What's New in Herd Health

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Beef Technical Service

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ZOETIS FOCUS: DELIVERING INNOVATIVE SOLUTIONS WHICH INTEGRATE ACROSS THE CONTINUUM OF CARE

SOLUTIONS SPANNING THE CONTINUUM OF CARE			
PREDICT	**PREVENT**	**DETECT**	**TREAT**
• Develop new markers for **genetics platforms** to enable prediction-based management • Investments in **data analytics** to provide user-friendly information regarding health and performance	• Invest in **novel vaccines** including Emerging Infectious Diseases • Continue to **update/improve existing vaccines** via lifecycle management	• Expansion of **diagnostic tools** to provide rapid on-farm results • Develop **sensors** to provide continuous, **automated monitoring** of animal welfare, health and production in real time	• Introduce new, **novel medicines and solutions** that address compliance and convenience

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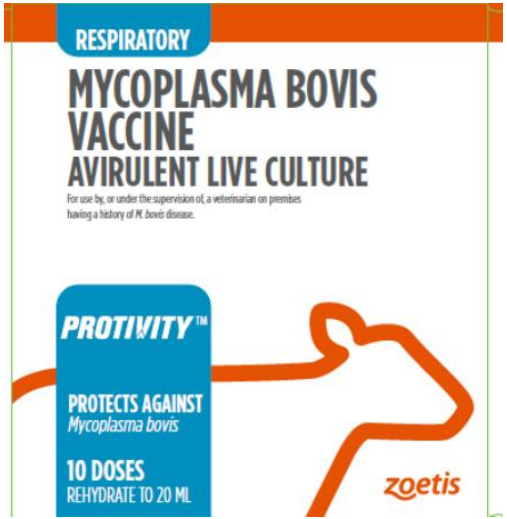
PROTIVITY™

Freeze dried avirulent modified live strain of *Mycoplasma bovis*

- Effective for vaccination of healthy calves 1 week of age or older against respiratory disease caused by *M. bovis*
- For use by or under the supervision of a veterinarian on premises with a history of *M. bovis* disease
- Two doses, 21 days apart administered SQ in neck
- First, and only, commercially available modified live avirulent *mycoplasma bovis* vaccine
- Proven efficacy in challenge studies



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Key Benefits of PROTIVITY™

First Modified Live Vaccine for *Mycoplasma bovis*

Early Administration

- PROTIVITY has the youngest administration age of any commercial *M. bovis* vaccine on the market with a label indication of one week of age.[1]
- The young administration age allows flexibility in the timing and convenience of vaccination while providing calves protection from *M. bovis* pneumonia at a younger age.

Two-Dose Regimen

- PROTIVITY requires two, 2-mL doses, with 21 days between doses
- There is flexibility in when PROTIVITY can be added to an on-arrival program or calf vaccination program.

Demonstrated Efficacy

- In a challenge study, two doses of PROTIVITY™ reduced overall lung lesion by 74%2

1. Based on approved labels of Protivity™, Mycoplaz®, Myco-B One Dose™, Myco-Bac® B and MpB Guard.
2. Data on file. Study Report No. B832R-US-17-665, Zoetis Inc.

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How PROTIVITY™ is different?

- Avirulent live *M. bovis* vaccines stimulate cell mediated immunity more effectively than bacterins.[1]
- Substantial reduction in lung lesions in challenge studies (74% reduction mean percentage of total lung with lesions).[2]
- Substantial reduction in duration of clinical signs in challenge studies (77% reduction in clinical signs, other than pyrexia).[2]
- Bacterins fail to adequately induce the cellular response which is related to protection
- Seroconversion is not predictive of protection.[3,4]

1. Chao J, Han X, Liu K. Calves Infected with Virulent and Attenuated Mycoplasma bovis Strains Have Upregulated Th17Inflammatory and Th1 Protective Responses. *Genes*. 2019;10:656.
2. Data on file. Study Report No. B832R-US-17-665, Zoetis Inc.
3. Mulongo M, Prysliak T, Perez-Casal J. Vaccination of feedlot cattle with extracts and membrane fractions from two Mycoplasma bovis isolates results in strong humoral immune responses but does not protect against an experimental challenge. *Vaccine*. 2013;31(10):1406-1412.
4. Soehnlen, Aydinb, Lengerichc et. al. Blinded, controlled field trial of two commercially available Mycoplasma bovis bacterin vaccines in veal calves . *Vaccine*. 2011;29: 5347– 5354.

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PROTIVITY™ use considerations

Live vaccine handling protocols and antibiotic considerations

- The vaccine must remain live to create the desired immune response.
  - Protect from disinfectants, antibiotics, and direct sunlight.
  - Two doses, 3 weeks apart are required for effective response.
- Beta Lactam antibiotics can be used concurrently because they have no activity against mycoplasma
- **Excede®** (*ceftiofur crystalline free acid*) Sterile Suspension, **Excenel® RTU EZ** (*ceftiofur hydrochloride*) Sterile Suspension or **Naxcel®** (*ceftiofur sodium*) Sterile Powder are suitable for use concurrent with PROTIVITY.
- Avoid use of antibiotics that can impact live *M. bovis* vaccine's ability to replicate.
  - The time frame for antibiotic moratorium will vary with class and duration of effect against *M. bovis*. This may vary from 7-21 days depending on pharmokinetics of product used.
  - If an animal must be treated with macrolides, fluroquinolones tetracyclines or fluorophenols revaccinate after antibiotics are no longer effective against *M. bovis*.

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Precautions

- The modified live strain of PROTIVITY™ may disseminate into joint fluid and cause arthritis.
- PROTIVITY may cause transient injection site swelling that usually resolves in 21 days.
- PROTIVITY has not been tested in pregnant or lactating cattle.
- Do not use chemically sterilized syringes to prevent inactivation of the live vaccine.
- Prolonged exposure to sunlight and high temperature may affect vaccine potency.
- Use entire contents when reconstituted.
- Do not slaughter within 21 days of administration
- As with any vaccine anaphylaxis may occur. Administer epinephrine and provide supportive therapy.

