

**interpath**  
the joint health experts

**4CYTE™**

# Veterinary Research & Product Guide



The only joint product  
patented to stimulate healthy  
cartilage production in  
horses and dogs.

[www.interpath.global](http://www.interpath.global)

**4CYTE™** is a game-changer for animal joint health. Scientifically developed to **reverse** or **repair** the pathological process responsible for joint disease. **4CYTE™**'s safety and efficacy has been demonstrated through 15 years of clinical and research studies.

## Six reasons to recommend 4CYTE™

1. Scientifically proven.
2. Sold through veterinarians - valuing your role in correct diagnosis and treatment protocols.
3. No long-term side effects or contraindications with other medications.
4. Small, cost effective and highly palatable daily oral dosing.
5. Targets the root cause/ailment, and not just the symptoms.
6. Applications for both **treatment** and **prevention** of joint disease.

<sup>1)</sup> Nutraceutical composition and methods of use 2008336267

<sup>2)</sup> Nutraceutical composition and methods of use 2008336268

## What makes 4CYTE™ unique?

**4CYTE™** contains Interpath's exclusive active ingredient, **EPIITALIS®**, patented for its revolutionary cartilage repair and pain relief properties.

## EPIITALIS® - the new superpower in joint health

**EPIITALIS®** is a patented oil extract from the seed of *biota orientalis*. Interpath utilises proprietary extraction methods to change the form of the **EPIITALIS®** from a triglyceride to a novel non-methylated interrupted free fatty acid form. This process significantly increases the potency and effect of the **EPIITALIS®** on controlling inflammatory mediator expressions such as Prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) and Nitric Oxide (NO).

### EPIITALIS®

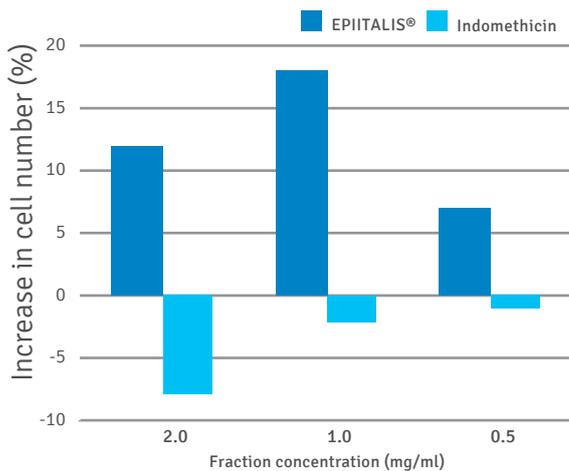
- ✓ Proliferates chondrocyte cells, which actively 'tips the balance' back in favour of the production of healthy cartilage instead of degeneration.
- ✓ Suppresses the inflammatory chemicals responsible for poor joint function and inflammation.

**EPIITALIS® has achieved international patents for cell proliferation<sup>1</sup> (in an inflamed environment - disease modifying) and anti- inflammatory properties.<sup>2</sup>**



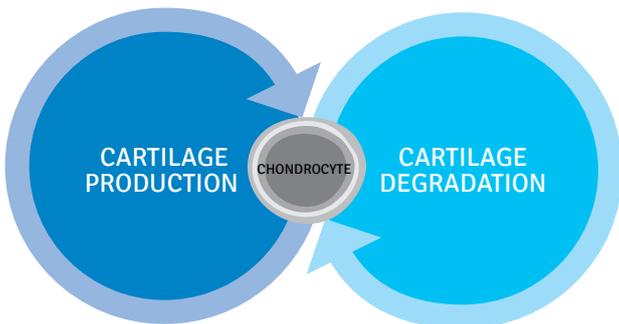
**EPIITALIS®**, an oil extract from the seed of *Biota Orientalis* (pictured)

# At A Glance: Research Highlights



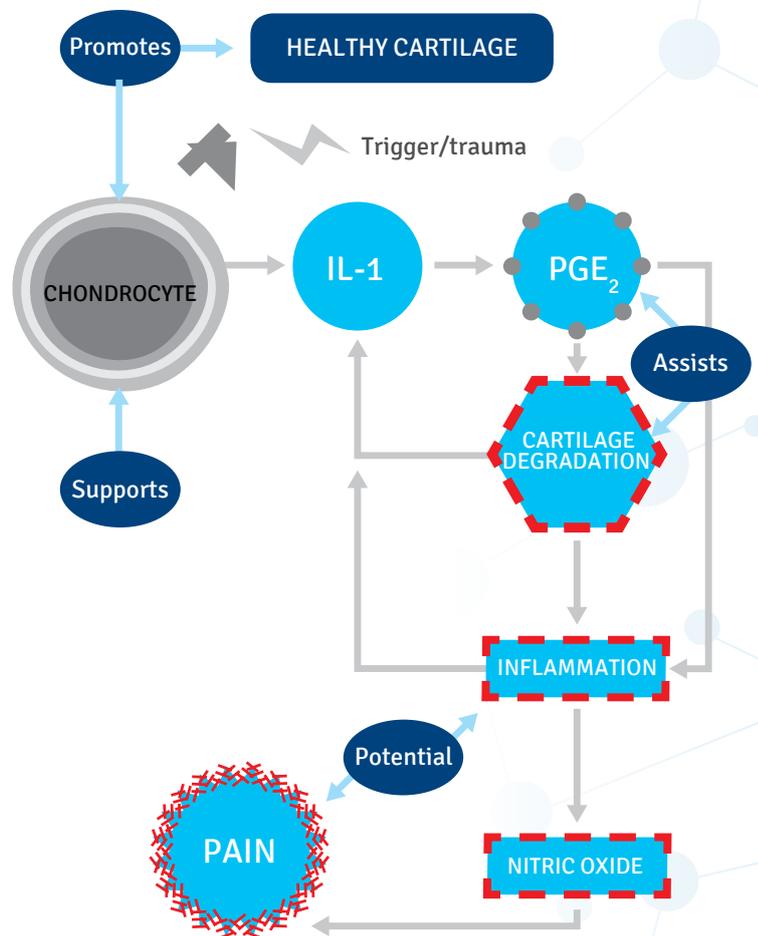
These bars represent mean and standard error and indicates significant increase in cell number, compared with control wells with culture medium only, in the absence of any treatment.

