

# Advancing Farm Animal Management with Improved Methods to Recognize and Manage Pain



Credit: Yann Arthus-bertrand



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# Current Disclosures (last 3 years)

- **Funded Research**

- USDA NIFA (#2008-35204-19238; #2009-65120-05729; #2013-67015-21332 and #2017-67015-27124). National Pork Board, AASV, AABP

- **Consulting**

- Boehringer Ingelheim; Bayer Animal Health; Merck Inc.; Midwest Veterinary Services Inc., and Zoetis

- **Sponsored CE**

- Local and State Veterinary Medical Associations

- **Patents**

- U.S 10,434,083B2, TRANSMAMMARY DELIVERY OF CYCLOOXYGENASE-2 INHIBITORS FOR ANALGESIA IN NEONATES. Coetzee JF. Issued October 8, 2019.
- U.S 8,791,105 B2, METHODS FOR ALLEVIATING CHRONIC PAIN AND IMPROVING PERFORMANCE OF CATTLE UNDERGOING DEHORNING OR CASTRATION. Coetzee JF and KuKanich SP. Issued 29 July, 2014.

- **Ethical Oversight: all studies cited had local IACUC approval**

# What are we going to discuss today?

1. Why is pain management in farm animals important?
2. What are the barriers to implementation of pain management strategies in livestock?
3. What are the new advances in pain assessment and pain management in livestock?
4. What are the unmet pain management needs?

# 1. What are the pain challenges in livestock production systems?

## **Elective Procedures**

→ Castration, tail docking (pigs/ sheep), dehorning (calves/ goats), branding, abdominal surgery, beak trimming (Poultry)

## **Pain associated with livestock management**

→ Lameness, calving, lambing, farrowing, infectious diseases



<https://www.theguardian.com/environment/2019/jan/19/curse-tail-docking-painful-truth-italy-pigs>



# Why are these procedures necessary?



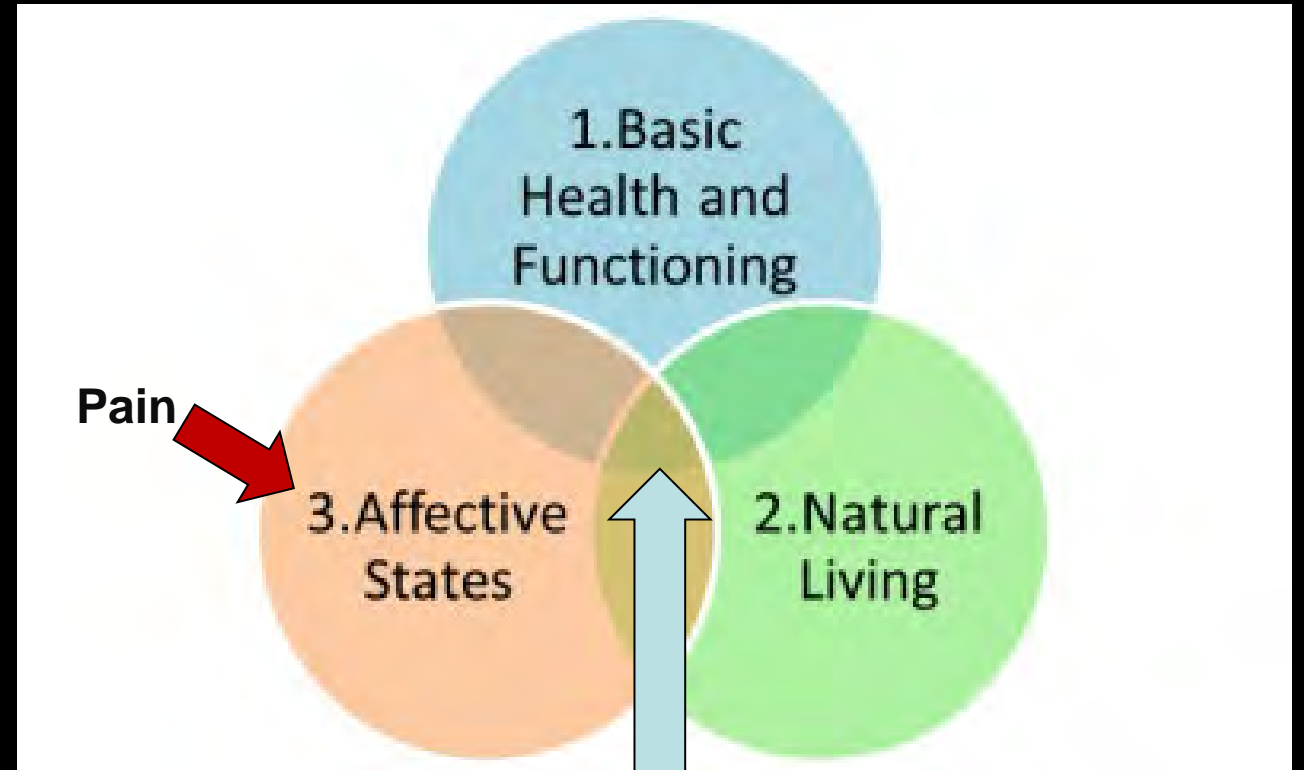
<https://timesoftexas.wordpress.com/tag/austin/>

- Castration reduces aggression and unplanned breeding events, and improves meat quality
- In pigs, castration reduces “boar taint”, an unpleasant taste that occurs during cooking pork from non-castrated male pigs after they reach puberty
- Dehorning reduces injury to other animals and caregivers
- Branding is used for animal identification especially in Western states.

# Why is pain management critical for farm animal welfare?



Brambell Report, 1965



David Fraser, UBC

**Good welfare**

**Pain management is a key part of assuring animal well-being**

# Pain mitigation is becoming a consumer expectation

FOX  
BUSINESS



MARKETS

POLITICS

FEATURES

FBN TV



## Food makers encourage dairy farms to end painful dehorning practice, breed hornless cattle

Published March 28, 2015 | Industries | Associated Press

- Addressing concerns related to dehorning, tail docking, and castration both with and without anesthesia



Starbucks Newsroom

## Views Animal Welfare-Friendly Practices

The animal welfare policy of Dunkin' Brands, which owns Baskin-Robbins ice cream, asks its suppliers to "support industry-wide efforts to promote the humane treatment of cattle, including the responsible use of polled breeding." And dining chain Denny's released a policy in February indicating a "purchase preference" for milk from polled dairy cattle.

## Progress! Dannon Works to End Dehorning of Calves

Fair Oaks Farms in Indiana, a Kroger supplier and one of the nation's largest dairy farms with 36,000 cows, is phasing out horned milk cows. About a quarter of its newborn calves are hornless due to selective use of bulls with the polled gene, CEO Gary Corbett said. It began to do so after genetics in polled bulls improved and there was proof that good traits like milk production weren't being lost.

PRODUCERS

## Wanted: More Bulls With No Horns

August 3, 2015 · 4:53 PM ET

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# How have food processors and retailers responded to consumer concerns about pain in livestock?



Tyson Fresh Meats, Inc.

