma cortisol concentration (nmol/L) was determined on days -3, 0, 1, 2, 3, 4, and 11.

   b. On days -3, 4, and 11, blood samples were collected prior to and one hour after intravenous injection of 1 mcg synthetic adrenocorticotropic hormone (ACTH) per kg for an ACTH-response test.

   c. On days 0, 1, 2, 3, and 4, blood samples were collected immediately prior to treatment with investigational drug article to determine baseline cortisol concentration.

9. Results (see Table 8)

Group A. Topically applied triamcinolone spray rapidly suppressed the HPA axis as indicated by decreased plasma cortisol concentrations the day after initial treatment. Repeated topical applications over the next four days continued the suppression as well as the reduced response to ACTH injection.

Group B. The systemic response (i.e., plasma cortisol reduction) to topically applied Vetalog® cream in one dog was similar to but not as significant as that achieved with the triamcinolone spray, while it was negligible in the other dog in this group.

Group C. Pre-ACTH and baseline cortisol concentrations remained relatively steady in control animals throughout the study. One control dog inadvertently received dexamethasone on day 10 for an injury, which accounts for its suppressed pre-ACTH cortisol level on day 11.

Table 8. Plasma cortisol concentration (nmol/L)

Group-Dog	D –3		D0	D1	D2	D3	D4		D11	
	Pre	Post					Pre	Post	Pre	Post
A-1	174.0	418.8	60.8	5.6	4.1	3.9	4.3	168.3	3.1	18.2
A-2	35.5	599.5	151.5	6.8	5.3	5.5	7.8	237.3	5.9	119.9
B-1	72.9	519.2	157.6	9.1	8.0	10.1	10.7	234.6	10.9	214.0
B-2	49.5	307.6	136.6	49.6	31.1	41.1	31.1	182.7	29.6	145.5
C-1	41.1	426.1	72.7	50.3	72.2	57.7	117.4	378.9	10.8	425.1
C-2	68.8	621.0	119.6	61.8	68.9	115.4	119.8	450.4	137.2	542.7

No adverse reactions were reported

10. Conclusions

Based on a sustained decrease in plasma cortisol concentrations in this study, triamcinolone acetonide is absorbed percutaneously from topically applied triamcinolone spray. Post-ACTH plasma cortisol concentrations on day 11 were low enough to indicate a continuing suppression of the HPA axis. Study duration was not sufficient to ascertain when pre-treatment status would return. The amount of triamcinolone spray administered in this study was approximately 5-6 times the maximum allowable dosage as presented on the labeling for Genesis Topical Spray.

B. Literature Review

1. Pharmacokinetics: Triamcinolone is a potent anti-inflammatory corticosteroid. It is rapidly absorbed (within 10 to 15 minutes) following intramuscular injection, and is primarily plasma-bound during its circulatory phase. Upon absorption it distributes into the extravascular compartment with a monophasic half-life of approximately 35 minutes. Within 15 minutes after intramuscular injection, triamcinolone distributes to all tissues with increased levels found in the adrenal glands, liver, and kidneys. In dogs, biliary metabolism and excretion is the primary means of elimination.

Approximately 80% of triamcinolone is excreted within 8 hours after injection, and the ratio of biliary to urinary excretion is 15:1.[1]

2. HPA Axis: It has been repeatedly demonstrated in human and veterinary medicine that the use of corticosteroids may adversely affect the HPA axis. Exogenous corticosteroids administered for prolonged periods or at excessive doses can disrupt the inhibitory feedback loop of cortisol and ACTH resulting in clinical signs of hyperadrenocorticism. These clinical signs include polydipsia, polyuria, nonpruritic alopecia, enlarged pendulous abdomen and thinning skin, impaired wound healing, lethargy, and myasthenia.[2,3]

   Controlled studies conducted in dogs indicate that triamcinolone administered intramuscularly, topically, or to the external ear canal at relatively high doses, increased dosing frequency, or extended duration can alter the normal function of the HPA axis. While the doses in these studies appear to be higher than most clinical applications, cases in veterinary clinical practice with overt signs of pathology occur with administration of corticosteroids.

