



Aptus[®]

SentrX[™]

**NATURAL WOUND HEALING
FOR DOGS AND CATS**



Aptus[®]

SentrX[™]

– 21st century biomaterials
to support natural wound healing in animals

Aptus[®] products are marketed by Orion Pharma which is a Finnish pharmaceutical company that develops and manufactures medicines, diagnostic tests and active pharmaceutical ingredients for global markets. Orion Pharma has been building well-being since 1917.

APTUS® SENTRX CORE TECHNOLOGY

When tissue is healthy, the extracellular matrix (ECM) provides support for cells and regulates intercellular communication. When an injury occurs, signals are released from the tissue that stimulate cells to repair the injury. Unfortunately, the process often leads to the formation of scar tissue rather than the appropriate new tissue.

Aptus® SentrX products provide matrices that work with the animal's natural repair system to encourage enhanced production of the appropriate ECM, leading to new healthy tissue.

Aptus® SentrX existing and coming products are based on chemically-modified glycosaminoglycans (GAGs), and other biopolymers in the extracellular matrix (ECM), to fabricate films and hydrogels.

These formulations are fully biocompatible, biodegradable at controlled rates, and non immunogenic.

Aptus® SentrX cross-linking technology permits in situ cross-linking of hydrogels that can be easily and quickly applied. These biomaterials have been described in a large number of scientific publications (see page 24).

An example of the synthesis of one proprietary version of the Company's biomaterial is shown below:

Hyaluronic acid (HA), is chemically modified to add sulfhydryl groups, producing Hyascent-S (also referred to as CMHA-S). CMHA-S is crosslinked using poly(ethylene glycol) diacrylate (PEGDA) to form a hydrogel. This hydrogel is then dried to form the Aptus® SentrX films.



A sheet of Aptus® SentrX film

PRODUCTS AVAILABLE ON THE MARKET WITH APTUS® SENTRX TECHNOLOGY ARE FOLLOWING:

For wound healing management

- Aptus® SentrX spray, 60 ml

For use in the prevention of post-surgical adhesions

- Aptus® SentrX film (adhesion prevention film), 3 X 7 cm (6 pieces), 10 x 15 cm (6 pieces)

For dry eyes

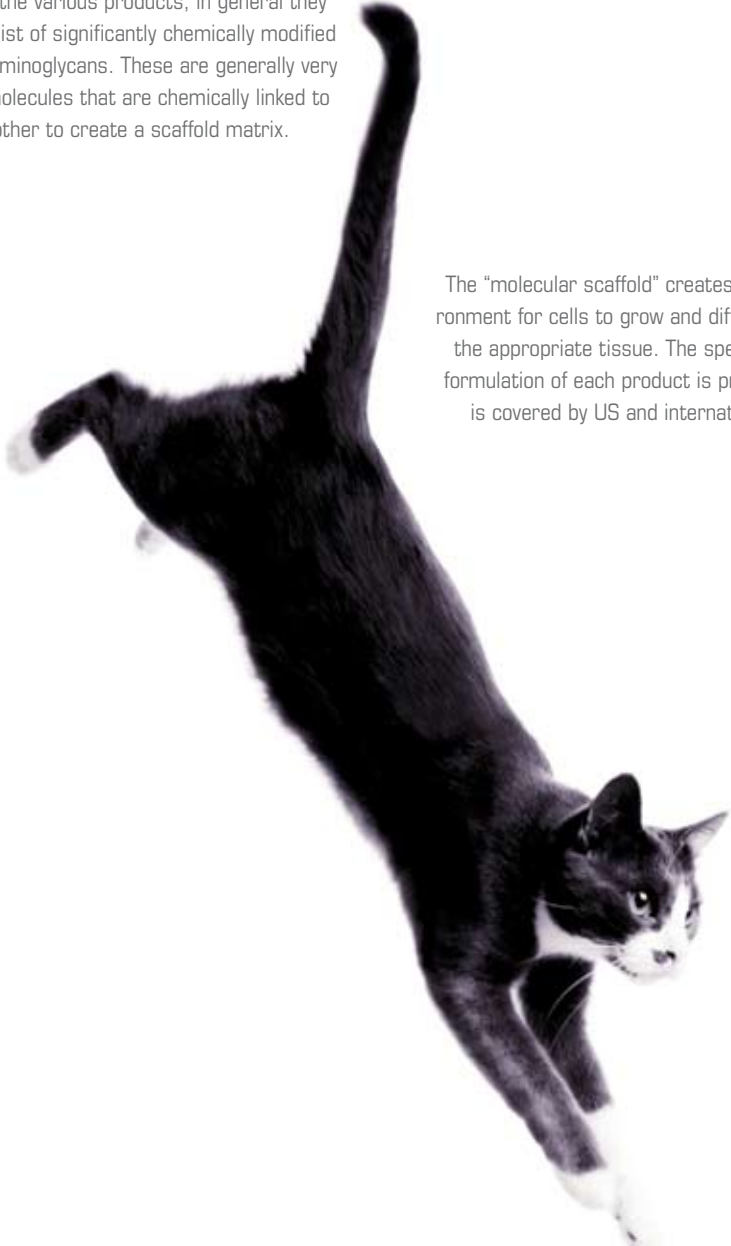
- Aptus® SentrX eye gel drops, 15 ml bottle
Can also be used for traumatic noninfected lesions.