January 8, 2014

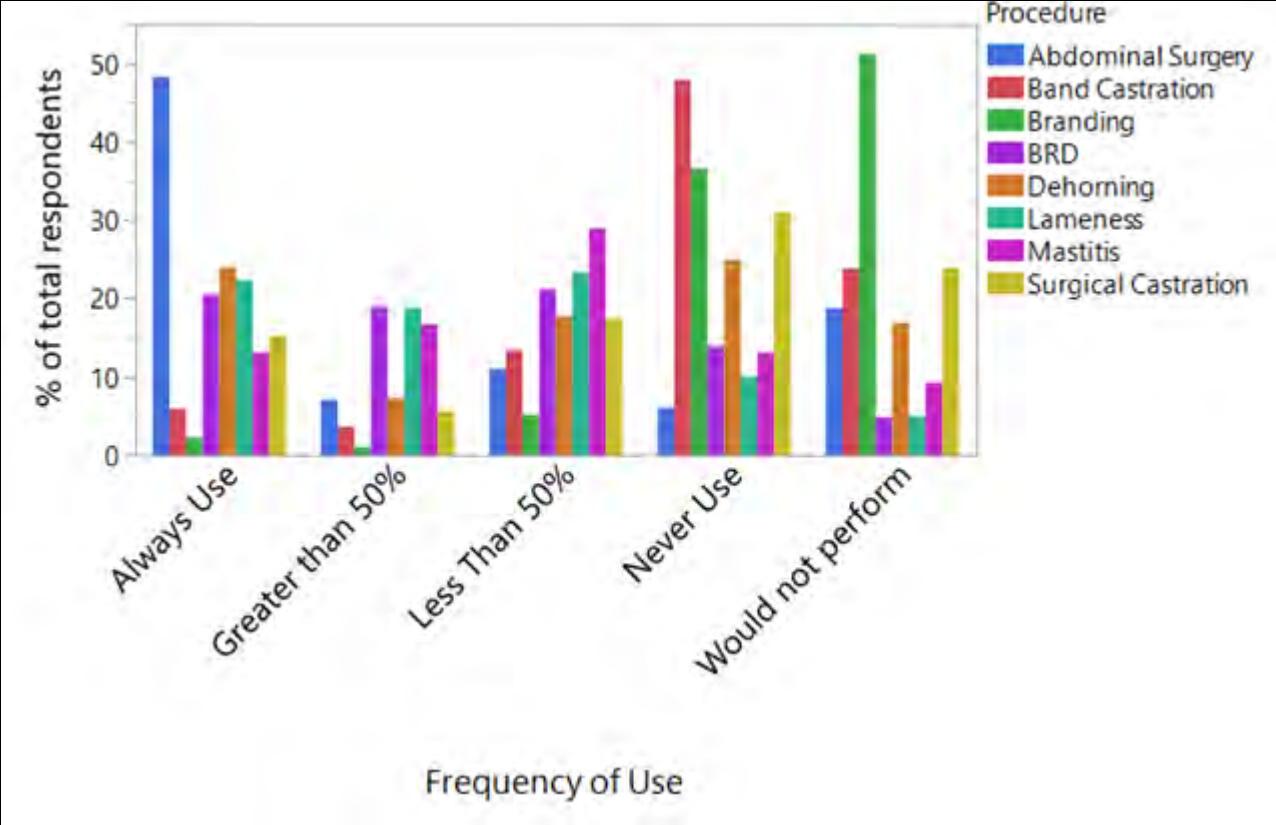


**We support the development and use of pain mitigation for tail docking and castration for piglets.** Although this is a topic of debate within our industry, we believe current practices need to improve. Tyson will fund research to further improve practical pain mitigation methods. In the meantime, we encourage producers to adopt practices that reduce or eliminate the pain associated with these procedures, including the use of anesthetics and analgesics that are approved for use in pigs and/or are permissible under the Animal Medicinal Drug Use Clarification Act (AMDUCA).

**It is noteworthy that there are currently no FDA-approved drugs labeled for pain relief in pigs**



# Current trends and attitudes towards pain management in cattle



## Change in All Respondents' (n=1,187) use of Pain Management in Their Operations or Practices in Last 10 Years

		% total (n)
Use of Pain Management	No Response	1.10% (n=13)
	Increased Use	57.49% (n=679)
	Stayed the Same	36.75% (n=434)
	Decreased Use	4.66% (n=55)

- **75%** of respondents agree that cattle benefit from receiving analgesic drugs as part of their treatment
- **33%** of respondents agree that analgesics may mask deterioration in the animal's condition
- **48%** of respondents agree that the benefits of analgesia outweigh the costs
- **64%** of respondents agree that FDA regulations limit their ability to use analgesic drugs in cattle

## 2. What are the barriers to the widespread adoption of pain management in livestock?

1. Pain assessment is difficult in livestock
2. Currently there is only one drug approved for pain management in cattle
  - Label does not include castration, dehorning and tail-docking pain
  - There are no drugs labeled for pain management in pigs
3. Time delay between drug administration and onset of activity (e.g. local anesthesia) → requires repeated handling that increases labor costs
4. Inconvenient routes of drug administration (IV, IM with large injection volumes)
5. Short duration of drug activity requires repeated injections
6. Cost of drugs and meat withhold periods
7. Nothing works well for treating chronic pain (Lameness/ tail docking)

# Why has the approval of pain management drugs for livestock in the USA been challenging?

## VI. LABELING

### 2. Pain

“We (FDA) recommend that this indication be based on the control of clinical signs of pain associated with a disease. We encourage the use of validated methods of pain assessment in the target species”.

FDA Guideline No. 123

DEVELOPMENT OF TARGET ANIMAL SAFETY AND EFFECTIVENESS DATA  
TO SUPPORT APPROVAL OF NSAIDS FOR USE IN ANIMALS

**Banamine transdermal® is the only approved drug for relief of pain specifically associated with infectious lameness in cattle**

# Currently pain management in livestock in the United States requires Extralabel Drug Use (ELDU)?

- The analgesics must be prescribed by a veterinarian
- The analgesic must be manufactured in an FDA-inspected facility
- The producer must keep a record of ELDU administration
- Drug administration in feed is prohibited
- A veterinarian must provide withdrawal period recommendations

**Under AMDUCA, veterinarians are responsible for ensuring that drug residues arising from ELDU, do not pose a risk to consumers**



# How do we know if it hurts?



Credit: Yann Arthus-bertrand

This research was supported by the Agriculture and Food Research Initiative Competitive Grant no. 2008-35204-19238 from the USDA National Institute of Food and Agriculture

## MODERATE

# UNIVERSAL PAIN ASSESSMENT TOOL

This pain assessment tool is intended to help patient care providers assess pain according to individual patient needs. Explain and use 0-10 Scale for patient self-assessment. Use the faces or behavioral observations to interpret expressed pain when patient cannot communicate his/her pain intensity.

