A clinical trial to determine the potential effects of Hydrolyzed Eggshell Membrane Powder (EMP) on joint mobility in dogs.

### November & December 2008

### **Background**

Older dogs suffer from canine osteoarthritis and other forms of degenerative joint disease and joint inflammation. This study reports clinical observations on joint mobility in dogs given a new nutritional supplement from eggshell membranes sourced from chicken eggs. Animal Medical Center (AMC) is a 36 year-old companion animal practice in Western Pennsylvania that is fortunate to have long term clients who are committed to providing their canine and feline companions with the highest possible quality of life within their means. AMC has developed a canine pain management program that includes the use of unique dietary supplements, non-steroidal anti-inflammatory agents and weight reduction to treat conditions associated with osteoarthritis. This program provides the highest standards of care. In 2008, eggshell membrane powder (EMP), a newly developed nutritional supplement originating from chicken eggshell membranes was commercialized\*. EMP is a >90% protein product that significantly increases palatability of dry food for dogs. Eggshell membranes contain some very powerful compounds including: a complex of glycosaminoglycans such as glucosamine, chondroitin and hyaluronic acid, elastin, collagen, desmosine, isodesmosine and transforming growth factor-β to name just a few. These compounds have a history of use for pain management associated with joint diseases. Because of the unique concentration of powerful, natural compounds in eggshell membranes, the potential effect of EMP on adult dogs with symptoms associated with Canine Osteoarthritis was tested.

### Purpose

The purpose of the clinical trial was to determine the effect of EMP on joint mobility in adult canine.

<sup>\*</sup>Eggshell membrane powder produced by BiOva, LLC, P.O. Box 394, Johnston, IA 50131-0394, http://biova.com

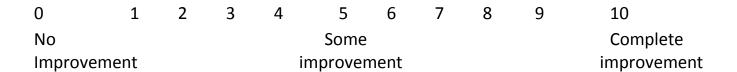
#### **Process**

In October of 2008, we began recruiting clients to participate in the study. We made this opportunity available to all clients with dogs exhibiting decreased joint mobility of any kind. We recruited participants to fall into the following four treatments:

Treatment Pre-trial		Trial supplementation	Number of
	supplementation		dogs
1. Naive	Nothing	EMP*	24
2. Boost	KnuBoost	KnuBoost + EMP	21
3. Supplement	Any supplement	Existing supplement + EMP	6
4. Switch	KnuBoost	EMP	6

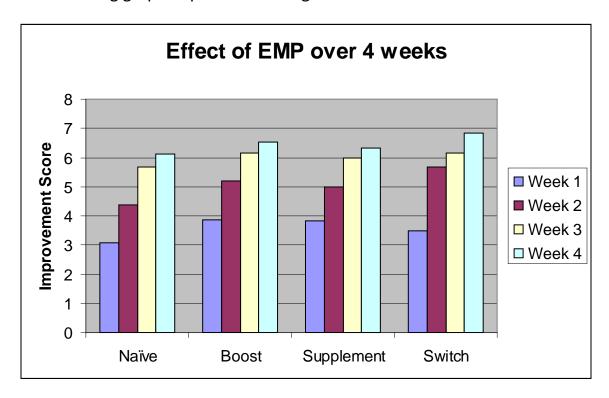
\*EMP supplementation consisted of a gel cap containing 5 mg of EMP/pound of body weight. The product was described to the clients as "KnuStuff". A 28-day supply of KnuStuff gel caps was compounded at a local pharmacy specific to each individual patient's body weight at the time of recruiting. The compounding agent was an inert ingredient. It was difficult to recruit clients into the Supplement and Switch treatment groups. There were very few clients on joint supplements other than KnuBoost and those who were on KnuBoost were very reluctant to switch off of it because of their confidence in the product.

On day zero, clients brought each of the patients into the clinic where the canine's general health condition was assessed and they were provided their supply of KnuStuff gel caps. They were instructed to give their dog one gel cap per day and to bring their dogs back in for review on a weekly basis. In compensation for compliance in the study, the clients were promised to receive \$125.00 upon completion. Every seven days, an AMC veterinary technician interviewed the clients, in person or on the phone, to assign joint mobility scores (JMS) in comparison to the day 0 status of the patient as a baseline for potential improvement. This does not imply the dogs were not in discomfort or pain on day zero. Instead, it serves as a baseline of joint mobility for the client to describe any changes taking place. The scale was as follows:



The Clients were responsible for assigning the joint mobility score and the veterinary technician asked them why they assigned that particular score for each week. The veterinary technician asked the client to provide examples of their dog's behaviors that led them to assign that particular score.