THE COMPOSITION OF APTUS® SENTRX EXISTING AND COMING PRODUCTS

Although there are differences in formulations among the various products, in general they all consist of significantly chemically modified glycosaminoglycans. These are generally very large molecules that are chemically linked to one another to create a scaffold matrix.

The "molecular scaffold" creates an ideal environment for cells to grow and differentiate into the appropriate tissue. The specific chemical formulation of each product is proprietary and is covered by US and international patents.



**WOUND HEALING
MANAGEMENT**





Package: Bottle, 60 ml

APTUS® SENTRX SPRAY

Aptus® SentrX wound healing spray provides wound management for chronic and/or traumatic wounds to the skin of dogs and cats. It is effective in promoting rapid wound closure by providing a matrix for cellular events that are required for normal healing to occur.

Frequency of application

This depends on a number of different factors. In young, healthy animals with a fresh, uncomplicated wound, a single application may be sufficient to accelerate wound closure. For older animals or ones that are in poor health, or wounds that have been chronically unresponsive to various therapies, multiple applications for weeks or months may be necessary. Slow responders may need repeated debridement as well.

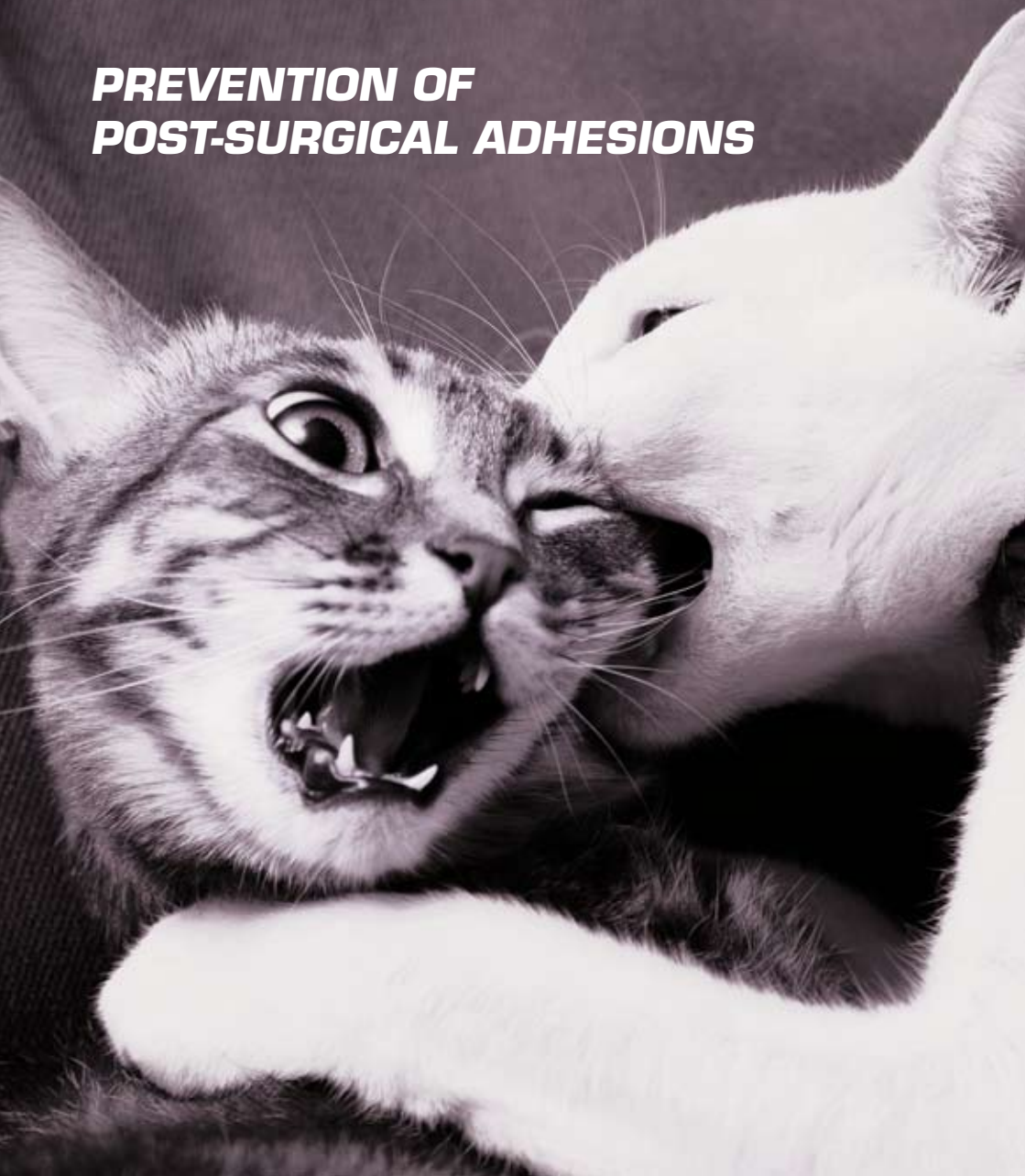
Aptus® SentrX spray is a sterile product and durable 2 years from day of manufacture. Store in room temperature.