   a. A dog was administered 1.76 mg/kg triamcinolone subcutaneously three times during a four-month period resulted in myasthenic rupture of the gastrocnemius muscle which could not be adequately repaired due to corticosteroid-induced impaired wound healing.[4] The dose administered was eight times the recommended clinical dose.
   b. A single intramuscular injection of triamcinolone at the maximum recommended therapeutic dose of 0.22 mg/kg resulted in a seven-fold reduction in endogenous cortisol levels and a two-fold reduction in ACTH-stimulated cortisol levels at 7 days after injection. Return to normal endogenous and ACTH-stimulated cortisol levels occurred 21 days after treatment. No overt clinical signs of pathology were observed.[5]
   c. Triamcinolone acetonide (0.1%) was applied topically to a group of five dogs (weight range from 7 to 15 kg). A 15x25 cm area of skin was clipped free of hair and the ointment containing 15 mg triamcinolone was applied topically for five consecutive days for a total available exposure of 75 mg triamcinolone per dog. The equivalent daily dose ranged from 1-2 mg/kg. Plasma cortisol and ACTH levels were decreased well below baseline and control levels for the five days of treatment. Plasma ACTH levels returned to normal by seven days after the last treatment. Endogenous cortisol and ACTH-stimulated cortisol levels remained below baseline and control levels at seven days after the final treatment. ACTH-stimulated cortisol levels were below baseline and control levels at 14 days after the last treatment. Plasma ACTH, cortisol and ACTH-stimulated cortisol levels were normal by 21 days after the last treatment. No overt clinical signs of pathology were observed.[6]
   d. Triamcinolone acetonide (0.1%) was applied into the external ear canal of four dogs (weight range of 9.2 to 17.6 kg) with normal ears. 1 mg triamcinolone was applied to each ear twice daily for three weeks. The equivalent daily dose ranged from 0.2-0.4 mg/kg. No adverse reactions were observed in the external ear canal and no overt clinical signs of pathology were observed. Plasma cortisol and ACTH-

stimulated cortisol levels were depressed for the duration of the three-week treatment period. Endogenous cortisol and ACTH-stimulated cortisol levels at weeks 4 and 5 remained below baseline and control but were increased compared to the treatment period, indicating ongoing recovery. Mild to moderate elevations in ALT, AST, and GGT occurred during the treatment period with evidence of a return toward baseline levels during the recovery period.[7,8]

Conclusion: Triamcinolone topical spray may be systemically absorbed and adversely affect the HPA axis. In order to minimize the likelihood for these effects, the product labeling provides for the following safeguards: 1) a dosing chart provides for a maximum allowable dosage of 0.1 mg/kg over the entire dosing period, 2) the dose is tapered from twice daily, to once daily and to once every other day and 3) the maximum treatment duration is limited to 28 days. This dosing regimen proved both clinically safe and effective in the well-controlled field study.

Citations

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2. R. D. Schechter. "Hyperadrenocorticism" in Current Veterinary Therapy VI. 1977. R. W. Kirk (ed). W. B. Saunders, Philadelphia. 1027-1032.

3. R.C. Thomas, D. Logas, L. Radosta, J. Harrison. "Effects of a 1% Hydrocortisone Conditioner on Hematologic and Biochemical Parameters, Adrenal Function Testing, and Cutaneous Reactivity to Histamine in Normal and Pruritic Dogs." 2000. Veterinary Therapeutics 1/1, 25-34.

4. J. M. Rewerts, A. M. Grooters, J. T. Payne, J. N. Kornegay. "Atraumatic rupture of the gastrocnemius muscle after corticosteroid administration in a dog." 1997. JAVMA 210:655-657.

5. R. J. Kemppainen, M. D. Lorenz, F. N. Thompson. "Adrenocortical suppression in the dog given a single intramuscular dose of a prednisone or triamcinolone acetonide." 1982. Am. J. Vet. Res. 42:204-206.

6. R. D. Zenoble and R. J. Kemppainen. "Adrenocortical suppression by topically applied corticosteroids in healthy dogs." 1987. JAVMA 191:685-688.

7. D. J. Meyer, K. A. Moriello, B. M. Feder, S. L. Fehrer-Sawyer, A. K. Maxwell. "Effect of otic medications containing glucocorticoids on liver function test results in healthy dogs." 1990. JAVMA 196:743-744.

8. K. A. Moriello, S. L. Fehrer-Sawyer, D. J. Meyer, B. Feder. "Adrenocortical suppression associated with topical otic administration of glucocorticoids in dogs." 1988. JAVMA 193:329-331.

VI. Human safety

Data on human safety, pertaining to consumption of drug residues in food, were not required for approval of this NADA. The drug is to be labeled for use in dogs, which are non-food animals.

Human Warnings are provided on the product label as follows: "User Safety: Wear gloves when applying the product. Spray in a well ventilated area. If the spray causes irritation to mucous membranes, discontinue use. Keep this and all drugs out of reach of children."

VII. Agency conclusions

The data submitted in support of this NADA satisfy the requirements of Section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The data demonstrate that Genesis™ (0.015% triamcinolone acetonide) Topical Spray, when used under labeled conditions of use, is safe and effective for the control of pruritus associated with allergic dermatitis in dogs.

The drug is restricted to use by or on the order of a licensed veterinarian because professional expertise is needed to diagnose and provide guidance in the treatment of allergic dermatitis. Furthermore, the veterinarian monitors patients for possible adverse effects of the drug.

Under Section 512(c)(2)(F)(ii) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for THREE years of marketing exclusivity beginning on the date of the approval.

Genesis™ (0.015% triamcinolone acetonide) Topical Spray is under U.S. patent number 6,300,326 which expires on November 2, 2014.

VIII. Attachments:

Facsimile Labeling is attached as indicated below:

1. Package insert
   Bottle Label