**Findings**The following graph depicts the average JMS for each treatment.



A single sample T- analysis for each of the four weekly observations was used to determine the statistical significance of the average JMS. A JMS of 2 was used as the threshold for improvement in the analysis (JMS  $\geq$  2). The Naïve and Boost groups exceeded this threshold

each week. The other two groups exceeded it for week 2 and beyond. The following charts contain the average Joint mobility scores for each treatment. A two sample T-analysis was used to make a pair-wise comparison of the weeks. In comparing two weeks, the week with the higher superscript letter has a significantly higher JMS than the other.

Naïve	WEEK=0	WEEK=1	WEEK=2	WEEK=3	WEEK=4	AVERAGE
AVERAGE	0.00	3.08 <sup>a</sup>	4.38 <sup>b</sup>	5.67 <sup>c</sup>	6.13 <sup>c</sup>	4.81
STD. DEV.	0.00	1.77	2.14	2.04	1.94	1.84

Boost	WEEK=0	WEEK=1	WEEK=2	WEEK=3	WEEK=4	AVERAGE
AVERAGE	0.00	3.86 <sup>a</sup>	5.19 <sup>b</sup>	6.14 <sup>b</sup>	6.52 <sup>bc</sup>	5.43
STD. DEV.	0.00	1.88	1.75	2.10	2.27	1.79

Supplement	WEEK=0	WEEK=1	WEEK=2	WEEK=3	WEEK=4	AVERAGE
AVERAGE	0.00	3.83 <sup>a</sup>	5.00 <sup>a</sup>	6.00 <sup>a</sup>	6.33 <sup>a</sup>	5.29
STD. DEV.	0.00	2.86	2.19	2.19	2.16	2.23

Switch	WEEK=0	WEEK=1	WEEK=2	WEEK=3	WEEK=4	AVERAGE
AVERAGE	0.00	3.50 <sup>a</sup>	5.67 <sup>a</sup>	6.17 <sup>a</sup>	6.83 <sup>ab</sup>	5.54
STD. DEV.	0.00	3.33	2.16	2.14	1.83	2.22

At the conclusion of the trial, a significant number of clients expressed their strong desire to purchase the trial product, EMP (KnuStuff). Clients began calling in with their requests to purchase as quickly as 3 to 7 days after discontinuing the EMP (KnuStuff) treatment. Accommodations were made to deliver commercial product in order to provide the clients with the highest possible standard of care. The following chart contains the total number of clients who purchased EMP (KnuStuff) after completing the trial.

Treatment	Total number of dogs	Number of clients refilling post-trial
1. Naive	24	15
2. Boost	21	16
3. Supplement	6	3
4. Switch	6	4
Total	57	38

The following chart contains the average joint mobility scores (JMS) of the dogs whose owner's purchased EMP (KnuStuff) after completing the trial.

Treatment	Average JMS of the entire treatment group	Average JMS of the dogs whose owners purchased EMP post-trial	Average JMS of the dogs whose owners did not purchase EMP post-trial
1. Naive	4.81	4.82	4.81
2. Boost	5.43	5.81	4.20
3. Supplement	5.29	7.00	4.50
4. Switch	5.54	5.25	4.75

### **Conclusions**

- 1. EMP increases joint mobility in adult dogs in as few as 7 days and continues to increase over time.
  - a. Joint mobility significantly increased in the Naïve and Boost treatment groups seven days after treatment began.
  - b. Joint mobility significantly increased in the Naïve treatment group from week 2 to week 3. The Boost treatment group exhibited significant improvements from week 2 to week 4.
- 2. None of the fifty seven dogs in any the four studies ever regressed in their individually observed JMS rating.

- 3. EMP increases joint mobility in adult dogs that are also on an existing pain management program including: supplementation of glucosamine and omega-3 fatty acids.
- 4. 66% of all clients participating in the trial came forward on their own volition to request and purchase the trial product, EMP (KnuStuff), upon completion of the study.
- 5. Supplementation of EMP is warranted as a standard of care for pain management in adult dogs.

I would like to express special thanks to Mrs. Beth Turtzer and the entire staff at AMC for their dedication to our client's needs and commitment to providing the highest standards of care to all patients.

Respectfully submitted,

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