For examples, see www.sentrxanimalcare.com.

Aptus® SentrX products are a vital part of the first aid kit and must be on-hand when you need them. Keep an inventory readily available in your practice.



**PREVENTION OF
POST-SURGICAL ADHESIONS**





Package: Adhesion prevention film, 3 x 7 cm, 10 x 15 cm (6 pieces)

APTUS® SENTRX FILM

Aptus® SentrX film is a medical device that provides a biodegradable, biocompatible temporary barrier between tissues which are likely to inappropriately heal together causing adhesions, while simultaneously providing post-operative tissue management. Aptus® SentrX film provide a physical adhesion barrier and accelerate the natural healing process of injured tissues.

Aptus® SentrX film can be used for tendon abdominal or neural adhesion prevention or in any subsequent surgeries that could be required to repair adhesions from earlier surgery(s). *See how to use the film on page 14-15*

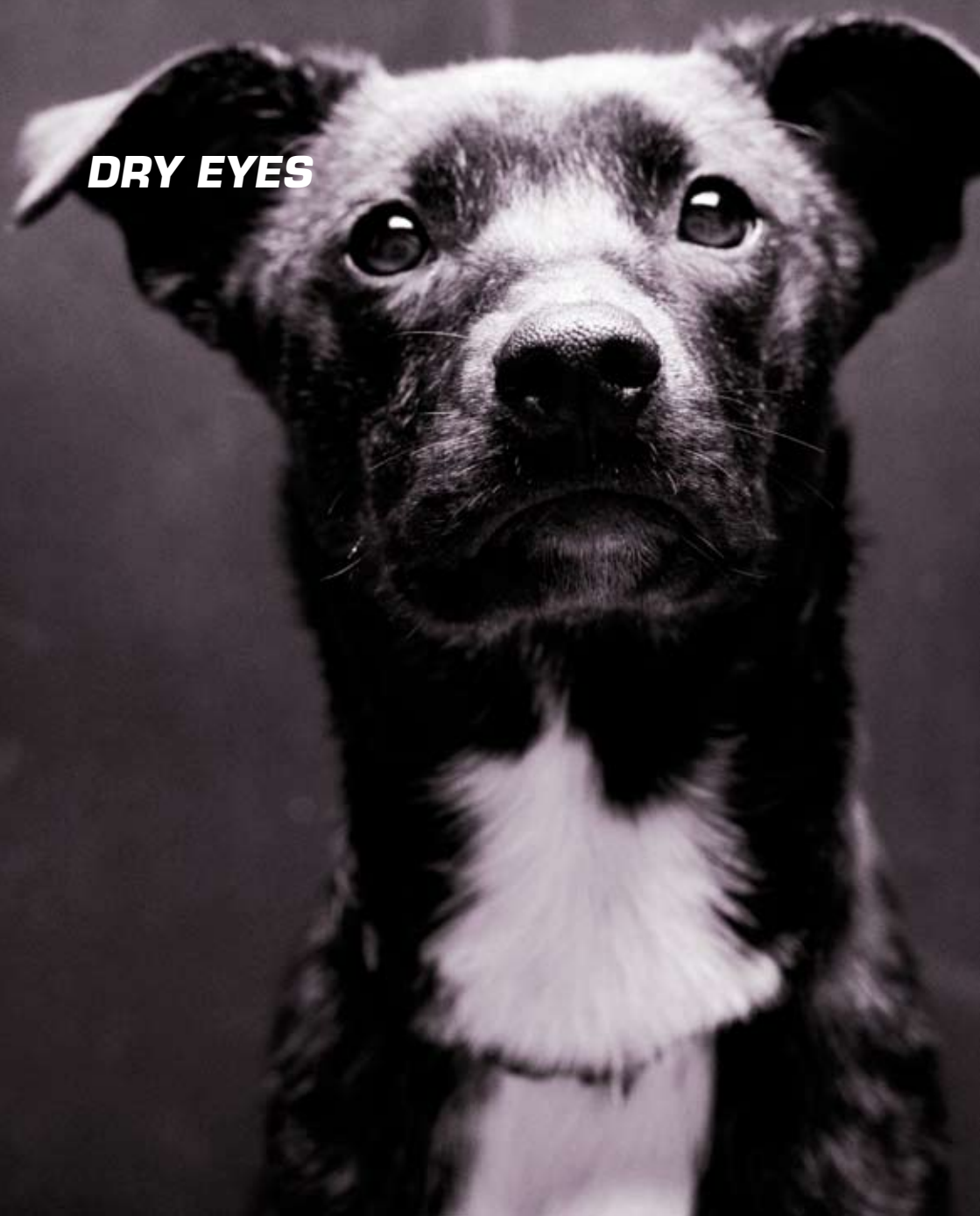
Aptus® SentrX film is a sterile product and durable 2 years from day of manufacture. Store in room temperature.