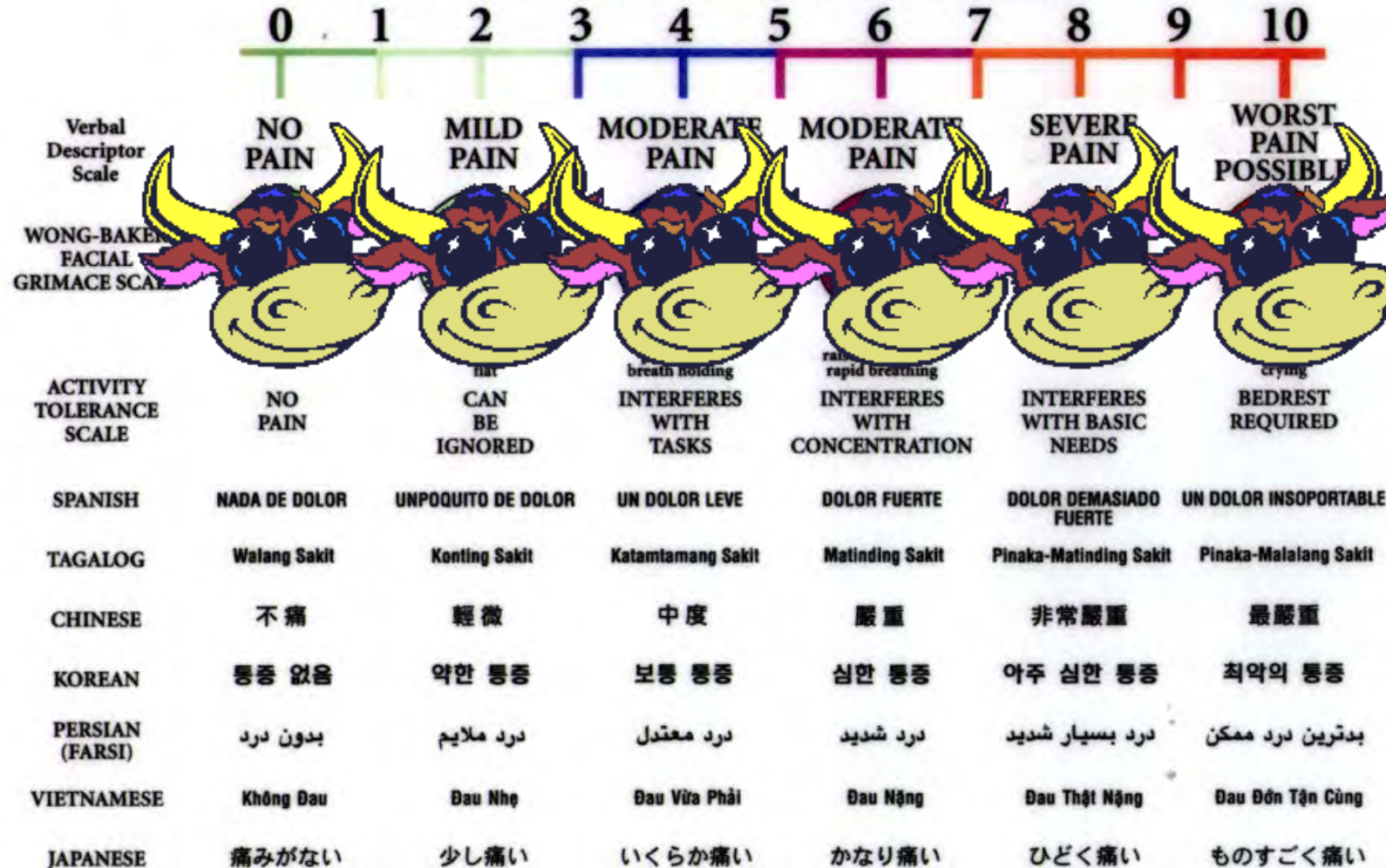
	0	1	2	3	4	5	6	7	8	9	10
Verbal Descriptor Scale	NO PAIN	MILD PAIN	MILD PAIN	MODERATE PAIN	MODERATE PAIN	MODERATE PAIN	MODERATE PAIN	SEVERE PAIN	SEVERE PAIN	SEVERE PAIN	WORST PAIN POSSIBLE
WONG-BAKER FACIAL GRIMACE SCALE											
	Alert Smiling	No humor serious flat	No humor serious flat	Furrowed brow pursed lips breath holding	Furrowed brow pursed lips breath holding	Wrinkled nose raised upper lips rapid breathing	Wrinkled nose raised upper lips rapid breathing	Slow blink open mouth	Slow blink open mouth	Slow blink open mouth	Eyes closed moaning crying
ACTIVITY TOLERANCE SCALE	NO PAIN	CAN BE IGNORED	CAN BE IGNORED	INTERFERES WITH TASKS	INTERFERES WITH TASKS	INTERFERES WITH CONCENTRATION	INTERFERES WITH CONCENTRATION	INTERFERES WITH BASIC NEEDS	INTERFERES WITH BASIC NEEDS	INTERFERES WITH BASIC NEEDS	BEDREST REQUIRED
SPANISH	NADA DE DOLOR	UNPOQUITO DE DOLOR	UNPOQUITO DE DOLOR	UN DOLOR LEVE	UN DOLOR LEVE	DOLOR FUERTE	DOLOR FUERTE	DOLOR DEMASIADO FUERTE	DOLOR DEMASIADO FUERTE	DOLOR DEMASIADO FUERTE	UN DOLOR INSOPORTABLE
TAGALOG	Walang Sakit	Konting Sakit	Konting Sakit	Katamtamang Sakit	Katamtamang Sakit	Matinding Sakit	Matinding Sakit	Pinaka-Matinding Sakit	Pinaka-Matinding Sakit	Pinaka-Matinding Sakit	Pinaka-Malalang Sakit
CHINESE	不痛	輕微	輕微	中度	中度	嚴重	嚴重	非常嚴重	非常嚴重	非常嚴重	最嚴重
KOREAN	통증 없음	약한 통증	약한 통증	보통 통증	보통 통증	심한 통증	심한 통증	아주 심한 통증	아주 심한 통증	아주 심한 통증	최악의 통증
PERSIAN (FARSI)	بدون درد	درد ملایم	درد ملایم	درد معتدل	درد معتدل	درد شدید	درد شدید	درد بسیار شدید	درد بسیار شدید	درد بسیار شدید	بدترین درد ممکن
VIETNAMESE	Không Đau	Đau Nhẹ	Đau Nhẹ	Đau Vừa Phải	Đau Vừa Phải	Đau Nặng	Đau Nặng	Đau Thật Nặng	Đau Thật Nặng	Đau Thật Nặng	Đau Đớn Tận Cùng
JAPANESE	痛みがない	少し痛い	少し痛い	いくらか痛い	いくらか痛い	かなり痛い	かなり痛い	ひどく痛い	ひどく痛い	ひどく痛い	ものすごく痛い



# MODERATE

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### 3. Advances in pain assessment and pain management in livestock



- Electrodermal Activity
- Chute Exit Speed
- Growth & Performance
- Accelerometers
- Behavior & Location in a pen
- Heart Rate Determination
- Plasma Cortisol
- Plasma Substance P
- EEG
- Algometers measuring MNT
- Thermography
- Pressure mat analysis