Treatment Innovation

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Draxxin® KP

Dr. Jeff Sarchet
Managing Veterinarian,
Beef Technical Services

DRAXXIN KP OVERVIEW

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CONCEPT: DRAXXIN + KETOPROFEN = DRAXXIN KP

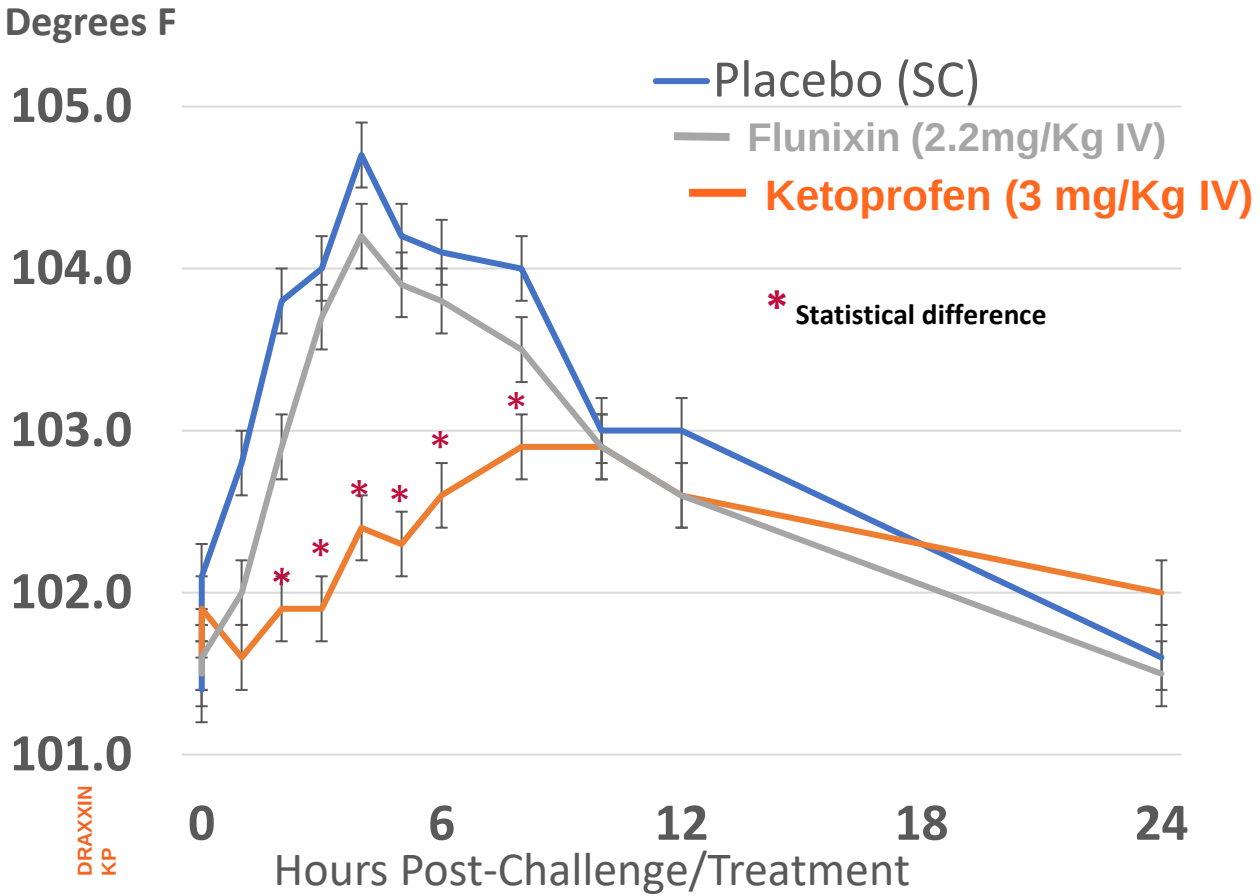
Treatment of BRD

- Macrolide: tulathromycin (**DRAXXIN**)
- Approved: 11/2003 (EU); 05/2005 (US)
- Dose: 2.5 mg/kg
- Clinical Claims: For the prevention and treatment of BRD associated with *Pasteurella multocida*, *Histopholus somni*, *Mannheimia haemolytica* and *Mycoplasma bovis*

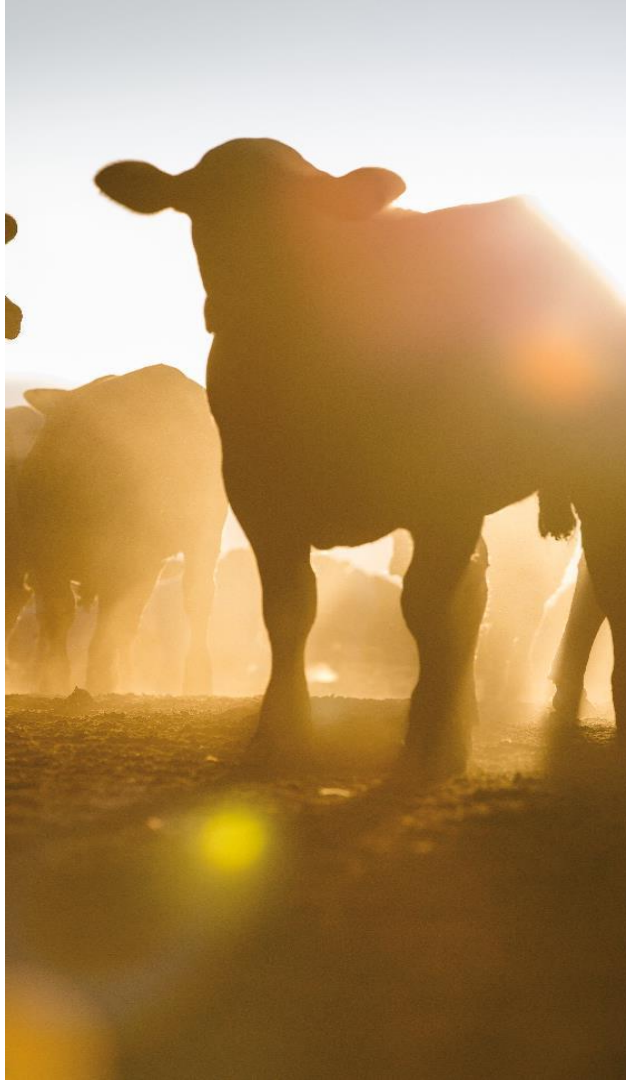
Alleviation of Inflammation and Pain

- NSAID: ketoprofen (**KETOFEN**)
- US: IV in horses only – NO cattle approval
- EU: several non-Zoetis approvals for cattle
- Dose: 3 mg/kg
- Clinical Claim (US): alleviation of inflammation and pain associated with musculoskeletal disorders in horses