For examples, see www.sentrxanimalcare.com.

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DRY EYES





Package: Bottle, 15 ml

APTUS® SENTRX EYE GEL

Aptus® SentrX eye gel is intended for moisturizing and lubricating dogs', cats' and horse's eyes. It is useful for dry eyes and for when there is a noninfected trauma involved. Aptus® SentrX eye gel relieves the discomfort animals can experience when having an injured eye.

Frequency of application

Aptus® SentrX eye gel works by directly drop the substance into the eye. The eyelids natural movement will distribute the eye gel evenly over the eye's surface. Aptus® SentrX eye gel can be used until normal function of the eyes are restored. Only use Aptus® SentrX eye gel under the supervision of a veterinarian.

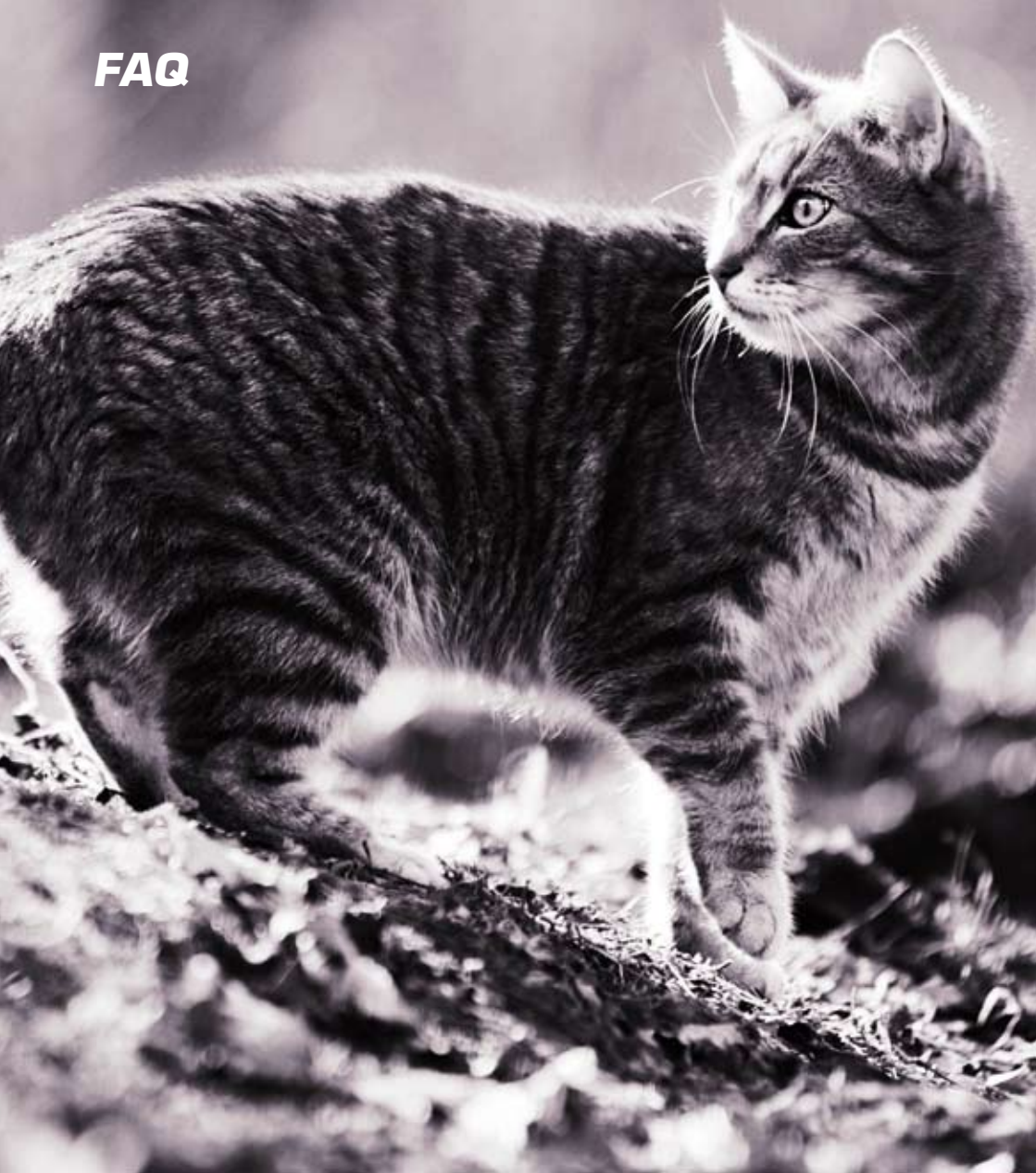
Aptus® SentrX eye gel is a sterile product and durable 2 years from day of manufacture. Store in room temperature.