## 4CYTE™ Supporting joints to restore the balance



Potential increase in production of cartilage due to more chondrocytes, more GAGs and higher cell viability. Potential decrease in degradation of cartilage, production of PGE<sub>2</sub>, GAG release and inflammation.

## Biochemical pathway with 4CYTE™ intervention

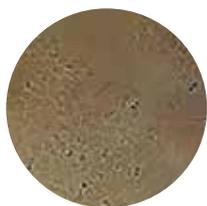


## Results: Demonstrated chondrocyte proliferation - In-Vitro

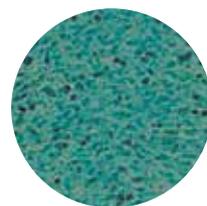
In cartilage explants stimulated with recombinant IL-1 $\beta$  (10 ng/mL), the prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) levels were significantly reduced by all of the **EPIITALIS®** - containing samples. The degree of inhibition ranged from 27.1% with the undigested extract to 48.8% with digested extract. This effect was fairly consistent with previously published data from the Pearson group (Pearson et al, 2008). Indomethacin almost completely inhibited PGE<sub>2</sub> production, as expected.



Shows chondrocytes at various stages of proliferation, starting with a small nest of cells and becomes 100% confluent.



Phase contrast light microscope images of chondrocytes at different stages of proliferation (10%, 60 and 100% confluency).



Alcian blue staining of chondrocytes. The darker blue spots are patches of glycosaminoglycan.

# The Evidence

**4CYTE™**, unlike many other products currently on the market, is backed by product specific research. **4CYTE™** has been scientifically developed targeting the root cause of the ailment and not just the symptom(s). The research utilised the latest molecular and cellular biology techniques, within the in-vitro and in-vivo studies providing a new, molecular level explanation of the effects of **4CYTE™** on the central inflammatory mediators associated with pain, inflammation and cartilage damage. **4CYTE™** has been proven to significantly affect the three major inflammatory mediator pathways.



## In-Vitro

Effects of stimulated digests of **EPITALIS®** and a dietary nutraceutical on IL-1 induced inflammatory responses in cartilage explants. W.Pearson, M.W. Orth, N. A. Karrow, M. Lindinger, AJVR, Vol 69, No.12, December (2008).

### Key Findings

Resulted in significantly improved NO and PGE<sub>2</sub> inhibiting properties, compared with effects of individual marine ingredients alone at same dose. Cell viability was significantly increased by **4CYTE™** in IL-1 challenged environment - the increases in viability resulted from an increase in live cell staining.

## In-Vivo (Equine)

Evaluation of inflammatory responses induced via intra-articular injection of IL-1 in horses receiving a dietary nutraceutical and assessment of the clinical effects of long-term nutraceutical administration. W. Pearson, M.W Orth, M. Lindinger. AMJVR, Vol 70, No.7, (2009).

### Key Findings

Feeding of **4CYTE™** inhibited the increase of PGE<sub>2</sub> (54.6%) and GAG induced by the intra-articular injection of IL-1 highlighting **4CYTE™** anti-inflammatory and chondroprotective properties as previously demonstrated in in-vitro studies - refer to figure 1. Feeding of **4CYTE™** lead to decrease in the circumference of joints swollen by the intra-articular administration of IL-1 consistent with inhibition of increased joint effusion seen in cases of arthritis and injury.

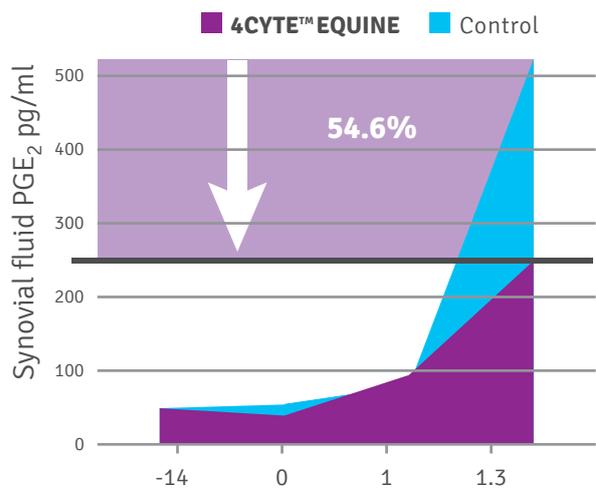


Fig 1: Feeding of DN inhibited the increase of PGE<sub>2</sub> (54.6% decrease) and GAG induced by the intra- articular injection of IL-1 highlighting DN anti-inflammatory and chondroprotective properties as also demonstrated in in-vitro studies.