Rectal Temperatures Following LPS Administration and Immediate Treatment

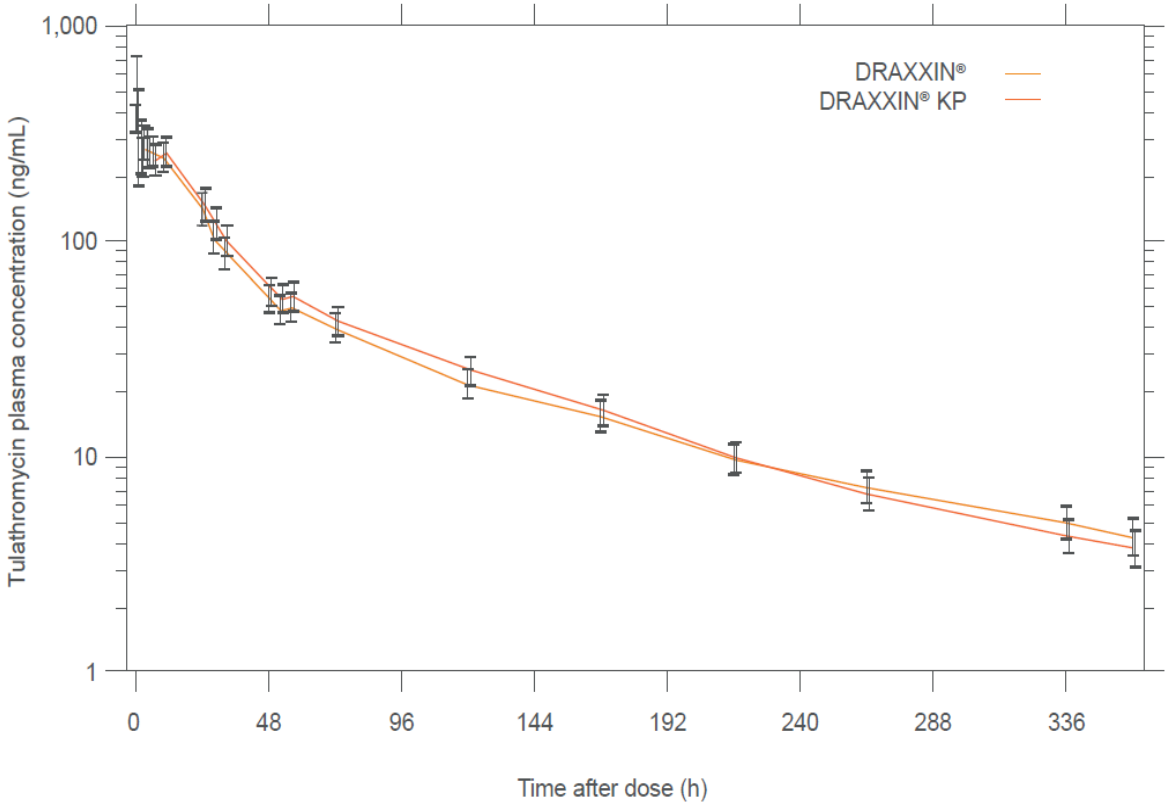


Study Report: AR32W-US-14-283



What Happens To Draxxin When We Combine Draxxin and Ketoprofen?

- **No Difference in Tulathromycin Concentrations**



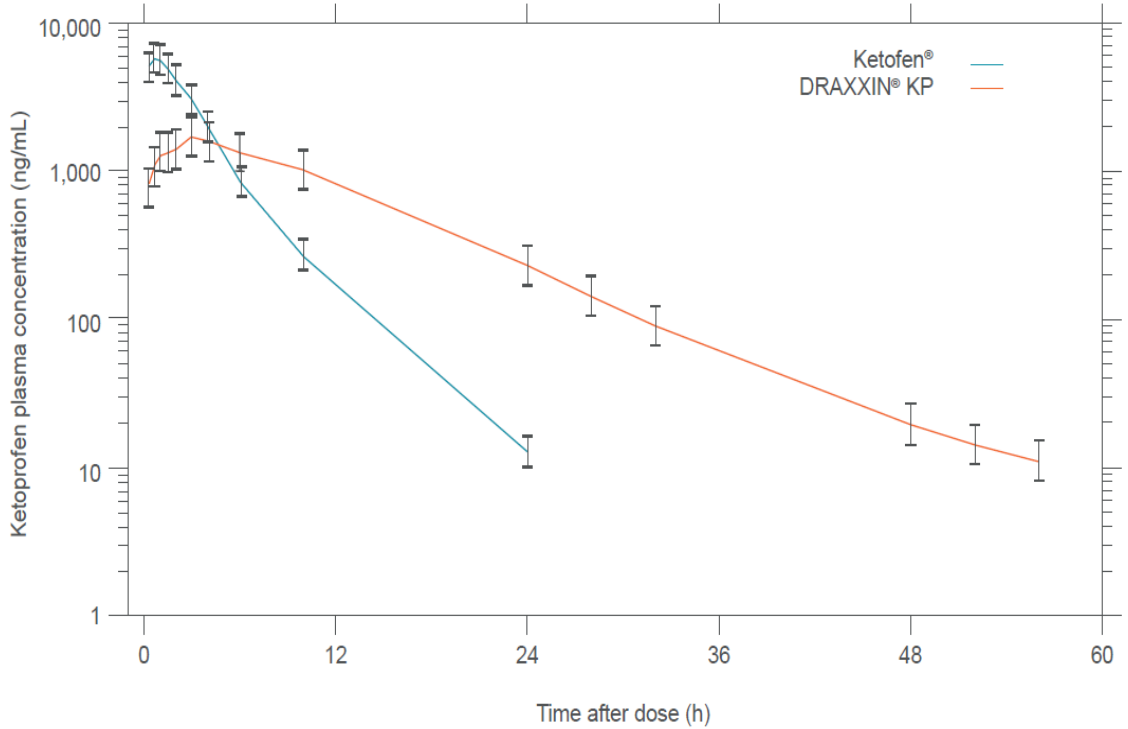
DRAXXIN KP

Study # A431N-US-16-418

What Happens to Ketoprofen When We Combine Draxxin and Ketoprofen?