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FAQ



How do the products accelerate wound healing?

When tissue is healthy, its extracellular matrix (ECM) provides support for cells and regulates communication between these cells. When an injury occurs, signals are released from the tissue that stimulates cells to repair the injury. Unfortunately, the process often leads to the formation of scar tissue rather than the appropriate new ECM. Aptus® SentrX products provide matrices that work with the animal's natural repair system to encourage enhanced production of the appropriate ECM, leading to new healthy tissue.

How and when should the products be used?

These films and gels are designed to be used on fresh or debrided wounds. Because the products need access to the appropriate cells for healing, they do not work when applied to a mature, scabbed wound. The products should be applied directly to the wound surface, which can be dressed in the normal way, as per the veterinarian's practice.

How long does the material remain on a wound from time to time of treatment?

The answer depends on the formulation. These materials can be engineered to biodegrade at various rates. The film for example degrades slower than the spray after application.

How often should a wound be retreated?

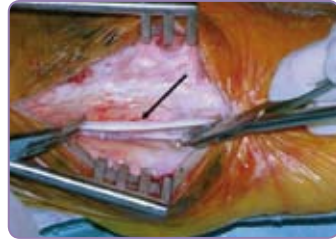
If a wound is dressed, then we recommend that a re-treatment should be done at each re-dressing. If the wound cannot be dressed, then treatment should be done daily until the wound is healed. Slow responders may need repeated debridement as well.

How should Aptus® SentrX film be used?

The films can be used externally on wounds but are mainly intended for internal use of post-surgical abdominal adhesions, neural adhesions and tendon/ligament adhesions. Films are placed between potentially sticky tissues to prevent adhesions, which would likely require a second surgery. Many surgeons are familiar with how to use films for these purposes. Sterile film may be pre-hydrated with sterile water/saline or with body fluid at the surgical site before placing them among or around potentially adhesion tissues such as tendons, neural tissues and/or internal abdominal anatomy. Upon hydration, the film may tend to curl because it is initially hydrated on one side. Flipping the film over, or first dragging it through the fluid and then flipping the film will result in flat film that can be easily handled and placed in the desired location.



*Flipping
Aptus Sentrx
film before
placing,
for easy
handling.*



*Placing
Aptus
Sentrx
film in
the
wound.*







CASE STUDIES

Note: The original company SENTRX SURGICAL, INC. has today been divided in to Sentrx Animal Care, Inc., Carbylan Biosurgery, Inc. and Glycosan Biosystems, Inc. Therefore other product names than Aptus® Sentrx are used in these case studies.