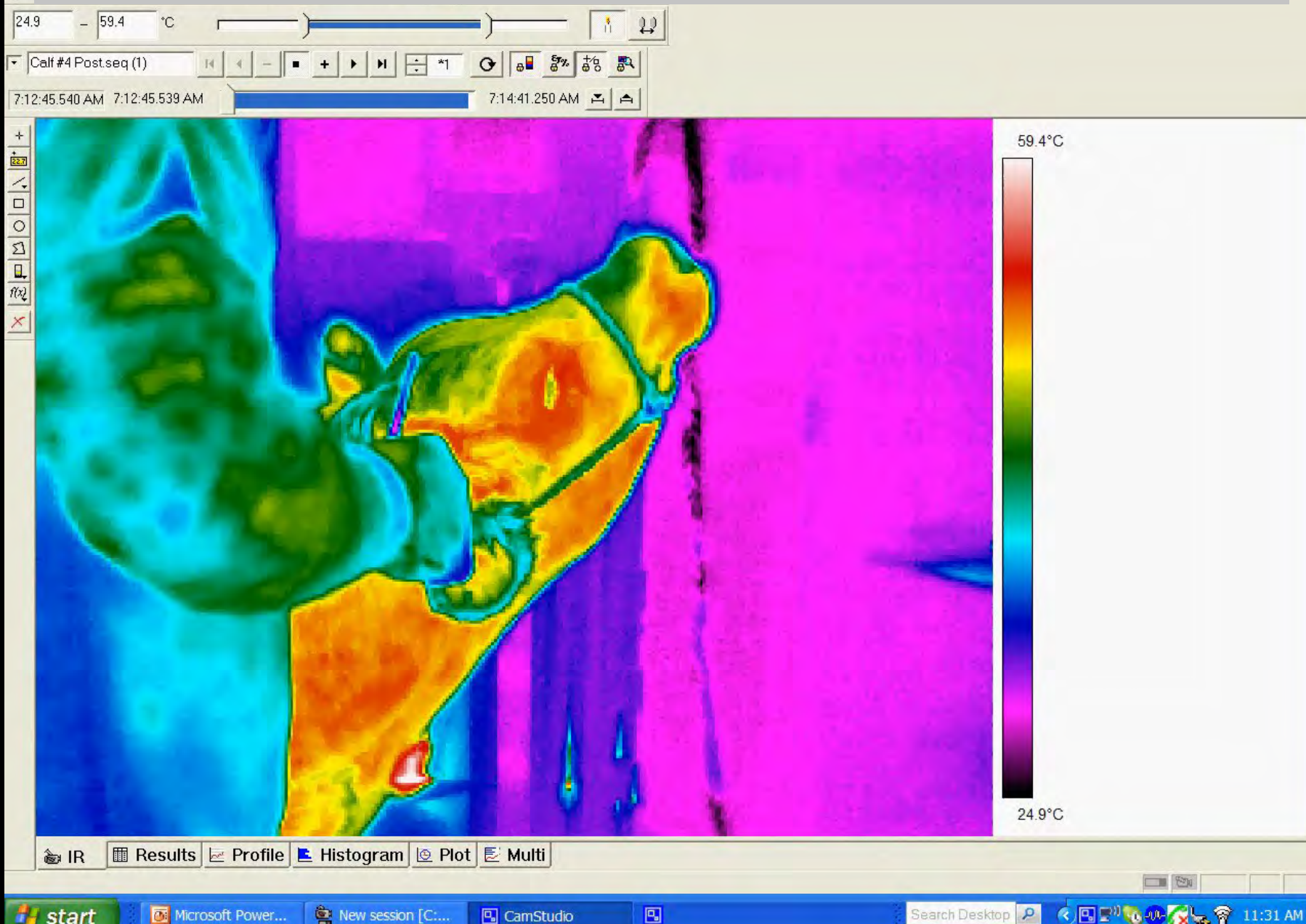


# Thermography



- Detects thermographic differences associated with changes in cutaneous perfusion
- Pain causes alterations in sympathetic tone
- Results in changes in superficial vascular blood supply.
- Gives rise to quantifiable changes in localized body temperature

# Infrared Thermography

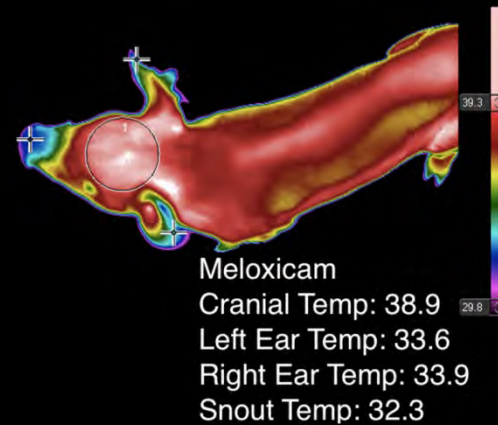
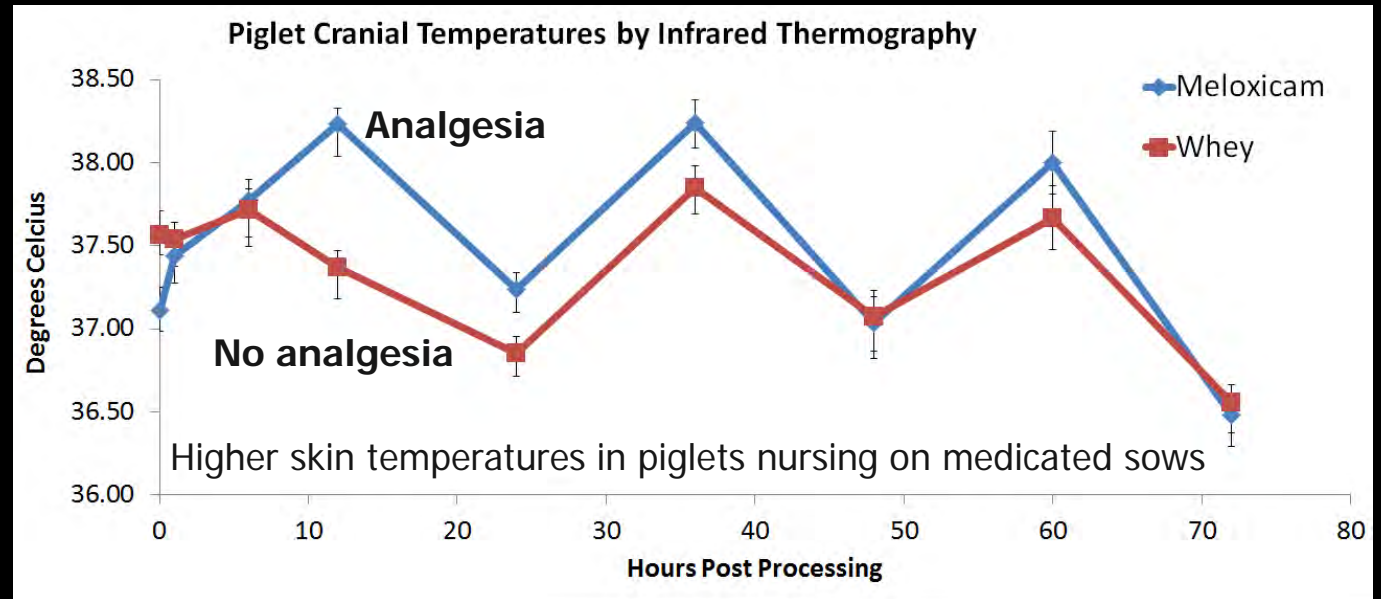


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National Institute of Food and  
Agriculture





