




Antimicrobial Stewardship in Dairy Production: Mastitis Examples

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Themes

- Dairy animal health drives much of antimicrobial use
 - Generally, dairy health has never better
- Dairy producers have strong incentive to prudently use antimicrobials
 - Animal well-being, profitability, and regulatory
- Record keeping helps: well-being, profitability, and compliance
 - Tools are available to help and a VCPR is important
 - (VCPR= veterinary patient client relationship)
- Stewardship
 - Not driven to a reduction number, but by decisions to when use an antimicrobial

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Info Sheet

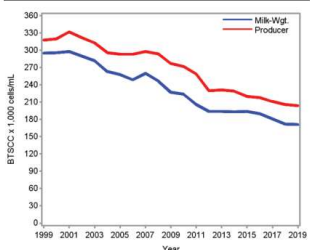
Veterinary Services
Center for Epidemiology and Animal Health
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Determining U.S. Milk Quality Using Bulk-Tank Somatic Cell Counts, 2019

Legal limit for BTSCC = 750,000 cells/mL

Similar improvement pattern as seen for udder health for calf health, reproductive health, respiratory health, metabolic health, etc. in dairy production

Figure 5. Milk-weighted and producer BTSCCs for the four monitored FMMOs, by year



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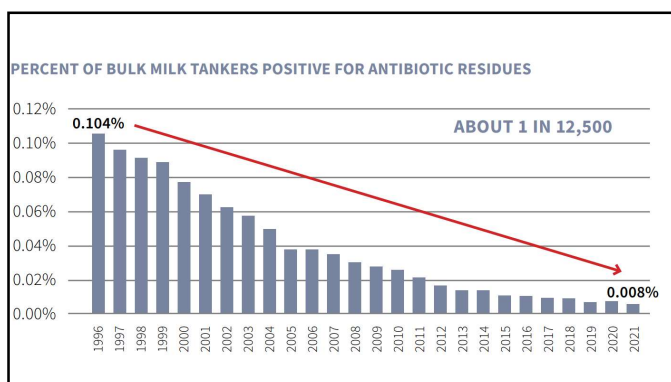


MILK & DAIRY BEEF
DRUG RESIDUE PREVENTION

Milk Drug Residue Testing

Pasteurized Milk Ordinance (PMO)
The Grade "A" Pasteurized Milk Ordinance (PMO), the rules that state regulatory agencies use to implement their Grade "A" milk programs, requires that all bulk milk tankers be sampled and analyzed for beta-lactam drug residues before the milk is processed. The PMO also requires states to test farm-level milk samples at least four times every six months for antibiotics (called Section 6 testing). Most states use an "inhibitor" test, which shows sensitivity to any antibiotic in milk. Additionally, customers (e.g., processors) may require additional testing for quality assurance purposes. **Any tanker found positive for any antibiotic residue is rejected for human consumption.**

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FDA approved antibiotics for adult dairy cows
(systemic infections)

Product	Active	Indication	Dosage	Treatment and Route	Meat withdrawal	Milk withdrawal
Excede	Ceftiofur cfa	Metritis, BRD, foot rot	1.5mL/100lbs (6.6 mg/kg)	Metritis: 2 doses, 72 hours apart base of ear BRD/foot rot: 1 dose base of ear	13 d	0 d
Excenel	Ceftiofur hcl	Metritis, BRD, foot rot	2mL/100 lbs	Metritis: 1x/d for 5d SQ or IM BRD/foot rot: 3-5d SQ or IM	4 d	0 d
Naxcel	Ceftiofur na	BRD, foot rot	2mL/100lbs	1x/d for 3-5 d SQ or IM	4 d	0 d
Polyflex	Ampicillin	Bacterial infections	2-5 mg/lb	1x/d for 3-7d IM	6 d	48 hrs
Penicillin	PPG	Bacterial pneumonia	1mL/100lbs (300,000 u/mL)	1x/d for 4d IM	10 d	48 hrs
Tetracycline	Oxytet 200	Pneumonia, BRD, foot rot, pinkeye, wooden tongue	3-5mL/100lbs (9mg/lb)	1x/d for 4d IV	28 d	96 hrs

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**FDA-APPROVED DRUGS FOR INTRAMAMMARY USE
LACTATING CATTLE**

ACTIVE INGREDIENT	DRUG TYPE	MILK WITHHOLDING TIME	MEAT WITHHOLDING TIME	PRODUCT NAME	MANUFACTURER/MARKETER
Amoxicillin trihydrate	Rx	60 hours	12 days	Amoxi-Mast*	Merck Animal Health
Ceftiofur hydrochloride	Rx	72 hours	2 days	SPECTRAMAST™ LC	Zoetis, Inc.
Cephapirin (sodium)	OTC	96 hours	4 days	Today*	Boehringer Ingelheim Vetmedica, Inc.
Hetacillin (potassium)	Rx	72 hours	10 days	PolyMast*	Boehringer Ingelheim Vetmedica, Inc.
Penicillin G	*OTC*	60 hours	3 days	Masticlear	Hanfords US Vet

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This is limited number of FDA approved antibiotics; and all have withdrawal times...