**CASE STUDY:
DR PATRICIA KUPANOFF,
FELINE MAY 2008,
FELITRX WOUND HEALING GEL**

This cat presented to Dr. Kupanoff on May 11, 2008 with a large wound at the base of his tail. The wound was infected and in need of debridement. Surgery was performed but the wound was not able to be closed with suture due to the difficult location and size.

On day 2, FelitrX gel was applied. Dr. Kupanoff continued to apply FelitrX every day. As the tissue granulated in, it became more feasible to surgically close the wound. Several surgeries were performed, as the wound had to be closed in stages. FelitrX was used throughout the treatment of this wound, and accelerated the healing process enabling Dr. Kupanoff to successfully close the entire wound 16 days after initial presentation.



Day 1, May 13 2008, FelitrX applied



Day 4 of use with FelitrX



*Day 9 of use with FelitrX.
Surgical closure performed.*



*Day 16 of use with FelitrX.
Surgical closure performed.*

Note: FelitrX wound healing gel is in our region marketed under the brand name Aptus[®] SentrX spray.

**CASE STUDY:
DR NIKLOS WEBER, DVM,
WHISPERING PINES PET
CLINIC, CANINE NOVEMBER-
DECEMBER 2008, CANITRX
WOUND HEALING GEL**

This chronic wound on a dog's neck had been open for 6 months after the dog was likely bitten by a rattlesnake. This chronic wound was previously diagnosed "untreatable" by another veterinarian that examined this dog prior to her coming to Whispering Pines. Once Dr. Weber

was able to get the wound free of infection and necrotic tissue, he began applying CanitrX wound healing gel at all bandage changes, every 2-3 days. In just 50 days, this wound had almost completely healed.



*CanitrX application begins.
November 5, 2008.*



November 12, 2008



November 17, 2008



December 1, 2008



December 12, 2008



December 19, 2008

Note: CanitrX wound healing gel is in our region marketed under the brand name Aptus[®] SentrX spray.

**CASE STUDY:
DR JEN TRIPPANY, WILLOW
RUN VETERINARY SERVICES,
ROCKFORD, MI CANDY, OCTO-
BER 2008, CANINE, CANITRX
WOUND HEALING GEL**

Candy is a 15-year old German Shepard. She has a granulomatous mass excised from her dorsal rear paw.

CanitrX wound healing gel was applied post-operatively and at each bandage change. In just a few weeks, the wound had completely healed.



October 14, 2008. Sugical excision of mass completed. CanitrX use begins.



