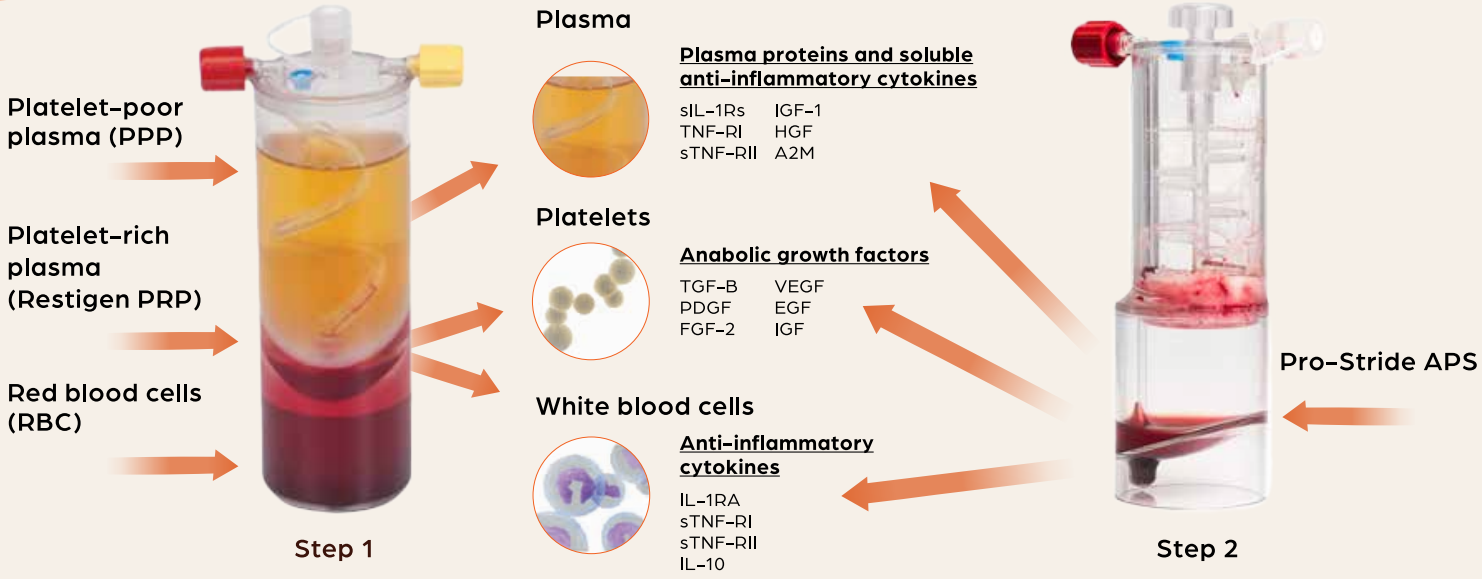
Pro-Stride® APS is a comprehensive orthobiologic device for managing equine osteoarthritis (OA).

What's in Pro-Stride® APS?