- **2.5X Increased Half Life for Ketoprofen**

- **Half life increases 2.5X from 2.72 to 6.78 hours**
- **16% higher AUC**
- **Reduction in C_{max}**

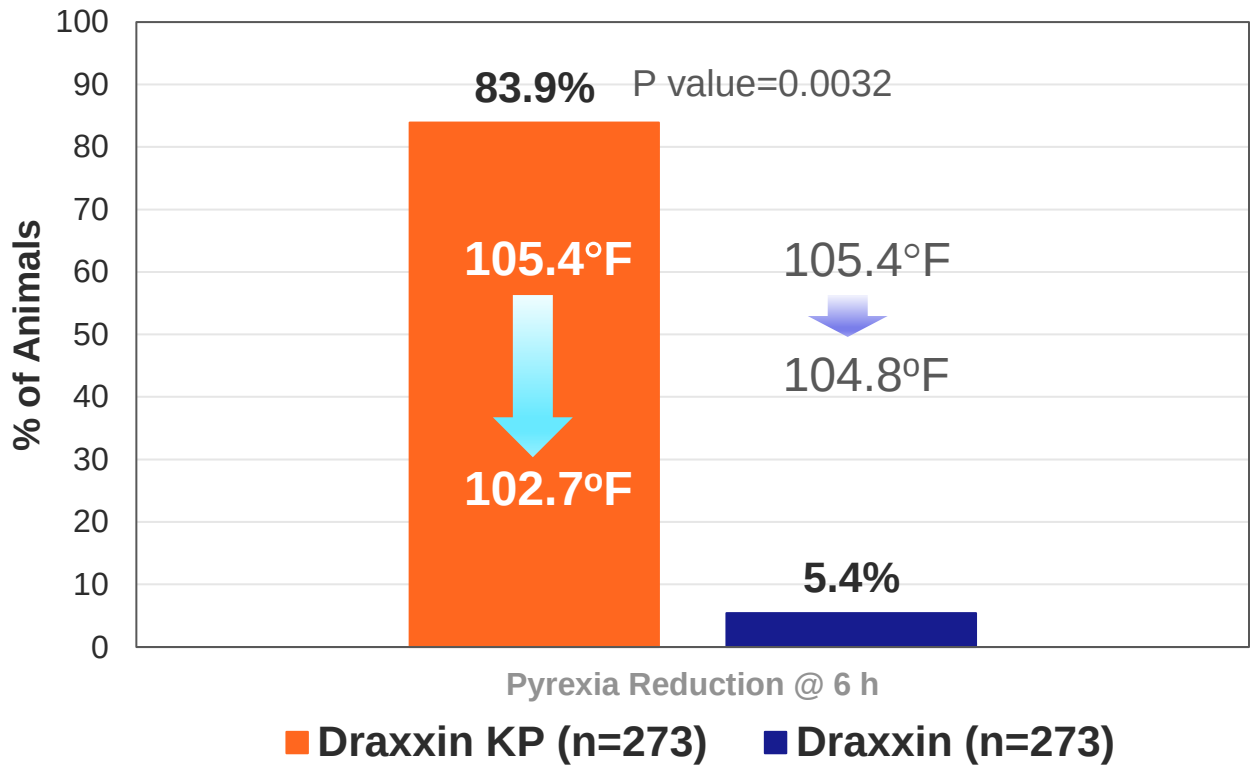


Study # A431N-US-16-418

DRAXXIN KP

UNITED STATES EFFICACY

6-HOUR FEVER REDUCTION



Label Indications

-Indicated for the ***treatment*** of bovine respiratory disease (BRD) associated with ***Mannheimia haemolytica, Pasteurella multocida, Histophilus somni,*** and ***Mycoplasma bovis***

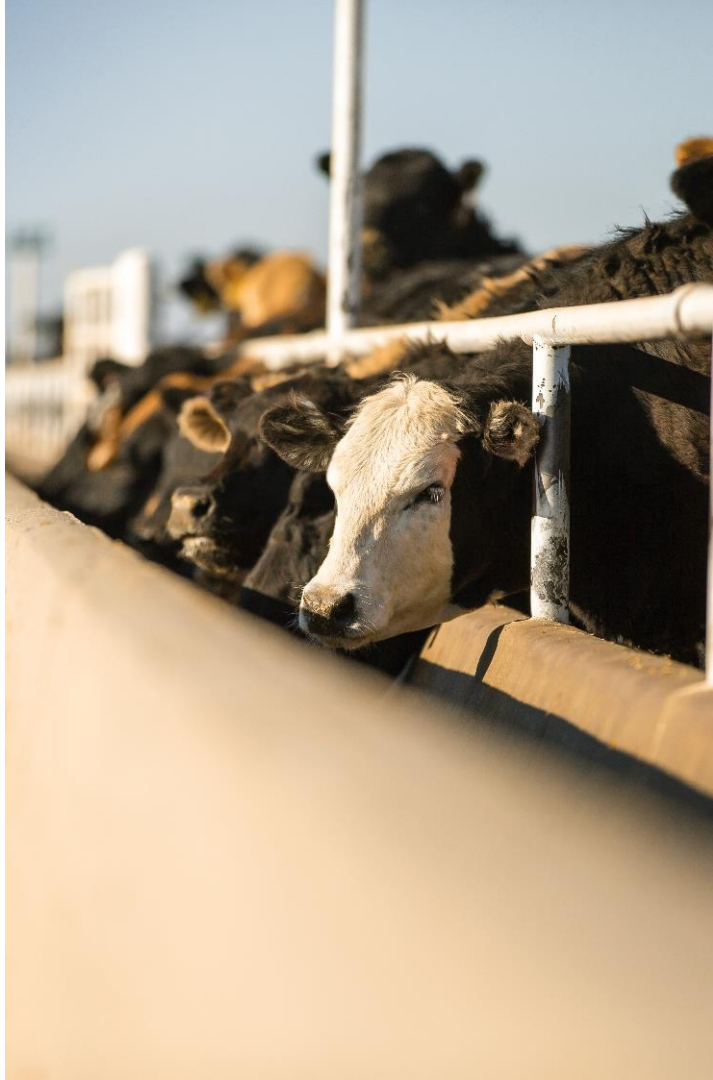
-Control of pyrexia associated with BRD in beef steers, beef heifers, beef calves 2 months of age and older, beef bulls, dairy bulls, and replacement dairy heifers

