Approval Date: September 30, 1998

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 122-578

B. Sponsor

Anika Therapeutics, Inc.

C. Proprietary Name

HYVISC® STERILE INJECTION

D. Established Name

Hyaluronate sodium

E. Dosage Form

The ingredients of Hyvisc® are formulated in a sterile injection for intra-articular injection in horses.

F. Dispensing Status

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

G. Dosage Regimen

A 2 mL dose containing 22 mg of hyaluronate sodium is injected intra-articularly in small joints (carpal and fetlock) and a 4 mL dose containing 44 mg of hyaluronate sodium is injected in large joints (hocks). Treatment may be repeated at weekly intervals for a total of three treatments. The maximum total of three treatments at weekly intervals applies to both small and large joints.

H. Route of Administration

Intra-articular injection

I. Indication

HYVISC® (Hyaluronate Sodium) Injection is recommended for treatment of joint dysfunction in horses due to non-infectious synovitis associated with equine osteoarthritis.

J. Effect of Supplement

To increase the concentration of hyaluronate sodium from 10 mg/mL to 11 mg/mL, and increase the dose from 20 mg to 22 mg for small joints and from 40 mg to 44 mg for large joints.

II. EFFECTIVENESS

Refer to the FOI Summary for the original April 3, 1986 approval.

III. TARGET ANIMAL SAFETY

Target animal safety was established in the original NADA approval dated April 3, 1986. These data were reevaluated due to the increase in dose when the drug concentration was increased from 10 mg/mL to 11 mg/mL.

The margin of safety in the original approval was 5X for carpal and fetlock joints based on the drug concentration of 10 mg/mL and the dose of 20 mg for small joints. The increase in drug concentration to 11 mg/mL increases the dose for small joints from 20 mg to 22 mg per joint. The increased dose reduces the margin of safety from 5X to 4.5X, which is adequate.

The margin of safety in the original approval was 3.58X for hock joints based on the drug concentration of 10 mg/mL and the dose of 40 mg for large joints. The increase in drug concentration to 11 mg/mL increases the dose for large joints to 44 mg per joint. This reduces the margin of safety from 3.58X to 3.2X, which is adequate.

IV. HUMAN FOOD 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 labeled not for use in horses intended for food.

V. AGENCY CONCLUSIONS

No new safety data were required to support this supplemental NADA. The data in the original approval dated April 3, 1986 were adequate to satisfy the requirements of Section 512 of the Act and 21 CFR 514.111 of the regulations. The data in the original approval were adequate to support the increased dose for both small and large joints. The data were adequate to demonstrate that Hyvisc® Sterile Injection when used under the labeled conditions of use, is safe and effective.

Hyvisc® Sterile Injection is restricted to use by or on the order of a licensed veterinarian because professional expertise, especially a knowledge of non- infectious osteoarthritis is needed to make an accurate diagnosis, safely administer the drug and monitor response to treatment. A veterinarian's expertise is required to determine if additional treatments are required and to evaluate the significance of any adverse reactions that may occur.