# Impact of transmammmary meloxicam on skin temperature of piglets



# Electroencephalography (EEG)

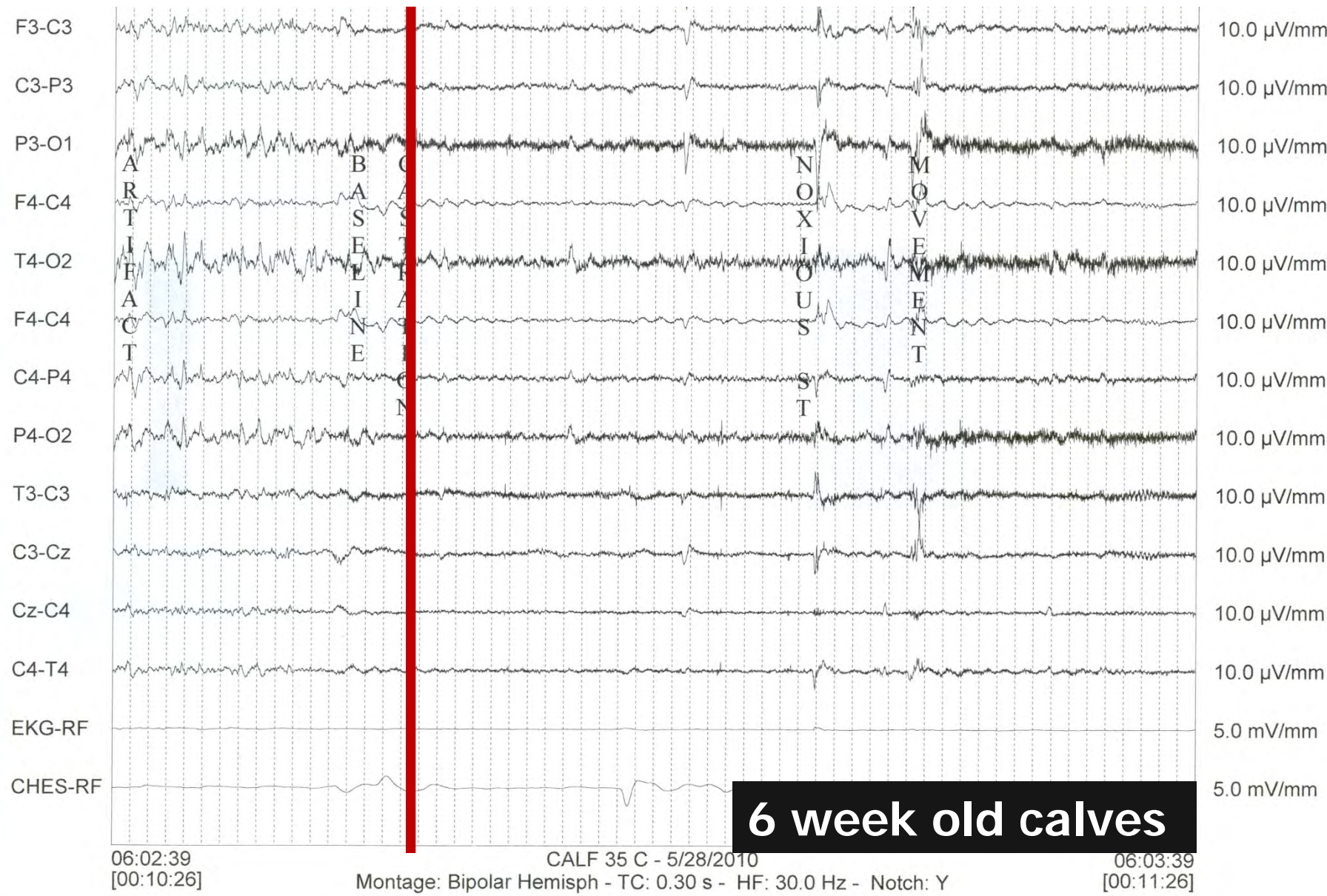


- Measurement of electrical activity on the scalp produced in brain
- ***Effects of Age:*** EEG responses in lambs undergoing castration under light halothane anesthesia varied with age.
- ***Effects of Method:*** EEG differences are seen with tonic pain (surgical castration) and phasic pain (non-surgical castration)
- ***Preemptive Analgesia:*** Quantitative EEG analyses are used to quantify anesthetic drug effects.

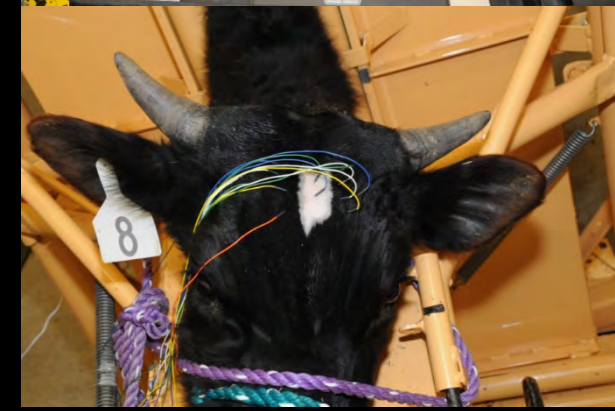
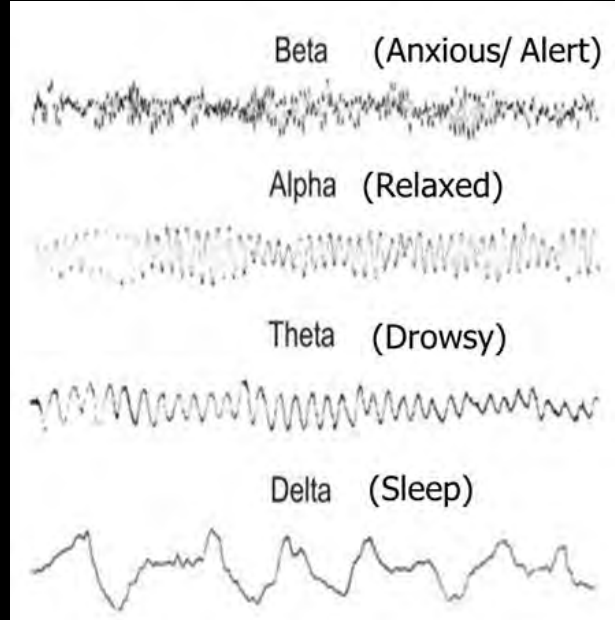