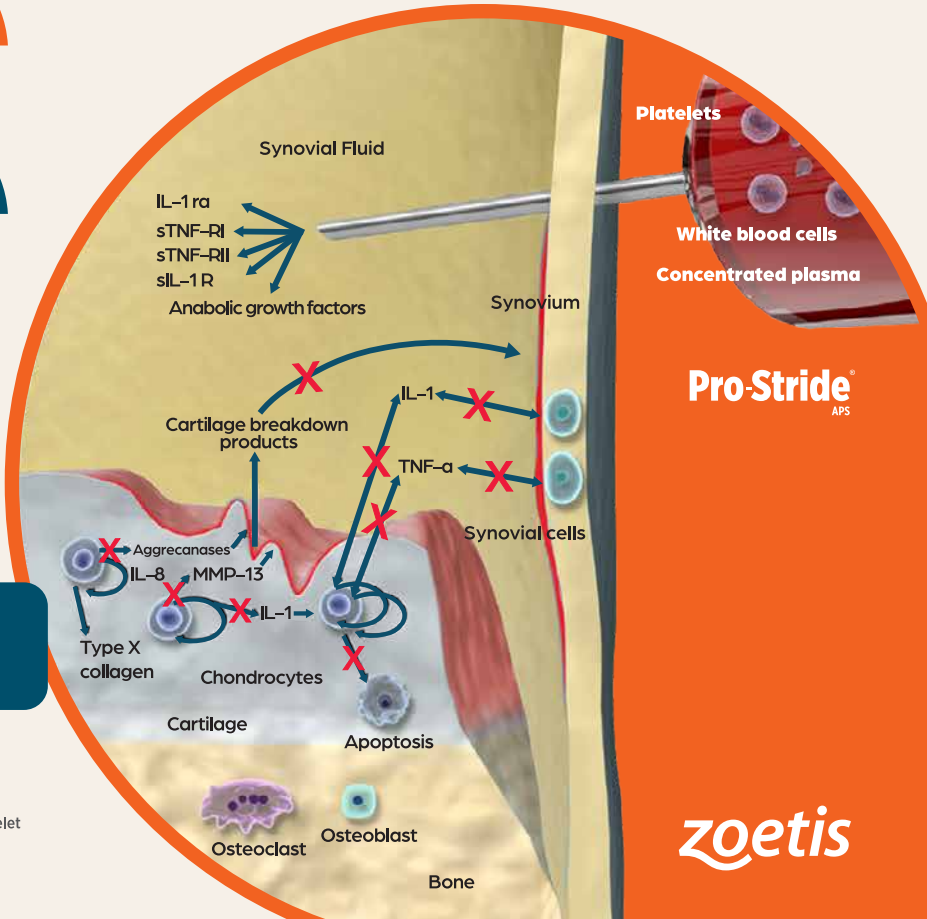
All three components (Plasma, Platelets and WBC) are optimal for comprehensive OA management.[1,2]

Comprehensive Orthobiologic Device for a Complex Process

OA is a complex process that ultimately breaks down cartilage. Inflammatory proteins like IL-1, TNF-α, MMP-13 and aggrecanase need to be neutralized to prevent joint deterioration.

The Pro-Stride APS device concentrates horses' naturally occurring anti-inflammatory proteins and growth factors to address this complex process.[1]

X Pro-Stride inhibits multiple inflammatory pathways and provides growth factors to support healing.



1. Muir et al. The concentration of plasma provides additional bioactive proteins in platelet and autologous protein solutions. *Am J Sports Med.* 2019 Jul;47(8):1955-1963.
2. nSTRIDE APS Scientific Narrative, Zimmer Biomet, Internal Document.

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STUDY 1: COMPARISON OF A2M IN THREE ORTHOBIOLOGIC DEVICES

Research study supported by zoetis

Evaluation of plasma protein composition in Restigen® PRP, Pro-Stride®APS and PPP compared to Alpha2EQ® devices[3]

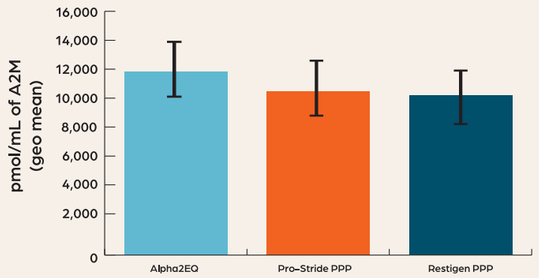
Study objective
To demonstrate concentrations of Alpha-2-macroglobulin (A2M) and other proteins found following processing with Restigen PRP, Pro-Stride APS and Alpha2EQ devices.

Study methods
Thirteen horses in three geographic locations were utilized (a private practice in Missouri, the University of Pennsylvania NBC and Colorado State University CVM). Blood samples were obtained and processed by independent veterinarians. Plasma protein analysis was performed by proteomics at Zoetis Veterinary Medical Research and Development in Kalamazoo, MI.

Results
- A2M concentration of plasma is equivalent between all three devices
- There are significantly higher concentrations of A2M in the final output of Pro-Stride APS and Restigen PRP versus Alpha 2EQ
- The PPP portion of Pro-Stride APS and Restigen PRP had identical protein profiles as compare to Alpha2EQ

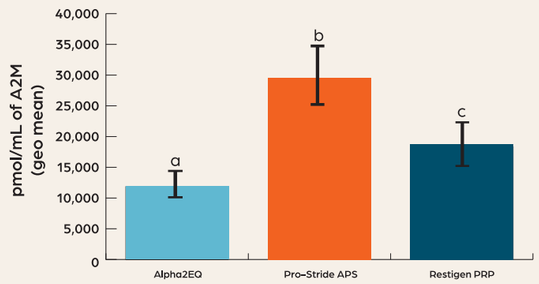
What does this mean?
In the study, the PPP portion of Restigen PRP and Pro-Stride APS is identical to the final output of Alpha2EQ.