-Not for use in reproducing animals over one year of age, dairy calves, or veal calves

DRAXXIN KP

Dosage and Administration

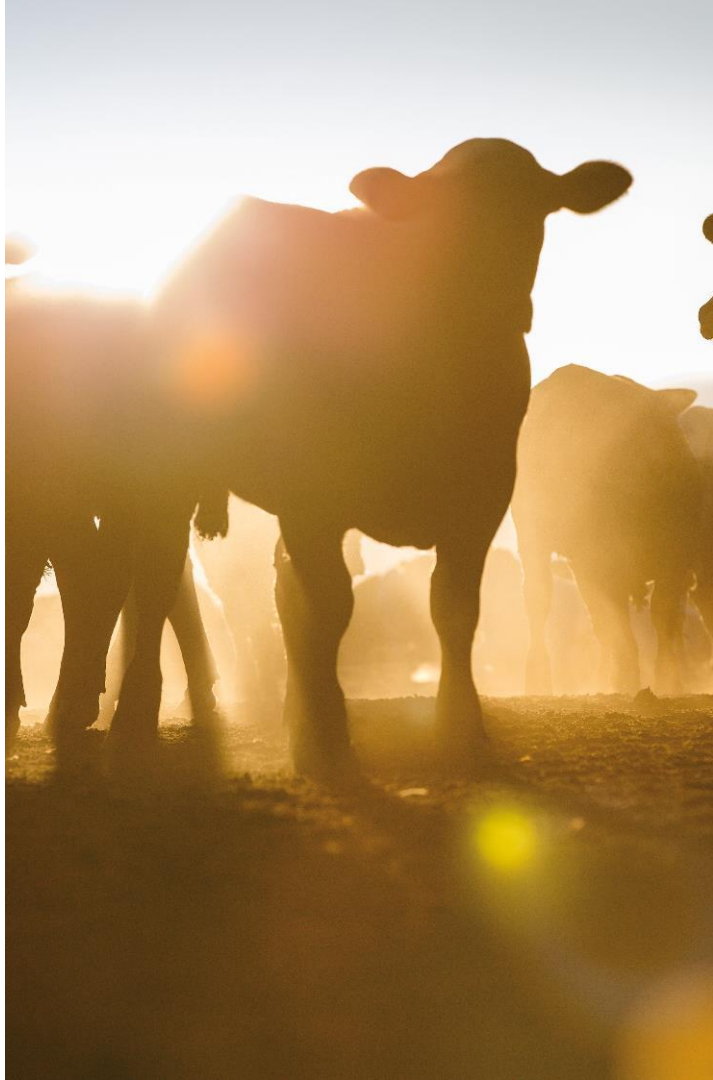
- 1.14 ml/100 lbs. bodyweight
- Subcutaneously
- No more than 10 ml per injection site
- Use within 56 days of first puncture
- Don’t puncture more than 20 times



DRAXXIN
KP

Withdrawal and Safety

- 18-day pre-slaughter withdrawal period
- No withdrawal time has been established for calves less than two months of age
- Do not use in calves to be processed for veal
- Mild injection site swelling



DRAXXIN KP

Label Summary

- Same low dose and short withdrawal times we have with Draxxin®
- Same treatment claims against main BRD bacterial pathogens
- Only labelled for BRD treatment and fever reduction
- Mild injection site swelling that are similar to Draxxin®

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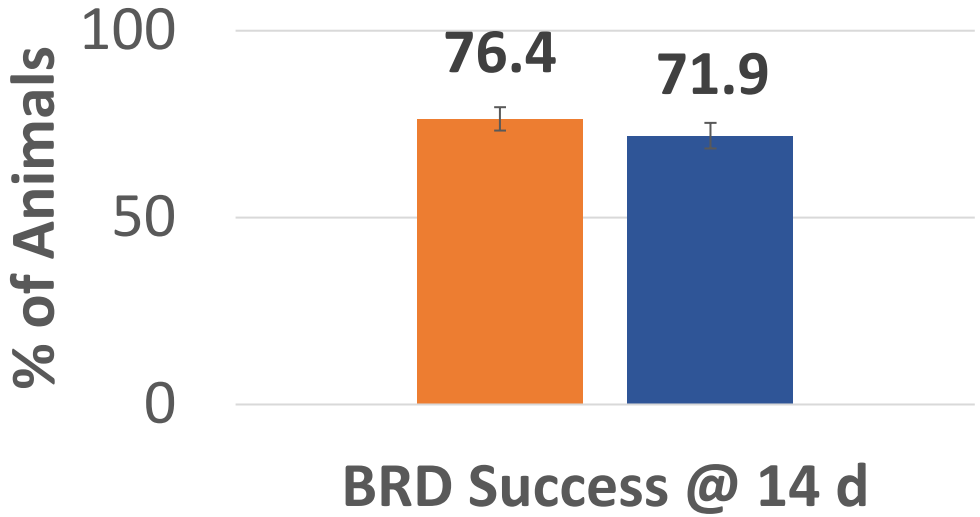
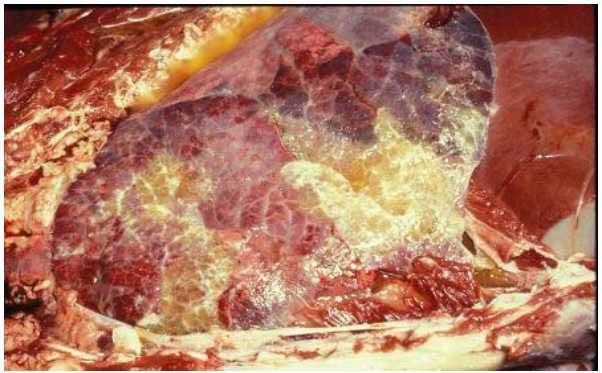
14 Day BRD Success