# Electroencephalography (EEG)

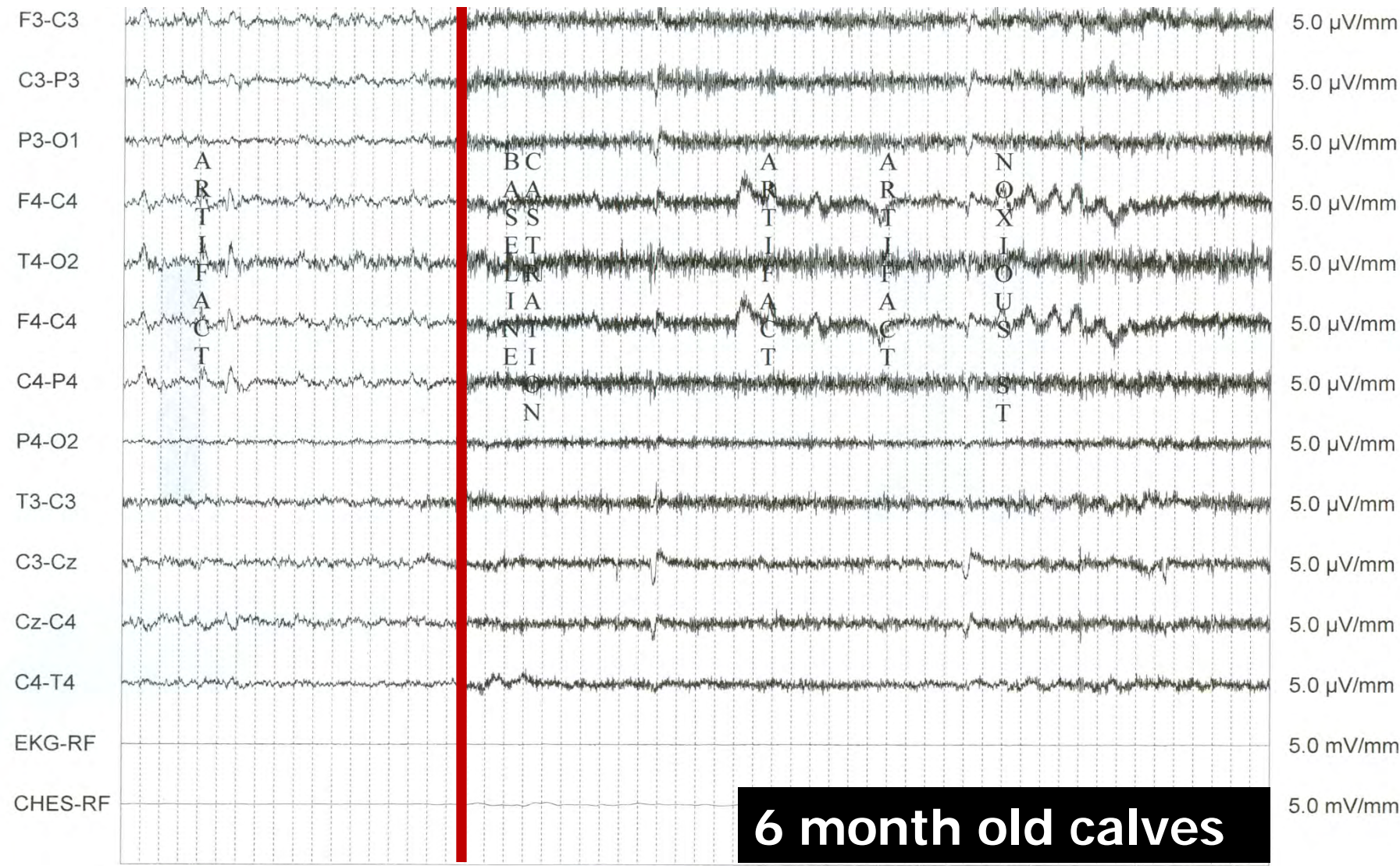


6 week old calves





# Electroencephalography (EEG)

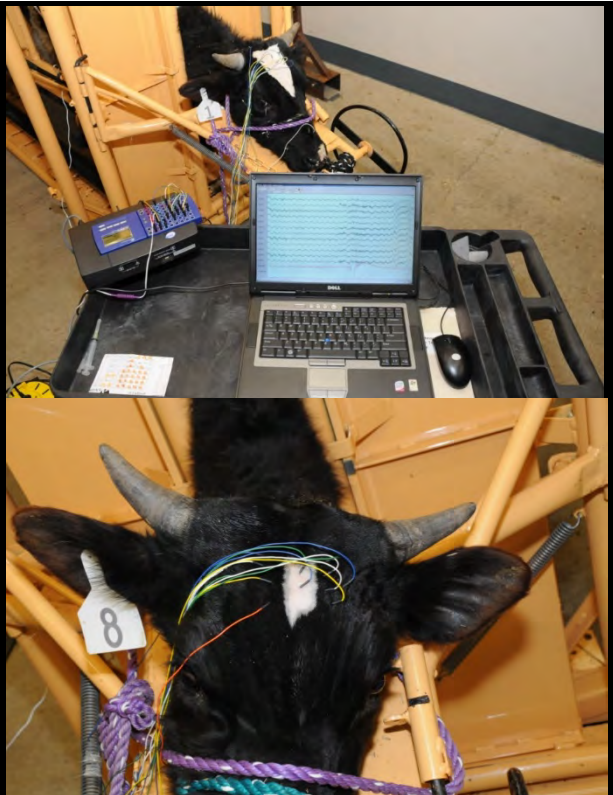
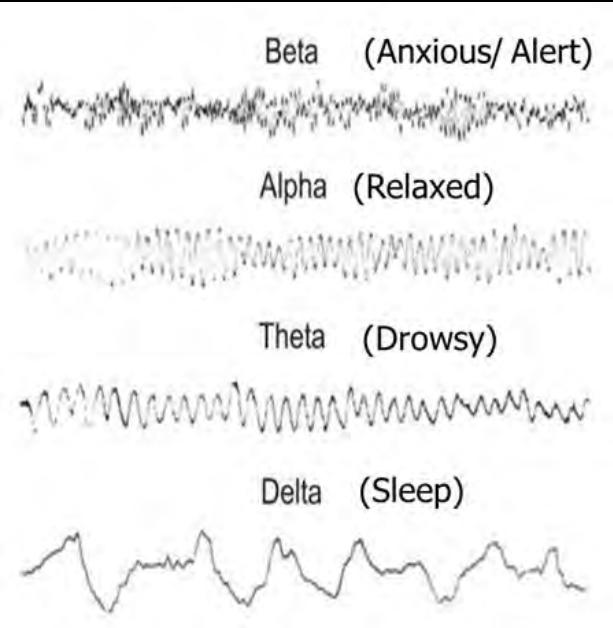


**6 month old calves**

07:28:30  
[00:08:11]

CALF 20C AGE - 5/25/2010  
Montage: Bipolar Hemisph - TC: 0.30 s - HF: 15.0 Hz - Notch: Y

07:29:30  
[00:09:11]

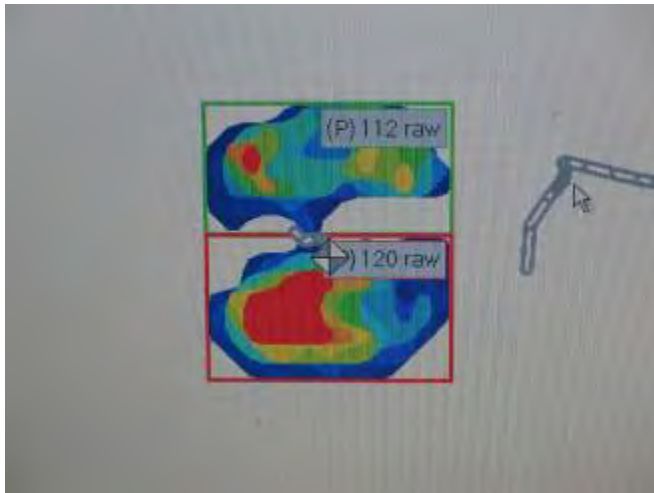




# How do we objectively measure lameness?



- Walkway with two sensor mats in series
- Computer software allows real-time recording of all phases of stride
  - the duration of stride,
  - length of stride,
  - force throughout the stride,
  - force distribution, and
  - moment of inertia.
- This allows complete characterization of how much weight is being carried on each foot



# FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

NADA 141-450

Banamine® Transdermal

flunixin transdermal solution

Steers, beef heifers, beef cows, beef bulls intended for slaughter,  
and replacement dairy heifers under 20 months of age

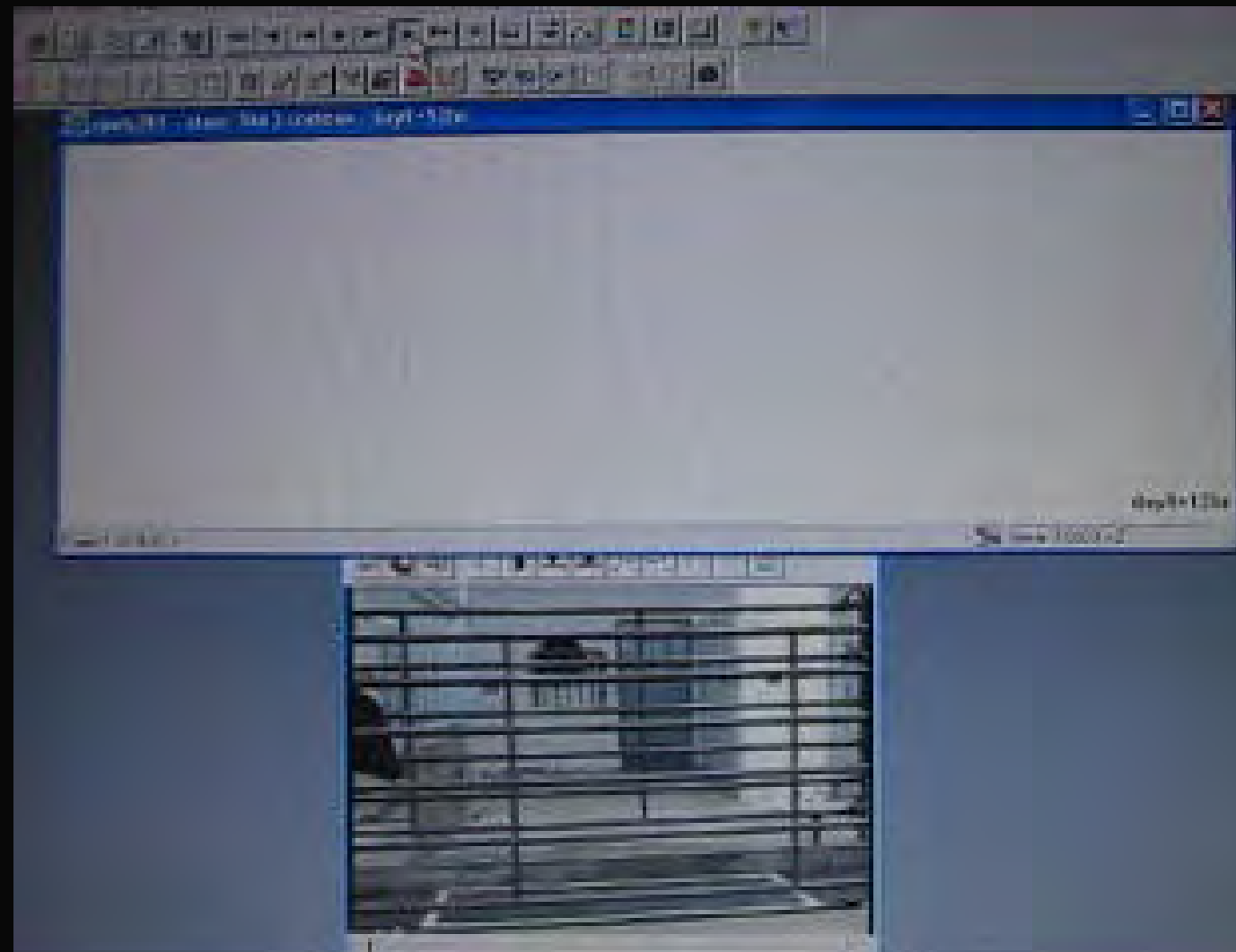
For the control of pyrexia associated with bovine respiratory disease and the control of pain  
associated with foot rot