A2M concentration of plasma compared by device



No statistical difference

A2M concentration in final outputs



a,b,c: Significant difference (p<0.05)

	A2M	Plasma proteins and soluable anti-inflammatory cytokines (TNF-R1, IGF-1)	Platelet-derived growth factors (PDGR, VEGF and others)	WBC-derived anti-inflammatory cytokines (Il1-ra, IL-10 and others)
Pro-Stride APS (3mL)	2.7X concentrated over plasma	✓	✓	✓
Restigen PRP (6mL)	1.8X concentrated over plasma	✓	✓	✓
Pro-Stride or Restigen PPP portion from device 1 (30 mL)	Plasma A2M and other protein composition equivalent between devices	✓		
Alpha2EQ (30 mL)	Plasma A2M and other protein composition equivalent between devices	No published data		

3. Ortved, KF, Alward, L, Cowles, B, et al. Use of quantitative mass spectrometry-based proteomics and ELISA to compare the alpha 2 macroglobulin concentration in equine blood-based products processed by three different orthobiologic devices. *Front. Vet. Sci.* 2024;11. doi: 10.3389/fvets.2024.1335972.

STUDY 2: SHORT-TERM NSAID ADMINISTRATION

Research study supported by zoetis

Effect of a Single Dose Administration of NSAIDs on Pro-Stride®APS and Restigen®PRP[4]

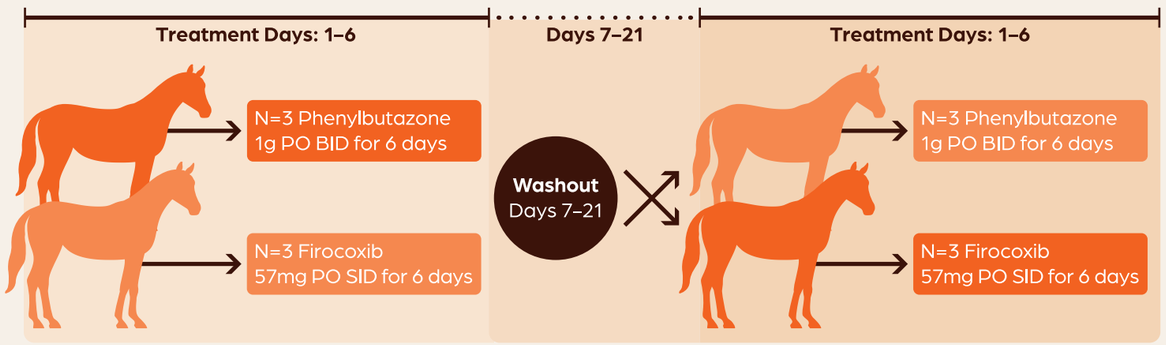
Results
A single dose of ketoprofen, flunixin meglumine, phenylbutazone or firocoxib did not significantly alter the cytokine or growth factor profile of APS or PRP when blood was obtained **6 hours** post administration.

STUDY 3: LONG-TERM NSAID ADMINISTRATION

The Effect of Prolonged Administration of NSAIDs on Concentrations of Cytokines and Growth Factors in Pro-Stride®APS and Restigen®PRP[5]

Study objective
To determine the effects of firocoxib and phenylbutazone on concentrations of growth factors and cytokines in Pro-Stride APS & Restigen PRP devices when given for six consecutive days.

Study methods
Prospective, cross-over study using six research horses at the University of Pennsylvania.



Blood collection and evaluation of end solution from Restigen PRP and Pro-Stride APS devices
Days 0 (pre-treatment), 7, 14 & 21 for each group

Looking at:
Platelet & leukocyte concentration
Cytokines: IL-1ß, IL-10, IL-6, IL-8, TNFα and
Growth factors: FGF, TGF-ß, PDGF-BB

Results
There were no statistically significant differences in concentrations of cytokines or growth factors in either Pro-Stride APS or Restigen PRP before or after **6 days** of administration of firocoxib or phenylbutazone.

What does this mean?
In the study, there was no impact to the final output of Restigen or Pro-Stride in horses receiving long term NSAID administration, so no need to stop administration prior to blood collection.

