Approval Date: August 26, 1997

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 141-052

B. Sponsor

Schering-Plough Animal Health Corporation
1095 Morris Avenue
Union, NJ 07083

C. Proprietary Name

Optimmune® ophthalmic ointment

D. Established Name

0.2% cyclosporine USP ophthalmic ointment

E. Dosage Form, Route of Administation, and Recommended Dosage

1. Dosage Form:

   The ingredients of OPTIMMUNE® are formulated into a topical ophthalmic ointment. A 1/4 inch strip is to be administered every 12 hours to the affected eye(s). The ointment may be placed directly on the cornea or into the conjunctival sac. Dogs afflicted with CSK will most likely require lifelong consistent therapy.

F. Dispensing Status

A prescription (Rx) product which includes the caution statement as follows: Federal Law restricts this drug to use by or on the order of a licensed veterinarian.

G. Indication

OPTIMMUNE® (Cyclosporine A) Ointment is indicated for the management of chronic keratoconjunctivitis sicca (KCS) and chronic superficial keratitis (CSK) in dogs.

H. Effect of Supplement

To add the label claim for the management of chronic superficial keratitis (CSK) in dogs. In addition, the label claim for treatment of chronic keratoconjunctivis sicca (KCS) was changed to management of chronic KCS. The term management reflects the complexity of therapy for the two diseases.

II. EFFECTIVENESS

The ingredients of OPTIMMUNE® are formulated into a topical ophthalmic ointment. A 1/4 inch strip is to be administered every 12 hours to the affected eye(s). The ointment may be

placed directly on the cornea or into the conjunctival sac. Dogs afflicted with CSK will most likely require lifelong consistent therapy.

1. Controlled Clinical Field Trial-Europe: Report Number A-27053

a. Type of Study

Multicenter, historical controlled clinical field study in dogs affected by chronic superficial keratitis (CSK).

b. Investigators

Seven referral veterinary ophthalmology clinics located in four European countries (France, Germany, Spain and the United Kingdom) served as the study sites in the clinical field study. Of these, six produced a sufficient number of cases to be included in the clinical efficacy analysis.

		Cyclosporine Cases	
Investigator	**Location**	**Enrolled**	**Analyzed**
K. Barnett	United Kingdom	7	6
S. Crispin	United Kingdom	3	3
B. Clerc	France	2	0
J. Jegou	France	3	3
W. Neumann	Germany	15	15
A. Alvaro	Spain	3	3
D. Schmidt-Morand	France	3	2
	Total	36	32

c. General Design

Purpose: To demonstrate that 0.2% cyclosporine ointment is safe and effective under clinical conditions for the management of chronic superficial keratitis in dogs.

Animals: A total of thirty-six (36) cases treated with cyclosporine were enrolled in this clinical field trial and thirty-two (32) were included in the efficacy analysis. Enrolled dogs were predominantly German shepherds.

Diagnosis: All enrolled dogs were bilaterally affected by CSK. Presence of at least one of three pivotal clinical signs; vascularization, pigmented opacity, or granulation tissue was a prerequisite for enrollment into this study. Overall evaluations were made and adverse events recorded.

Controls: Historical, based on the knowledge that the disease is progressive and does not spontaneously resolve.

Dosage Form: 0.2% cyclosporine ointment.

Dose Tested / frequency of treatment: Approximately a 1 cm (1/4 inch) ribbon of cyclosporine was administered twice daily for 42 days.

*Route of Administratio*n: Ophthalmic topical

Test Duration: The study was conducted in two phases: a treatment phase of six weeks and a post treatment phase of three weeks to assess the need for long-term therapy.

d. Results

Vascularization: Cyclosporine statistically significantly reduced the severity of vascularization from baseline (Day 0) when evaluated on Days 7, 21, and 42. Statistically significant worsening was not noted in the cyclosporine group after treatment termination.

Pigmented Opacity: Pigmented opacity was not observed to improve over the 42 day treatment period.

Granulation Tissue: Cyclosporine statistically significantly reduced the extent of granulation tissue from baseline (Day 0) when evaluated on Days 7, 21, and 42. Statistically significant worsening was noted after treatment termination.

Overall Response: The investigators evaluated 90.3% of eyes treated with cyclosporine to be improved after 42 days of treatment. Approximately 39% of eyes were unchanged and 50% worsened within the 21 day period after treatment was withdrawn.

Adverse Reactions: Of 36 cases evaluated for safety, adverse reactions were noted in two animals. One involved transient hyperemia, epiphora, and mild discomfort of the eye and the other involved periocular/palpebral inflammation and mild alopecia.

e. Conclusion

Optimmune (0.2% cyclosporine ointment) was safe and efficacious in the management of chronic superficial keratitis. The results of the efficacy study and the previously established target animal safety support the long-term use of the drug.

III. ANIMAL SAFETY

Target animal safety was established in the original NADA approved on August 2, 1995.

IV. HUMAN SAFETY

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

V. AGENCY CONCLUSIONS

The data submitted in support of this supplemental NADA satisfy the requirements of Section 512 of the Act and 21 CFR 514.111 of the regulations. The data demonstrate that

OPTIMMUNE Ophthalmic Ointment (0.2% cyclosporine USP), when used under the labeled conditions of use, is safe and effective.

OPTIMMUNE Ophthalmic Ointment is restricted to use by or on the order of a licensed veterinarian because professional expertise, specifically knowledge of veterinary ophthalmology and a correct diagnosis of chronic superficial keratitis (CSK) are needed for safe use and treatment success. A veterinarian is required to monitor the results of treatment and determine the importance of adverse reactions.

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for THREE years of marketing exclusivity beginning on the date of approval because the application contains substantial evidence of the effectiveness of the drug involved, or studies of animal safety required for the approval of the application and conducted or sponsored by the applicant.

Patent number 4839342 for this product expires on June 13, 2006.

The format of this FOI Summary document has been modified from its original form to conform with Section 508 of the Rehabilitation Act (29 U.S.C. 794d). The content of this document has not changed.