# Clinical Trial Equine

Equine Medical Centre Ocala (Unpublished),  
Dr Frederick W. Benker, DVM

## Objective

To establish the clinical efficacy of dose rates in **EPITALIS®** in a gel oral application and its ability to reduce arthritis symptoms.

## Sample Group

10 Horses - 5 horses in both Group 1 and Group 2.

## Protocol

- Horses selected were showing signs of arthritis/joint inflammation. Horses were assessed in good health and not on NSAID's or other joint medications/supplements. Randomly allocated horses to Group 1 or Group 2:
  - Group 1: Receive 8g from day 1-14 then 4g from day 15-42.
  - Group 2: Receive 8g from day 1-28 then 4g from day 29-42.
- Administration of **EPITALIS®** Forte gel was once daily direct into the mouth. Note: Can be mixed with feed/supplement.
- Cases were assessed at each time point by the same Veterinarian.

## Assessment

The following measures were utilised at pre-treatment, after 2 weeks, 4 weeks and 6 weeks:

- Veterinary Lameness Score (0 - 4) adapted from AAEP.
- Joint Circumference Measurement.
- Handler Mobility Score (completed by handlers).

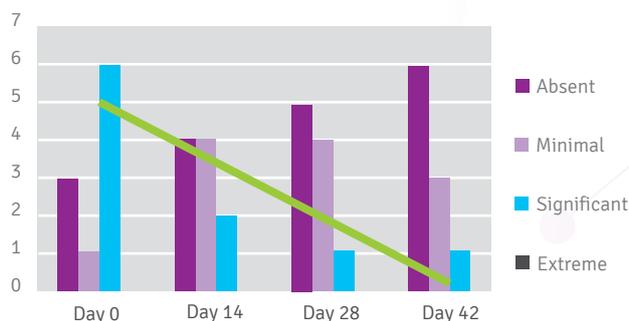
## Results

Findings were generally consistent across both groups which reinforced the efficacy in having a loading dose (8 grams) for the first 14 days and being able to reduce to a maintenance dose (4 grams). However it was raised by Dr Benker that in a severe case there may be a need for a slightly increased daily dose of between 4 - 8 grams (case dependent). In the trial there was 1 horse that did not benefit or improve throughout the 42 day trial, it is felt this horse has adhesions in his digital sheath. Joint circumference measurement; 10 horses in the trial did not have significant joint effusion and therefore no results can be actively drawn from this measurement. Some of the veterinary comments made on individual cases at the conclusion of the clinical trial:

- Much sounder, no longer requiring other NSAID medication to trail ride.
- Went from retirement back to being able to compete in barrel racing.
- Terrific results working better than IA treatment protocol.
- Miracle for this horse - running, bucking, playing like a foal for the first time in several years.
- Helped this horse significantly.

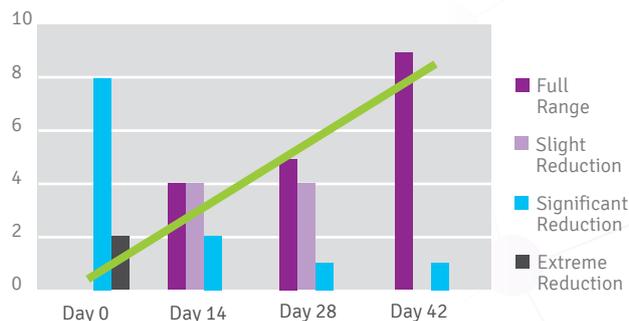
## Heat & Swelling

- 6 of the 10 horses had Significant Heat and Swelling at Day 0.
- 8 of the 10 horses were only showing Nominal to Absent levels after 14 days.



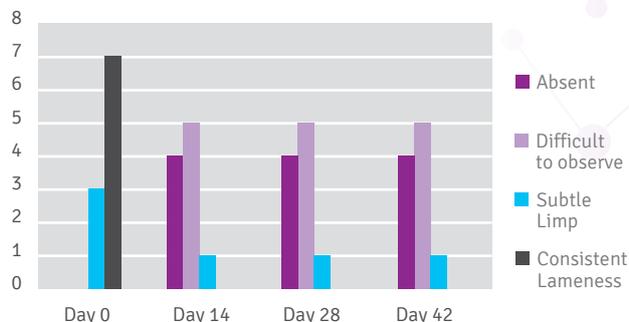
## Range Of Movement

- 8 of 10 horses had a Significant Reduction in Range of Movement/Mobility at Day 0.
- At Day 14, only 8 horses were showing Full Range or a Slight Reduction in Range of Movement/Mobility.
- At Day 42, 9 of the 10 horses had Full Range of Movement Mobility.



## Lameness

- 7 of the 10 horses had a Consistent Lameness at Day 0.
- 8 of the 10 horses at Day 14 had an Absent or Difficult to Observe Lameness.
- Only 1 horse had a subtle limp after 42 days.