**Table II.5: Site 1 Results**

Primary variable	Control group	Flunixin transdermal solution- treated group	P-value
Lameness score improvement success (number of animals classified as a treatment success/number in treatment group)	6.67% (1/15)	100% (15/15)	0.0263*
Mean change in maximum force (kg-force) between enrollment and 6 hours post-treatment (95% confidence interval)	-4.14 kg-force (-19.82:11.54)	43.08 kg-force (30.65:55.52)	<0.0001
Mean change in contact area (cm <sup>2</sup> ) between enrollment and 6 hours post-treatment (95% confidence interval)	-2.70 cm <sup>2</sup> (-8.19:2.80)	16.76 cm <sup>2</sup> (11.48:22.04)	<0.0001

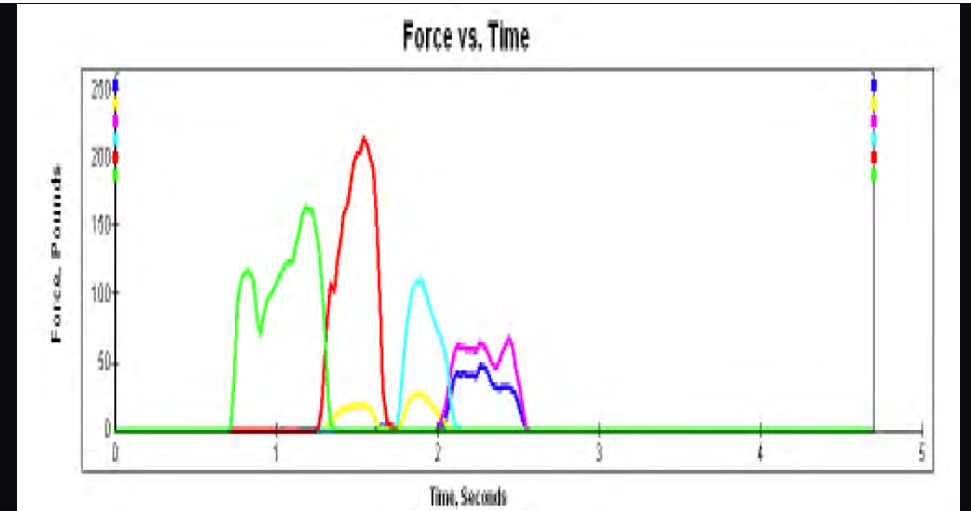
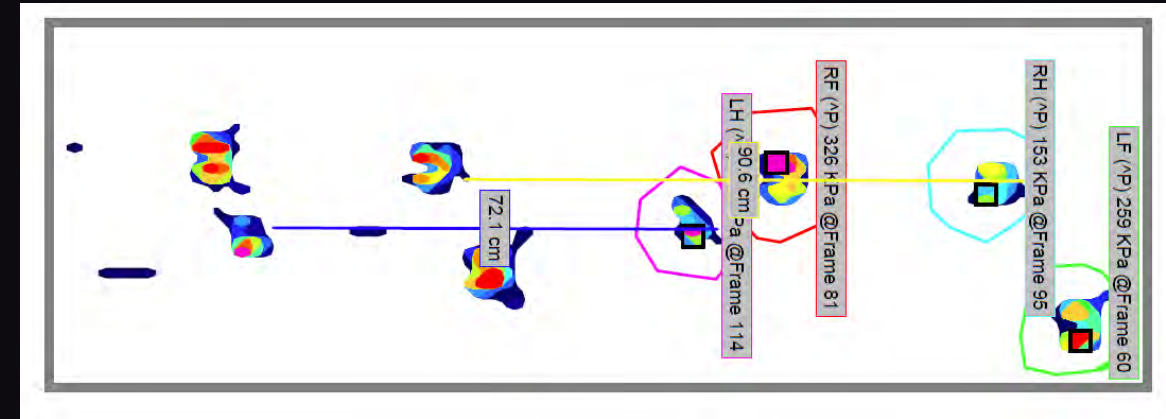
\* The p-value is from a sensitivity analysis in which one success in the flunixin transdermal solution-treated group was artificially changed to a failure. The original model did not converge because there were no failures in the flunixin transdermal solution-treated group.

Research funded by the Agriculture and Food Research  
Initiative Competitive Grant no. 2008-35204-19238  
**directly supported** the approval of the first drug for  
pain relief in livestock in the United States