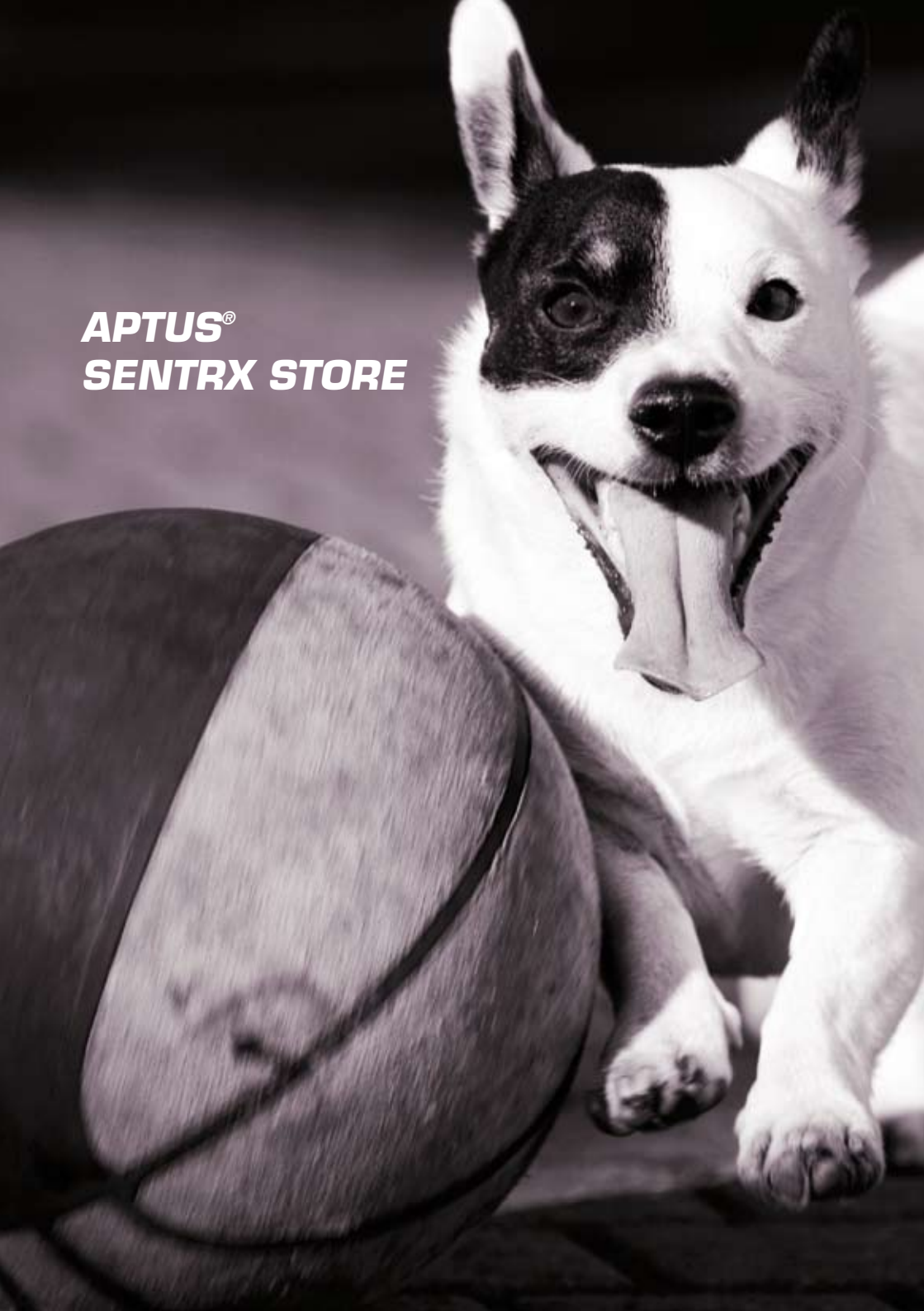
October 28, 2008



November 11, 2008

Note: CanitrX wound healing gel is in our region marketed under the brand name Aptus[®] SentrX spray.

APTUS[®]
SENTRX STORE



FOR FURTHER INFORMATION ABOUT APTUS® SENTRX PRODUCTS, CONTACT:

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832 10 37
www.orionvet.pl



PUBLICATIONS



PUBLICATIONS REGARDING APTUS® SENTRX WOUND HEALING TECHNOLOGY

Wound healing

K.R Kirker, Y Luo, J.H. Nielson, J. Shelby, and G.D. Prestwich, "Glycosaminoglycan Hydrogel Films as Biointeractive Dressings for Wound Healing." *Biomaterials*, 23, 3661-3671 (2002).

Y. Liu, X.Z. Shu, and G.D. Prestwich, "Reduced Postoperative Intra-abdominal Adhesions Using Carbylan-SX, a Semisynthetic Glycosaminoglycan Hydrogel," *Fertil. & Steril.*, 87, 940-948 (2007).

Y. Liu, A. Skardal, X.Z. Shu, and G.D. Prestwich, "Prevention of Peritendinous Adhesions Following Flexor Tendon Injury with Carbylan-SX, a Semisynthetic Glycosaminoglycan Hydrogel," *J Orthop Res.* 2008 Apr;26(4):562-9.

Mann BK, Scott JA, Rees R, Brown J, Seppi M, Burns G, Prestwich GD. "Enhanced wound Healing in Horses and dogs using crosslinked hyaluronic acid-based films" Poster presented at the Society for Biomaterials Annual Meeting, Chicago, IL, April 2007.

G. Yang, L. Espandar, N. Mamalis and G.D. Prestwich, "A cross-linked hyaluronan gel accelerates healing of corneal epithelial abrasion and alkali burn injuries in rabbits". *Veterinary Ophthalmology* 13, (3), 144 – 150 (2010).

Tissue Engineering

X.Z. Shu, Y. Liu, Y. Luo, M.C. Roberts, G.D. Prestwich, "Disulfide Cross-Linked Hyaluronan Hydrogels". *Biomacromolecules* 2002, 3, 1304-1311.

X.Z. Shu, Y. Liu, F. Palumbo, Y. Luo, and G.D. Prestwich, "In situ Crosslinkable Hyaluronan Hydrogels for Tissue Engineering," *Biomaterials*, 25, 1339-1348 (2004).