# Clinical Trial Canine

Melbourne University, Faculty of Veterinary Science, (2012)

## Study 1

The objective of this study was to compare the efficacy of **4CYTE™** with a positive control NSAID, for the treatment of naturally occurring osteoarthritis in the dog. A randomised controlled clinical trial was used to assess response to therapy with 66 dogs completing the trial. Outcomes were evaluated for non-inferiority.

### Key Findings

**4CYTE™** was found to be non-inferior to control (NSAID) at day 14 for the Owner Mobility Scoring and non-inferior to all three assessments (Owner Mobility Score, Owner Lameness Score, Veterinary Lameness Score) at day 28.

**4CYTE™** was at least as effective as Control in relief of pain and lameness resulting from osteoarthritis in adult dogs (i.e. Clinical end-point bioequivalence was demonstrated).

## Study 2

Study objective was to determine the efficacy of **4CYTE™ EPIITALIS® FORTE** for Dogs for the treatment of naturally occurring osteoarthritis in the dog. Evidence had already been established that **4CYTE™** both relieves the signs of Osteoarthritis in the dog and alters the disease progression. This study was to determine the efficacy of the new gel presentation. This study was a masked, placebo controlled, parallel group, intention clinical trial on 54 dogs with radiographical evidence of osteoarthritis.

### Gait Lameness Score

To qualify the degree of lameness dogs were walked along the Gait Pressure Sensing Walkway which gave them a Gait Lameness Score (a patented way of evaluating how affected by osteoarthritis a dog is when it is in motion.)

### Gait Lameness Score % Outcome

Based on comparison data from Day 0 to Day 28 the grading was recorded as "IMPROVED" or "NOT IMPROVED" **4CYTE™ EPIITALIS® FORTE** had improvement in 72% of cases.

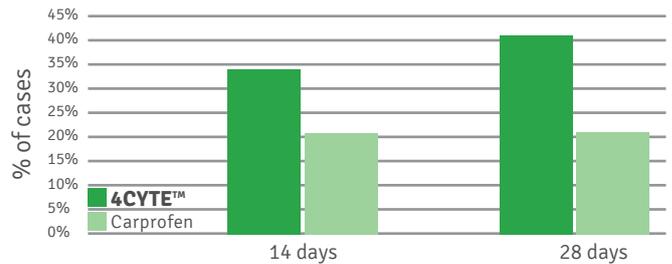
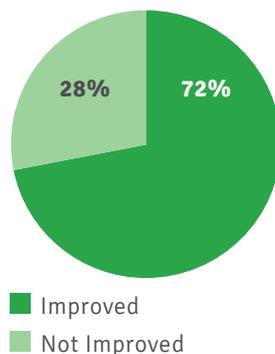


Fig 2: At day 28 twice the proportion 41.4% of dogs on **4CYTE™** Canine improved, compared to 21.6% that received the control.

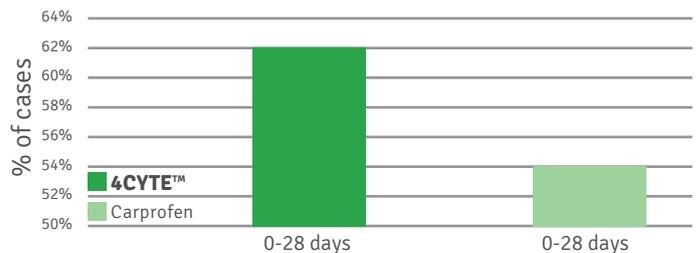
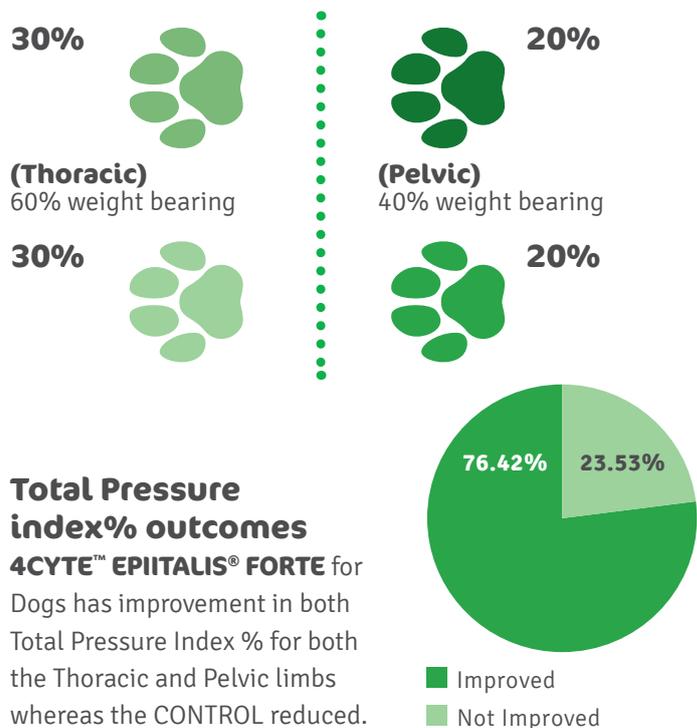


Fig 3: Between day 0 and day 28 at any given time point, 62.1% of dogs that received **4CYTE™** improved, compared to 54.1% of the control.