- Draxxin KP is not inferior to Draxxin (15% NI margin)
- Control was 31.6% at 14 days



DRAXXIN KP

Study Report: A131C-US-17-531

Treatment Innovation

VALCOR™

(doramectin and levamisole injection)

TOUGH ON TOUGH WORMS.
EASY ON YOU.

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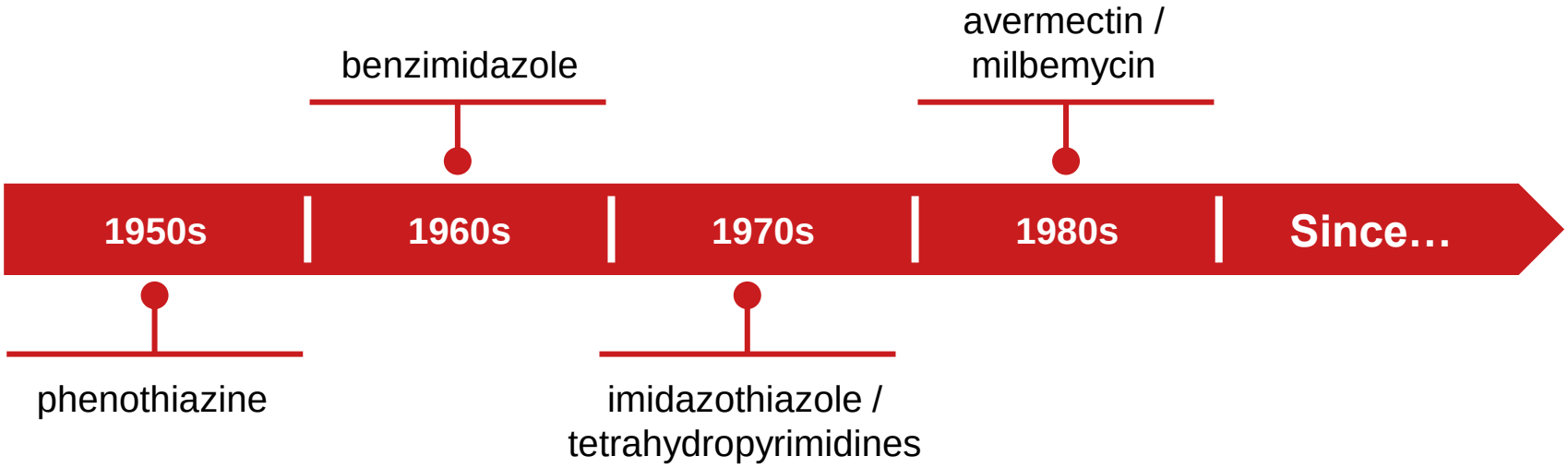
PARASITICIDE HISTORY

VALCOR™
(doramectin and levamisole injection)



FDA LABEL REQUIRED CHANGES – KEY POINTS

VALCOR™
(doramectin and levamisole injection)

- Parasite resistance may develop to any dewormer
- Do not underdose
- Effectiveness of treatment should be monitored

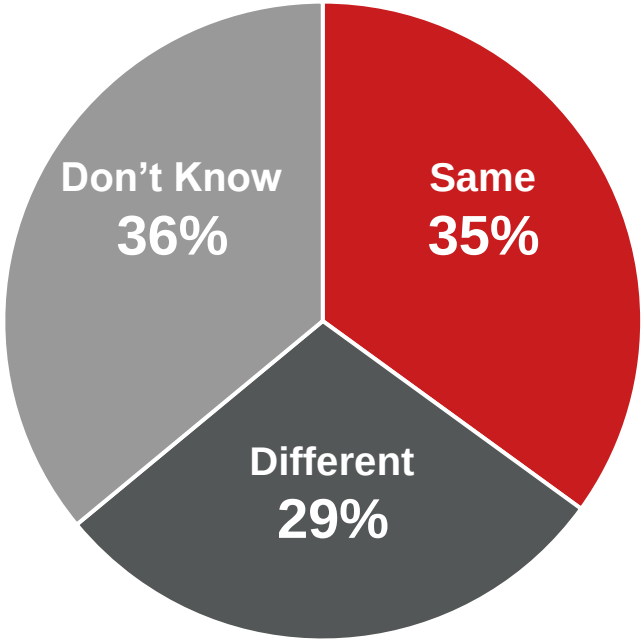
Other Warnings

Macrocyclic lactones provide prolonged drug exposure that may increase selection pressure for resistance. This effect may be more pronounced in extended-release formulations