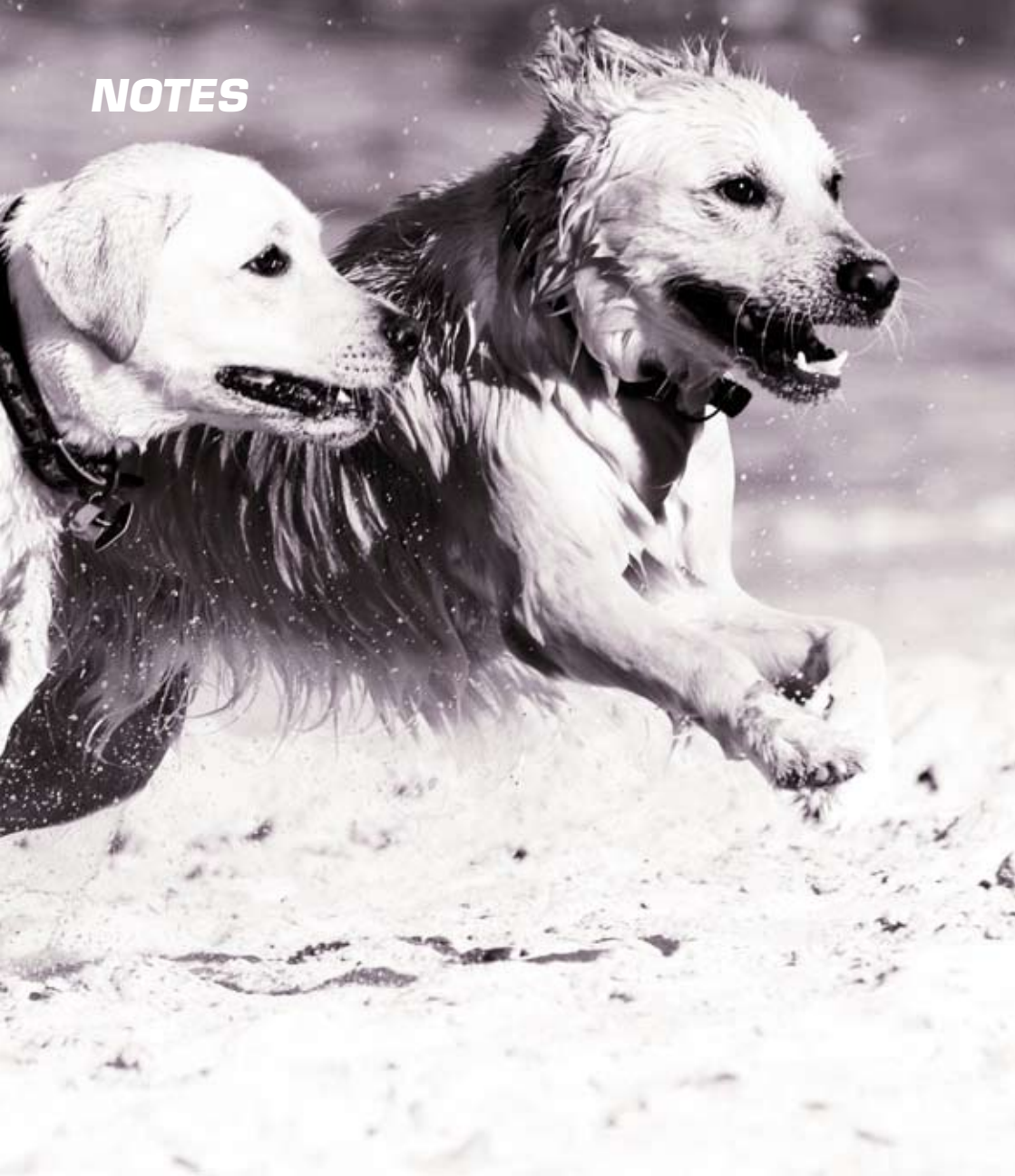
General

Y. Liu, X.Z. Shu, and G.D. Prestwich, "Biocompatibility and Stability of Disulfide-Crosslinked Hyaluronan Films," *Biomaterials*, 26, 4737-4746 (2005).

K. Ghosh, X.Z. Shu, R. Mou R, J. Lombardi, G.D. Prestwich, M.H. Rafailovich, R.A.F. Clark. "Rheological Characterization of in Situ Cross-Linkable Hyaluronan Hydrogels". *Biomacromolecules*. 2005 Sep-Oct;6(5):2857-65.

G.D. Prestwich and J.W. Kuo, "Chemically-Modified HA for Therapy and Regenerative Medicine," invited article, *Curr. Pharm. Biotech.*, 2008 Aug;9(4):242-5. Review.

NOTES



Aptus® SentrX products are developed to support natural wound healing in animals.

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must be on-hand when you need them.

To find out more visit

www.apтусpet.com

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