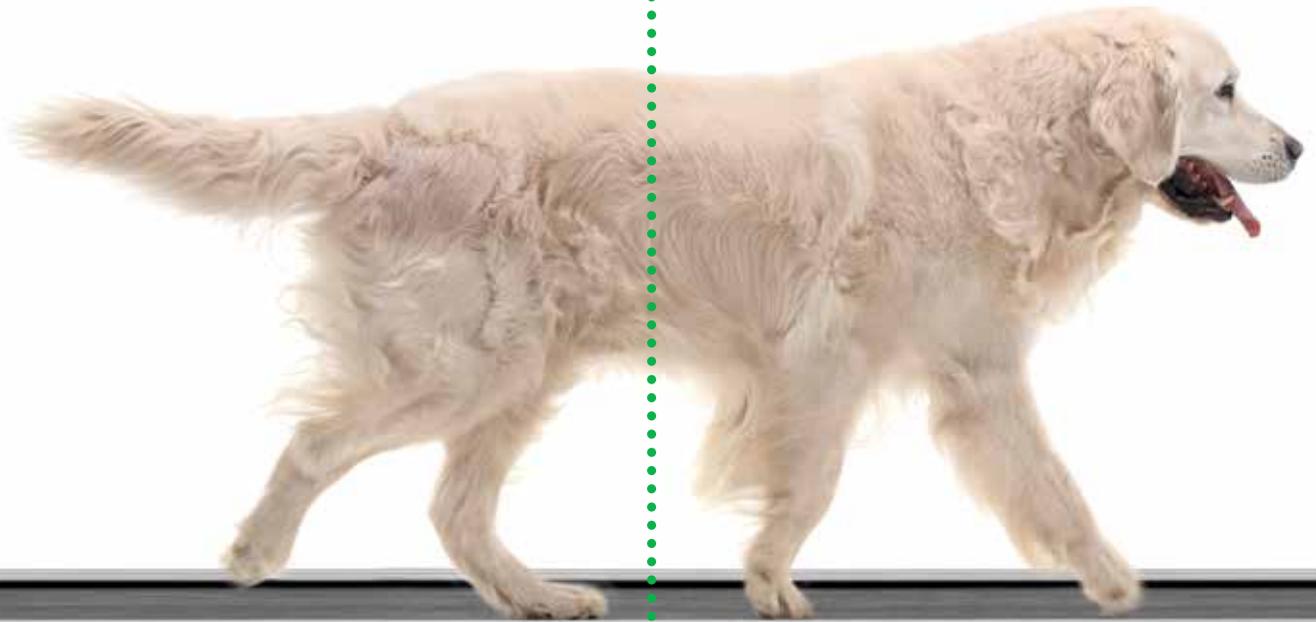
### Total Pressure Index %

In assessing Gait, the Total Pressure Index percentage (TPI%) is an important measure, Most breeds place more of their weight on their forelimbs (Thoracic) compared to their hind (Pelvic) limbs. For the majority of breeds this distribution falls somewhere between 60% on Thoracic (30% each limb) and 40% Pelvic (20% each limb).



## Pelvic Limb

## Thoracic Limb

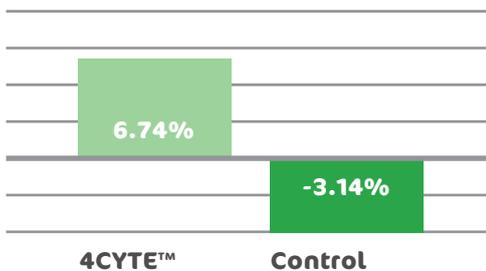


In this clinical trial we assessed both the overall TPI% for Thoracic and Pelvic as well as the ratio of weight borne on the Thoracic vs. Pelvic Limbs (T/P TPI%). As this study was looking at osteoarthritic cases not a specific limb lameness large variation was not expected, however we have seen fantastic results across both assessments. For improved weight bearing on both Thoracic and Pelvic limbs.

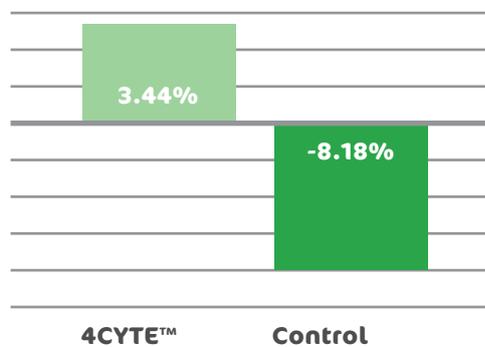
### Ratio of Weight Borne on the Thoracic Vs. Pelvic Limbs (T/P Tpi%) Outcome

#### Total TPI% Comparisons

##### (Pelvic)



##### (Thoracic)



# The 4CYTE™ Granule Range for Prevention & Maintenance

Available Units:

**4CYTE™** 50g and 100g chicken-flavoured granules for dogs.

**4CYTE™** 700g and 3.5kg berry-flavoured granules for horses.

The **4CYTE™** Granule Range comprises premium daily joint supplements used to protect damaged joints, and actively maintain joint health. Safe to take long-term, **4CYTE™**:

- ✓ Improves and maintains healthy joints at any stage of life.
- ✓ Addresses symptoms such as stiffness and lack of willingness to play, jump, run/canter/gallop.
- ✓ Boosts the body's ability to meet performance and recuperation demands in athletic, working and high performance animals.
- ✓ Acts as a prophylaxis in large breed dogs or breeds highly susceptible to joint-related problems and disease.
- ✓ Complements prescription joint pain treatments.
- ✓ Targets and addresses the cause of joint disease.