4. Brown KA, Gregoria E, Barot D, et al. Single-dose nonsteroidal anti-inflammatory drugs in horses have no impact on concentrations of cytokines or growth factors in autologous protein solution and platelet-rich plasma. AJVR, Feb 15, 2024.
5. Brown, KA, Gregorio, E., Barot, D, et al. The effect of prolonged administration of non-steroidal anti-inflammatories on concentrations of cytokines and growth factors in autologous protein solution and platelet rich plasma. Proceedings ACVS Surgical Summit. Presented abstracts Page 7, 2023.

Research study supported by zoetis

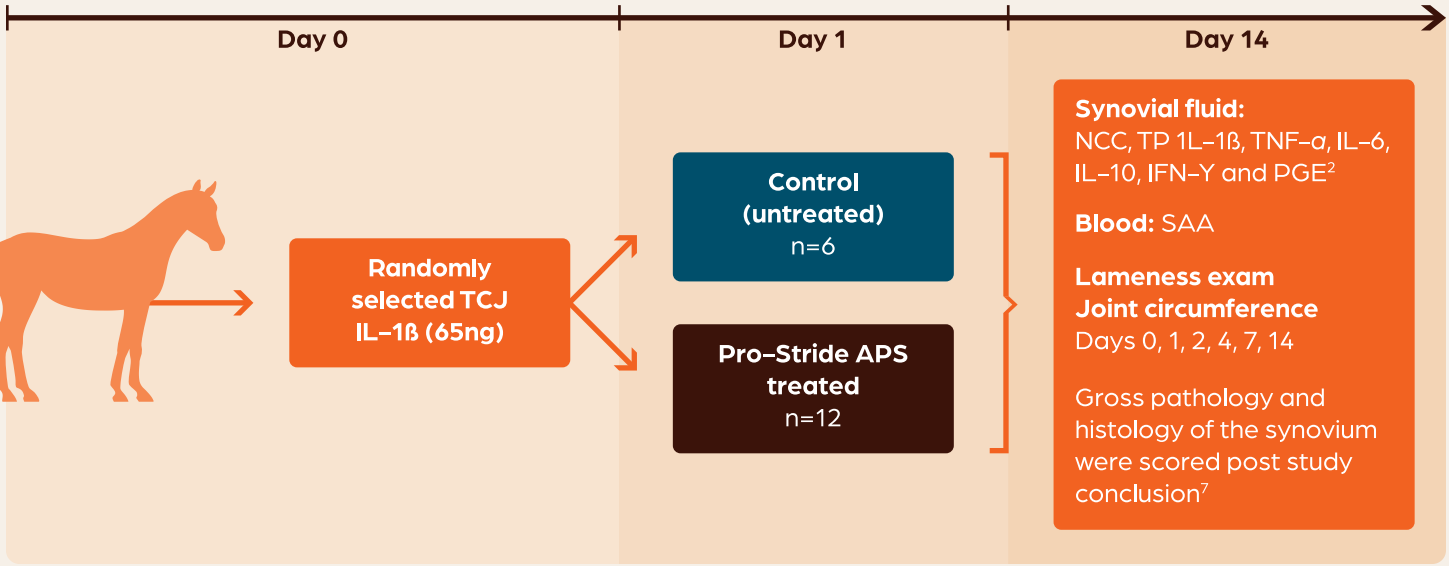
Effects of Pro–Stride® APS in horses with acute synovitis[6]

Study objective

To investigate the effects of a single intra–articular Pro–Stride injection on horses with acute, IL–1ß–induced synovitis in a tarsocrural joint.

Study methods

Randomized control study using 18 research horses at the University of Pennsylvania NBC.



Results

- IL–1ß effectively induced synovitis
- No significant differences in synovial fluid cytokine concentrations between groups
- No significant differences in lameness parameters between groups
- **Gross and histopathology scores of Pro–Stride APS–treated joints were similar to normal joints**
- **Untreated control joints showed more damage (synovial hypermia, edema, discoloration and hemisiderosis)**

What does this mean?

In the study, Pro–Stride APS appeared to have a disease modifying affect in this synovitis model, protecting the joint from acute inflammation.

6. Usimaki A, Ciamillo S, Linardi R, et al. Effects of autologous protein solution in horses with acute synovitis. Proceedings ACVS Surgical Summit, 2023.
7. McIlwraith C, Frisbie D, Kawcak C, et al. The OARSI histopathology initiative – recommendations for histological assessments of osteoarthritis in the horse. Osteoarthritis and Cartilage. Oct 2010 (18:3), pages S93-S105 2010.