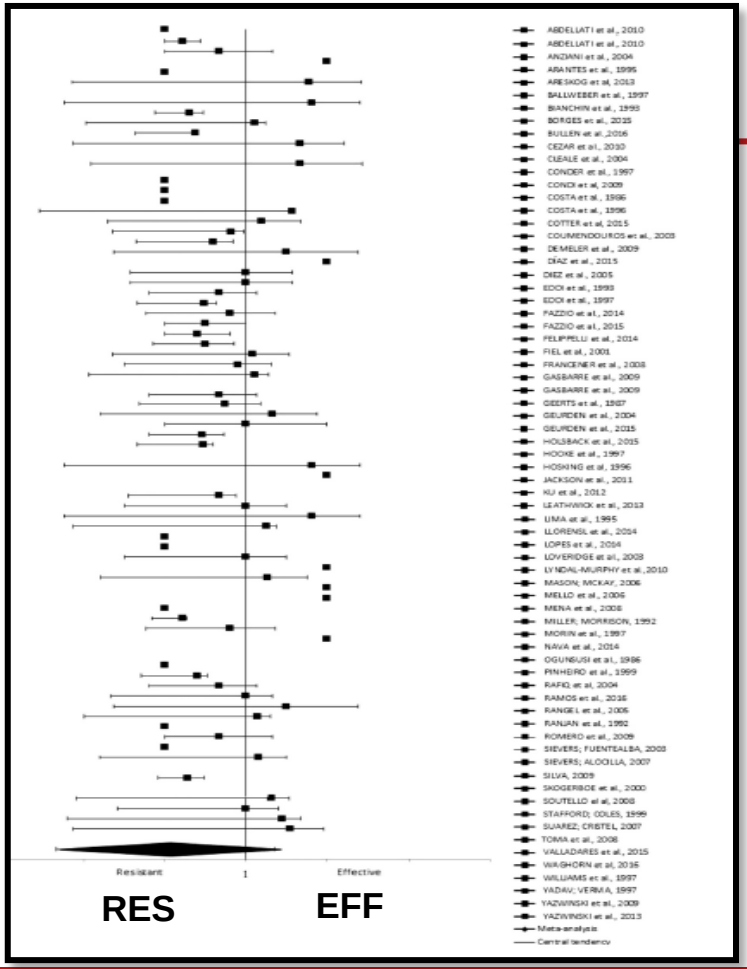
DOES A POUR-ON PRODUCT AND INJECTABLE PRODUCT WITH THE SAME NAME HAVE THE SAME OR DIFFERENT ACTIVE INGREDIENT? (N=194)

VALCOR™ (doramectin and levamisole injection)

There is confusion among producers regarding active ingredients in different products and forms



Beef Parasite Resistance Survey Results. January 2021. Bader Rutter, on behalf of Zoetis



VALCOR™
(doramectin and levamisole injection)

- Resistance present on several continents
- Likely present longer than we expected
  - *Cooperia* more so than *Ostertagia*

Baiak, et al. *Livestock Science*, 217, 127-245, 2018

THEORETICAL ADDITIVE MODEL IN A POPULATION OF SUSCEPTIBLE PARASITES

VALCOR™ (doramectin and levamisole injection)

Goal is 99-100% Efficacy to Mitigate Resistance Development

Drug 1 (% Efficacy)	Drug 2 (% Efficacy)	Drug 3 (% Efficacy)	Combination (% Efficacy)
80	80		96
80	80	80	99.2
90	90		99
90	90	90	99.9
60	95		98
60	60	95	99.2
99	99		99.99

Kaplan, *Vet Clinics NA FA*, 36, 17-30, 2020

PRODUCT PROFILE

VALCOR™
(doramectin and levamisole injection)

DESCRIPTION

- VALCOR injection is a **ready-to-use**, sterile injectable solution containing:
  - 0.5% w/v (5 mg/mL) of **doramectin** (a macrocyclic lactone) and
  - 15% w/v (150 mg/mL) of **levamisole hydrochloride** (an imidazothiazole)
- Labeled for **subcutaneous administration at a dose rate of 1 mL/55 lbs. of body weight**.
- *Federal law restricts this drug to use by or on the order of a licensed veterinarian*

Amber-colored, ultraviolet light resistant vial

Branded Injector

Card box packaging

MODE OF ACTION

VALCOR™
(doramectin and levamisole injection)

VALCOR IS THE FIRST APPROVED DUAL ACTIVE ENDECTOCIDE FOR CATTLE WHERE BOTH ACTIVE INGREDIENTS ARE EFFECTIVE AGAINST GASTROINTESTINAL NEMATODES.

- With different mechanism of actions, both active ingredients ultimately lead to paralysis and death of the parasites.
  - The active ingredient, **doramectin**, modulates the activity of chloride ion channels in the nervous system of nematodes and arthropods to inhibit the electrical activity of nerve cells.
  - The active ingredient, **levamisole**, is a nicotinic acetylcholine receptor agonist that continuously stimulates worm muscles.

INDICATIONS

VALCOR™
(doramectin and levamisole injection)

VALCOR IS INDICATED FOR THE TREATMENT AND CONTROL OF GASTROINTESTINAL ROUNDWORMS, LUNGWORMS, EYEWORMS, GRUBS, SUCKING LICE, AND MANGE MITES IN BEEF CATTLE 2 MONTHS OF AGE AND OLDER AND IN REPLACEMENT DAIRY HEIFERS LESS THAN 20 MONTHS OF AGE.

GI Roundworms (adults and fourth stage larvae)

- *Ostertagia ostertagi* (including inhibited larvae)
- *O. lyrate*
- *Haemonchus placei*
- *Trichostrongylus axei*
- *T. colubriformis*
- *T. longispicularis**
- *Cooperia oncophora*
- *C. pectinata**
- *C. punctata*
- *C. surnabada*
- Bunostomum phlebotomum*
- Strongyloides papillosus*
- *Oesophagostomum radiatum*
- Trichuris spp.*
- *Nematodirus helvetianus**

* Adults only

INDICATIONS

VALCOR™
(doramectin and levamisole injection)

NOT FOR USE IN BEEF BULLS INTENDED FOR BREEDING OVER 1 YEAR OF AGE, DAIRY CALVES, AND VEAL CALVES

Lungworms (adults & fourth stage larvae)	**Eyeworms** (adults)	**Grubs** (parasitic stages)	**Sucking Lice**	**Mange Mites**
> *Dictyocaulus viviparus*	> *Thelazia spp.*	> *Hypoderma bovis* > *H. lineatum*	> *Haematopinus eurysternus* > *Linognathus vituli* > *Solenopotes capillatus*	> *Psoroptes bovis* > *Sarcoptes scabiei*

PRODUCT PROFILE

VALCOR™
(doramectin and levamisole injection)

DOSING AND ADMINISTRATION

- Inject subcutaneously in the neck as a single dose at a dosage of 2 mL/100 lbs.
- Do not inject more than 10 mL per injection site.
- Do not underdose. Underdosing may result in ineffective treatment and encourage the development of parasite resistance.
- Use this product within 45 days of the first puncture.
- Puncture 100 mL vial a maximum of 6 times and the 250 mL and 500 mL vials a maximum of 28 times, using a luer-lock syringe and needle no larger than 18 gauge.