## Administration

Mix granules with daily feed.

### How Long Does It Last?

**Dogs** (20kg Dog) 100g lasts approx 125 days on a maintenance dose. 50g lasts approx 62 days.

**Horses** (500g Horse) lasts approx. 67 days on a maintenance dose. 3.5kg lasts approx. 334 days on a maintenance dose.

### Active Ingredients

- ✓ EPIITALIS®
- ✓ Abalone
- ✓ New Zealand Green-Lipped Mussel
- ✓ Marine Cartilage

## The Case for Preventative Treatment: A vet's perspective

**We all know prevention is better than a cure. Accordingly, veterinarians are increasingly recommending 4CYTE™ Granules for younger horses and dogs, rather than waiting for the signs of pain and discomfort to develop.**

Australian Veterinary Association Ballarat Branch President Dr Rob Page recommends preventative treatment for degenerative joint disease, particularly in very active

dog breeds, working dogs and large breeds. "Why wait for pain and discomfort in a client's pet before acting?" he says.

"At our clinic, we promote to our clients that prevention is better than a cure, and we have utilised **4CYTE™** and its disease-modifying capabilities to that effect.

We are pleased to see **4CYTE™** has quality research validating its capabilities, which has given our team and our clients confidence that the product they are using in their pets is providing genuine benefit.

Clients with dogs and/or horses should be encouraged to combine joint health supplements with strategies including:

- **Balanced Exercise.** Appropriate exercise can reduce stiffness in joints and keep muscles, tendons and ligaments in good condition. It also helps reduce an animal's weight, which reduces stress on joints and improves mobility.
- **Keeping Them Warm.** A well-fitting rug, coat or jumper keeps joints warm and comfortable.
- **Good Hoof/Nail/Foot Care:** It is important that toenails and hooves are kept trimmed to maintain a healthy, well balanced foot. Improper balance and overgrown nails/feet can increase the strain on joints.



### Suggested Dog Granule Dosage

Weight	1-4kg 2-10lbs	5-10kg 11-22lbs	11-20kg 23-44lbs	21-30kg 45-66lbs	31+kg 67+lbs
Loading Dose	1 scoop	2 scoop	4 scoop	6 scoop	8 scoop
Maintenance Dose	½ scoop	1 scoop	2 scoop	3 scoop	4 scoop

Weight	1-5kg	6-10kg	11-20kg	21-30kg	31+kg
Maintenance Dose	½ scoop	1 scoop	2 scoops	3 scoops	4 scoops
Doses per 50g Foil	250	124	62	42	31
Doses per 100g Foil	500	250	124	82	62

\*Dosage can be increased by ½ a scoop if desired

### Suggested Horse Granule Dosage

Product	Loading dose	Maintenance Dose
<b>4CYTE™</b> 700g horse	21 grams for 4 weeks (1 scoop)	10.5 grams daily (1/2 scoop)
<b>4CYTE™</b> 3.5kg horse	21 grams for 4 weeks (1 scoop)	10.5 grams daily (1/2 scoop)

# The 4CYTE™ Gel Range for Treatment

Available Units:

**4CYTE™** Dog 50ml, 100ml, 200ml

**4CYTE™** Horse 250ml, 1 Litre

The **4CYTE™ EPIITALIS®** Forte Gel range comprises premium daily feed supplements for the treatment of acute joint disease, injury and pain. Safe to use long-term, **EPIITALIS®** Forte:

- ✓ Use in acute care protocols including: joint injury, post orthopaedic surgeries and severe dysplasia.
- ✓ Complements prescription joint pain treatments.
- ✓ Addresses initial osteoarthritis, symptoms such as:
  - Intermittent lameness.
  - Reluctance to rise or move.
  - Stiffness (especially after vigorous exercise or prolonged periods of rest).
  - Swollen joints (may be warm or tender).
  - Visible joint deformities.
  - Painful joints when touched, palpated or moved.
- ✓ Large breed dogs requiring ongoing support of severe joint disease symptoms.

**Active Ingredient: EPIITALIS®**



**Other benefits:**

- ✓ Non-swabbable.
- ✓ Surgeon and Veterinarian endorsed.
- ✓ Backed by in-vitro, in-vivo and clinical studies.
- ✓ Should produce clinical improvements in 7-14 days.
- ✓ Simple, non-invasive application.
- ✓ Small, cost effective, once-daily dosing.

**Administration**

Draw accurate volume of suspension from bottle/foil using the applicator supplied.

**How Long Does It Last?**

**Dogs:**

- 50ml lasts approx. 50 days on a maintenance dose for dogs up to 20kg.
- 100ml lasts approx. up to 100 days on a maintenance dose for dogs 20-30kg.

**Horses:**

- 250ml lasts approx. 63 days on a maintenance dose.
- 1 litre lasts approx. 250 days on a maintenance dose.