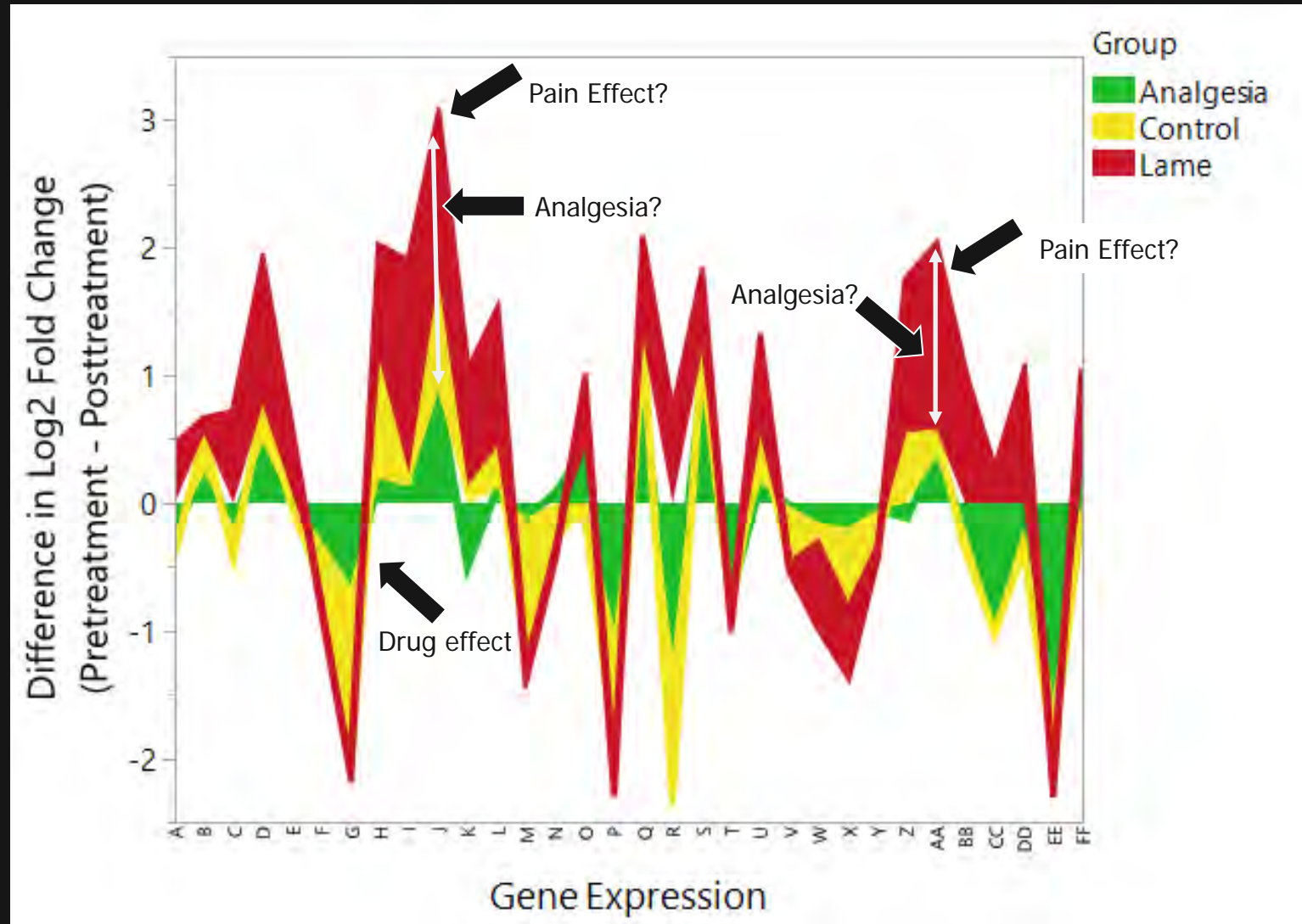




# This technology could this also be a “validated method of pain assessment” for use in pigs?



# Work in Progress- Using genetic biomarkers for pain detection



Untargeted gene expression profiling after lameness and pain relief in goats

### 3. What can we do to minimize pain? The 3 S's

- **SUPPRESS** the source of pain

- ✓ Hornless "Polled" genes to eliminate dehorning
- ✓ Sexed Semen to reduce need for castration
- ✓ Selection (boar taint, lameness, temperament)

- **SUBSTITUTE** with less painful alternative

- ✓ Optimize timing and methods used to perform painful procedures
- ✓ Immunocastration

- **SOOTHE** pain with an analgesic drug

- ✓ Cost and convenience will determine if use of pain management becomes routine



# How have we lowered barriers to on-farm analgesic use in livestock production systems?



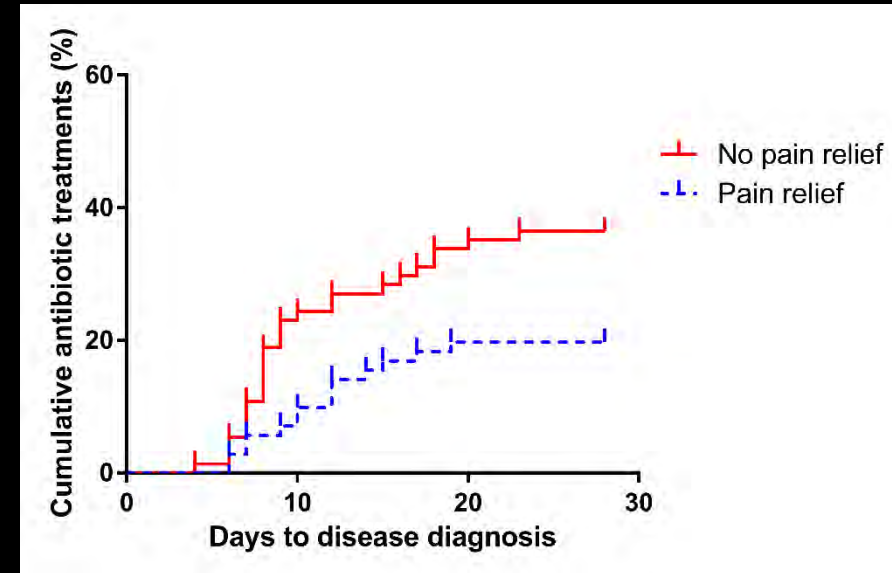
With support from USDA-NIFA we identified oral meloxicam as an effective pain relief drug for use in cattle and pigs

- Meloxicam is a prescription-only NSAID used to treat arthritis in people
- **Meloxicam tablets are rapidly absorbed from the gut of animals**
- Human generic tablets are very inexpensive (< \$0.50/calf)
- Pain relieving effects of oral meloxicam lasts for several days after a single administration

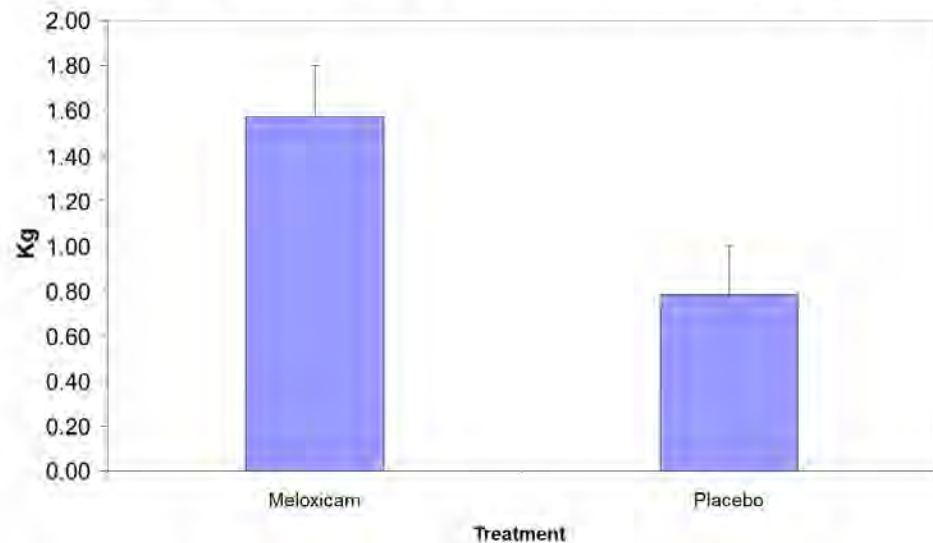




# How have we lowered barriers to on-farm analgesic use in livestock production systems?



Mean Average Daily Gain (ADG) (Kg) (+/- SEM) over 10 days in Holstein calves following meloxicam or placebo administration at prior to dehorning ( $p=0.0365$ )



- Providing pain relief improved weight gain in calves for 10 days after dehorning
- Pain relief reduced the number of calves requiring antibiotic treatment for pneumonia

# Transmammary drug delivery of pain relief to reduce pain in piglets



- Reduces the need to inject every piglet before surgery
- Caregivers only handle each piglet only once at processing
- Fewer needle sticks
- Less stress on both pigs and workers
- Long acting and potentially cost effective
- Piglets nursing medicated sows have increased growth rates

# Non-pharmaceutical alternatives for reducing pain in livestock



- **SUBSTITUTE** with less painful alternative
  - Immunocastration vaccine
  - With support received from USDA (2017-67015-27124) we have developed a novel ear implant that releases vaccine over the lifetime of the animal
  - The implant would eliminate the need for surgical castration
  - The implant also eliminates any risk to the operator of accidental self-injection



# What are the unmet needs for pain management in livestock?

- We currently do not have any drugs with FDA-approval to relieve pain in pigs
- We currently do not have any drugs with FDA-approval to relieve pain associated with castration, dehorning and branding in cattle
- Identification and validation of robust pain biomarkers
- The absence of analgesic drug approvals places a regulatory burden on veterinarians and livestock producers who are responsible, under AMDUCA, to ensure that drug residues do not enter the food supply

# Take Home Messages

- **Considerable progress has been made in validating methods of pain assessment**
  - With financial support from USDA, considerable progress has been made towards developing biomarkers of pain in livestock to support analgesic drug approvals
  - Oral meloxicam provides a convenient and cost effective approach to providing analgesia in livestock
- **Analgesic drug approvals in food animals are urgently needed**
  - Routine use of pain management is rapidly becoming a consumer expectation
  - The absence of FDA-approved analgesic drugs for use in livestock is a significant barrier to the widespread adoption of analgesic drug protocols on farms
  - Incentives, such as waiving ADUFA user fees, may encourage pharmaceutical companies to pursue analgesic drug approvals in livestock
  - Alternatives to painful procedures are an area of ongoing investigation

# Acknowledgements

- This research was supported by the Agriculture and Food Research Initiative Competitive Grants no. 2008-35204-19238; 2009-65120-05729; 2013-67015-21332 and #017-67015-27124 from the USDA National Institute of Food and Agriculture.



United States  
Department of  
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# Questions?



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