Body Weight, lb	Dose Volume, mL
110	2
220	4
330	6
440	8
550	10
660	12
770	14
880	16
990	18
1100	20
1210	22

ENHANCED PERFORMANCE LED TO SIGNIFICANT RETURN ON INVESTMENT IN VALCOR

VALCOR™
(doramectin and levamisole injection)

GREATER WEIGHT GAIN SUPPORTED BY VALCOR'S EFFICACY PAID OFF

- Improved herd productivity can have a tremendous impact on customers' bottom line
- Even when priced at almost 5 times more than the competitor product, VALCOR delivered greater return on investment
- Pricing concerns may be successfully overcome by focusing on the value of consistent efficacy and its impact on performance

$183.50/cwt = $14.03

$240.00/cwt = $22.37

	VALCOR	NOROMECTIN
Average weight at Day 0	521.59 lbs	522.75 lbs
Average weight at Day 56	689.35 lbs	681.19 lbs
Total weight gain per head	**167.76 lbs**	**158.44 lbs**
Value of weight gain per head[1]	$308.68	$291.53
Treatment cost per head[2]	**$3.97**	**$0.85**
Net value gain per head	$304.70	$290.68
Additional return per head for VALCOR	**$14.03**	---

1. Based on $183.50/cwt (mean price per USDA National Daily Feeder and Stocker Cattle Report, St. Joseph, MO, February 10, 2023)
2. Based on NOROMECTIN retail price ($89.95/500 mL per Valley Vet Supply) and on predicted producer cost for VALCOR in the US ($210.00/500 mL). Access February 10, 2023

QUESTIONS?

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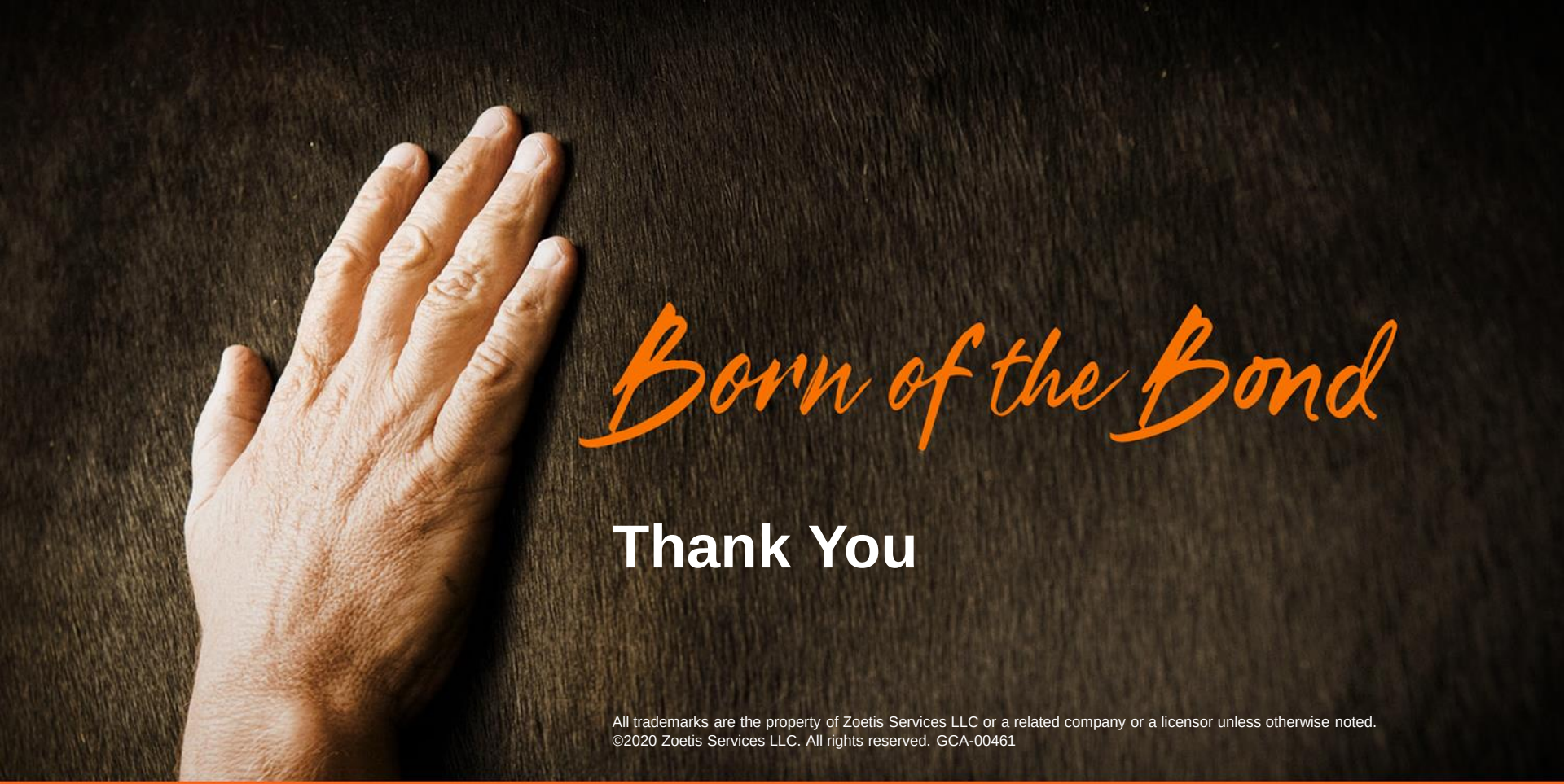

Thank You

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