**Suggested Dog Gel Dosage**

Unit Selection Guide			
Unit	50ml	100ml	200ml
Dog weight	Less than 20kg	20kg - <40kg	40kg - <60kg
Daily Dosing between	0.5ml - 1ml	1.5ml - 2ml	2.5ml - 3ml
Doses Per Unit	100 - 50 days	67 - 50 days	80 - 67 days

**Suggested Horse Gel Dosage**

Unit Selection Guide	250ml	1 Litre
	- First time user - Single Horse - Post Surgery Protocol	- Multiple Horse Owner - Studs - Horse trainers with multiple horses in care
Horse Dose	Loading 8ml for 14 days	Maintenance 4ml Daily



# Post-Operative Care Instructions

## Dog Post surgery care

**4CYTE™ EPIITALIS® FORTE Gel.**

**4CYTE™ EPIITALIS® FORTE** will help your pet have a fast recovery from surgery. Your vet has discharged your pet with care instructions including the product **4CYTE™ EPIITALIS® FORTE** to assist in post surgery recovery.

### What is EPIITALIS® and what will it do for my pet?

- ✓ **EPIITALIS®** is a patented plant extract with unique properties that will promote joint health.
- ✓ **EPIITALIS®** may suppress the inflammatory chemicals making your dog feel more comfortable during recovery.
- ✓ **EPIITALIS®** may proliferate chondrocyte cells which actively assists the production of healthy cartilage enabling the rebuilding of a previously damaged joint.
- ✓ With over 15 years of trial data supporting its safety and efficacy, **4CYTE™** comes with our palatability and efficacy **GUARANTEE**.

### How will EPIITALIS® help in the recovery of my pet post surgery?

- ✓ Alongside other prescribed medications and treatment regimes recommended post surgery, **4CYTE™** will assist in the fast recovery and wellbeing of your pet.
- ✓ The patented active **EPIITALIS®** will take effect from 24 hours of the first dose starting to work on the regeneration of healthy chondrocyte cells to rebuild the cartilage and repair the affected joint.
- ✓ Continued administration will provide ongoing care of joints post surgery for longevity of performance.

**Pack sizes available** 50ml, 100ml, 200ml.

**Dosage and after care** Your vet will advise on post surgery dose rates-below is a guide:



Suggested Dog Dosing/ Unit Selection Guide			
Unit	50ml	100ml	200ml
Dog weight	Less than 20kg	20kg - <40kg	40kg - <60kg
Daily Dosing between	0.5ml - 1ml	1.5ml - 2ml	2.5ml - 3ml
Doses Per Unit	100 - 50 days	67 - 50 days	80 - 67 days

Note: **4CYTE™** can be safely used in conjunction with other medications with no side effects. Should you have any questions please contact your prescribing veterinarian.

# Our Offer

Interpath is unique in our approach to our products, your business and the pet owner. We truly value the role all have to play from manufacturer to pet and look to add value to all parties ensuring we provide total satisfaction. **4CYTE™** is a unique joint product due to the high levels of validating safety and efficacy studies and also because of its patented properties.

## Benefits 4CYTE™ will bring to your Hospital or Clinic

- ✓ Provide you with a reliable joint health product to recommend with confidence.
- ✓ Satisfied clients who will see visual benefit in using **4CYTE™**.
- ✓ Safe efficacious product with no known side effects that can be used long-term.
- ✓ Engaged team – through training and mentoring provided by the Interpath team.
- ✓ Increased sales activity in the joint health segment of your business with solid margins available.
- ✓ Formal guarantee for clients should you or your clients be dissatisfied with the product.

## Customised Promotional Plan

A suite of promotional resources are available to suit any clinic or hospital and can be accessed online through [www.provet.com.au](http://www.provet.com.au) or through your Provet Business Account Manager.

## Team Education & Training

Your team is the number one asset and we believe they are often not invested in enough. We focus on training programs to educate your team on the complete opportunity from the product and its applications to the growing segment and how this fits in with your clinic.

## Client Education

Clients are becoming far more educated and often go seeking information about ailments, diseases and possible treatments. We believe the most important part of any treatment is correct veterinary diagnosis. We work with you to provide tailored support with client education activities to engage with your clients.

To access client education activities contact your Provet Business Account Manager or Interpath team.

# Our offer to you

## Highest Quality Product

- ✓ Made using only premium grade and patented ingredients.
- ✓ Strict manufacturing and testing regimes to ensure the highest level of quality.
- ✓ Supported by 15 years of formulation specific research including safety and toxicology.

## 100% Commitment

- ✓ Technical support – Access to industry experts for in-depth technical responses as well as the Interpath team with a wealth of knowledge on **4CYTE™**, joint disease and function.
- ✓ Solid Margins - Profitable Joint Health Segment, we know this market has grown and will continue to grow substantially. Hospitals and Clinics are seeing significant bottom line impacts by embracing this segment through **4CYTE™** along with other treatment modalities.
- ✓ Satisfied Clients – we care about your clinics and the benefits our products bring to the animals. **4CYTE™** has been researched and developed to ensure where used appropriately it will provide benefits.
- ✓ Partnership – we value your work and strive to be a significant partner to your business that adds value beyond supply of a quality product.



# Our 4CYTE™ Guarantee

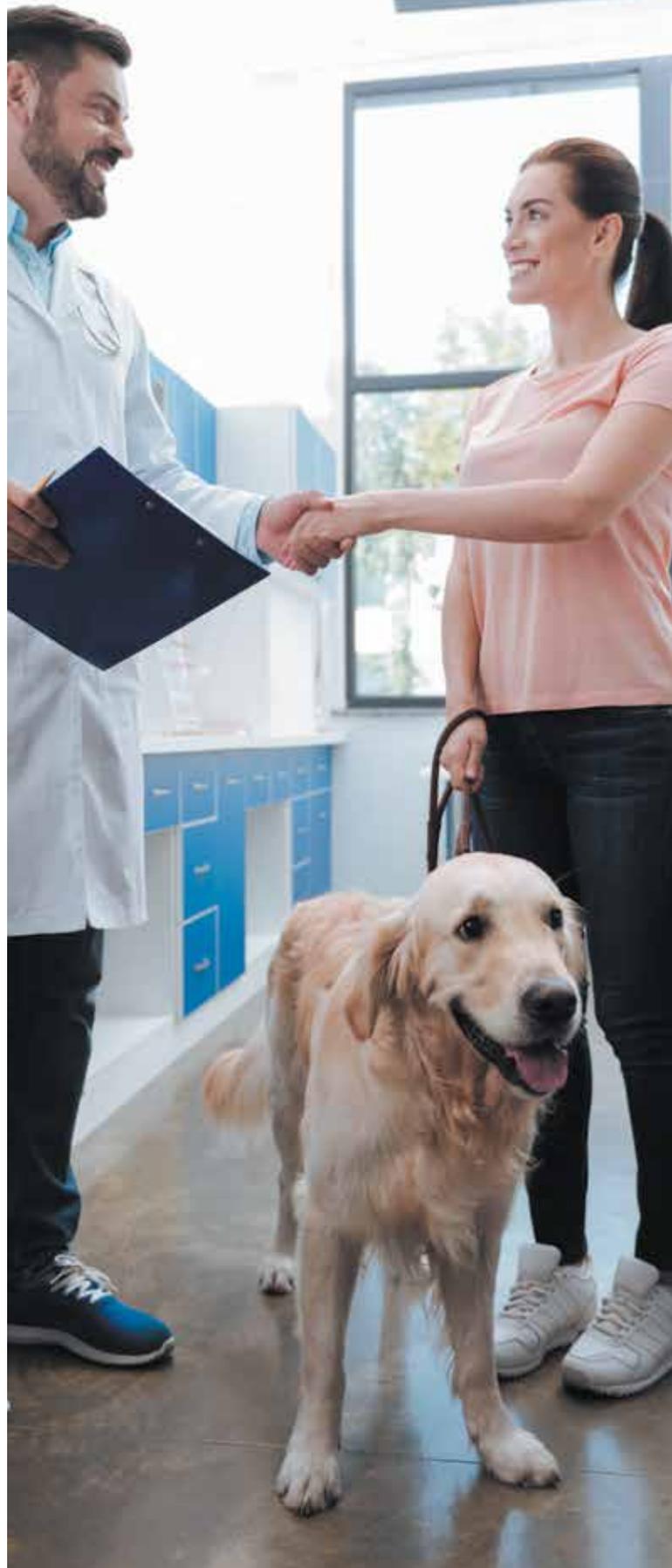
**By engaging with us in our OFFER, we can guarantee you will see the following positive outcomes:**

- ✓ Increased results in **4CYTE™** sales.
- ✓ Improved confidence and passion in clinic staff selling joint health products.
- ✓ Engaged front of house staff in the sales process.
- ✓ Satisfied and engaged clients.

## How the Money Back Client Guarantee works?

**If a client believes 4CYTE™ has not given the results expected under the guidance of the veterinarian the Interpath team will provide a money back guarantee. This will work by:**

- ✓ Client encouraged to come to the clinic and talk with a staff member about concern.
- ✓ Clinic staff will talk through with Client, ensuring correct dosing is being used.
- ✓ Once clinic staff are satisfied client has followed correct directions, they will request proof of purchase (must be from that clinic to be valid).
- ✓ Clinic staff will reimburse client for purchase value.
- ✓ Clinic staff will request a replacement from exclusive distributor Provet for reimbursed product.



# Home Grown and Family Owned

The Interpath brand has become synonymous with quality research programs supporting revolutionary product development. Having undergone in-vivo, in-vitro and clinical studies, our **4CYTE™** product gives you and your clients the confidence of a scientifically developed and proven joint health treatment.

Interpath Pty Ltd is an Australian family owned innovative company specialising in research, development and marketing of products for the treatment of cellular and tissue inflammation. Interpath applies an evidence based medicine approach to its research and development.

This involves the development of safe, clinically proven products which not only provide symptomatic relief but which also halt underlying disease processes. We have been listening to the ongoing comments and feedback provided by veterinarians, surgeons and end users and believe we have now developed a product range capable of meeting the needs of the Australian Veterinary industry.

**“Our mission is to develop safe efficacious products for the prevention and treatment of inflammatory disorders for the human and veterinary health markets that provide genuine relief!”**

Our team is highly respected in all clinics and hospitals we work with because our team listen, understand your business and look to give you a solution. In short - we deliver!

- We are passionate about what we do and we enjoy our work with you.
- We have extensive technical knowledge to support you and your team with further access to experts within the field.
- Over 20 years experience in the joint health research and development.
- We remain a proud family owned and operated business.



**Dan & Corina Bright**  
with family dog Jayda

**interpath**  
the joint health experts

**4CYTE™**

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