- Strong economic incentive to prudently use them
 - Milk from treated cows cannot be sold to enter food chain
 - Cows go into a treated hospital pen and milk is separated
- No medically important antibiotics continuously administered to lactating dairy cows (e.g. not in feed or water...)
 - Could never sell milk...

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Antimicrobial Stewardship
 Antimicrobial stewardship goes beyond an individual dairy farmer's actions. It extends across all livestock production, and includes use of antimicrobials in companion animals and humans, even extending to some types of crop production systems. Misuse and overuse of antimicrobials is one of the world's most pressing public health concerns. Infectious organisms adapt to antimicrobials designed to kill them, making the drugs less effective. The Food and Drug Administration Center for Veterinary Medicine (FDA CVM) has committed to antimicrobial stewardship for use in animals through principles and key initiatives.

According to the American Veterinary Medical Association (AVMA): "Antimicrobial stewardship cannot be ranked by intent of use for prevention, control or treatment. Strategic uses of antimicrobials for the purposes of prevention, control and treatment of disease may each meet the requirements of antimicrobial stewardship. Stewardship is better defined by decisions that influence the need for antimicrobial therapy in the first place and that maintain the effectiveness of antimicrobials when they are used."

Factors include the following:

- Systems of husbandry that reduce the risk of disease
- Careful diagnostic evaluation
- Good decision-making to use or not use antimicrobials
- Prudent choice of drugs, dosage and duration
- Records indicating appropriate follow-up and re-evaluation

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~ 60% of AMU in dairy production is for control or treatment of mastitis

- ~2/3 of that 60% is for dry cow therapy
- ~6 FDA approved DCT formulations
 - No meaningful differences in bioeconomic health and production outcomes

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Randomized noninferiority study evaluating the efficacy of 2 commercial dry cow mastitis formulations

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Randomized noninferiority clinical trial evaluating 3 commercial dry cow mastitis preparations: II. Cow health and performance in early lactation

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1960s "Blanket DCT"

Treat all 4 quarters of all cows

Treat & Control Mastitis

Quality Milk Production Services

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A bit of perspective...

- 1, 500mL PLASTET of, for example, Dry-Clox has 500mg beta-lactam antibiotic
- = 2g/cow/year
- www.cdc.gov/groupastrep/diseases-hcp/strep-throat.html
 - Strep throat (group A strep pharyngitis)
 - 500 mg amoxicillin BID for 10d
 - =10g/case

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Selective Dry Cow Therapy for Treatment and Control of Mastitis

Why do this?

Improving Udder Health
>50% subclinical infections -> <20% presently

- Save money on tubes (and maybe labor)
- Decrease risk of residues
- Bogey man
 - Someone tells you that you have to
 - Mitigate risk of antimicrobial resistance
- (Sell more milk?)

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Summary: Teat sealants + DCT

Equally effective

↓ new IMI at calving & Clinical mastitis

Addition of DCT lowers SCC

Rabee & Lean, 2013 (Meta-analysis of 12 trials)

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Randomized controlled non-inferiority trial investigating the effect of 2 selective dry-cow therapy protocols on antibiotic use at dry-off and dry period intramammary infection dynamics

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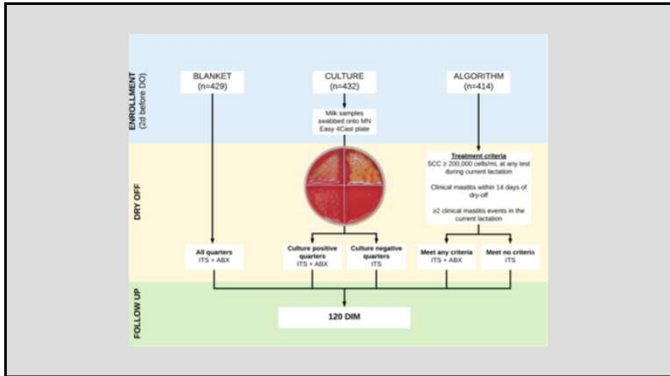
J. Dairy Sci. 100:6485-6491
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Randomized controlled trial investigating the effect of 2 selective dry-cow therapy protocols on udder health and performance in the subsequent lactation

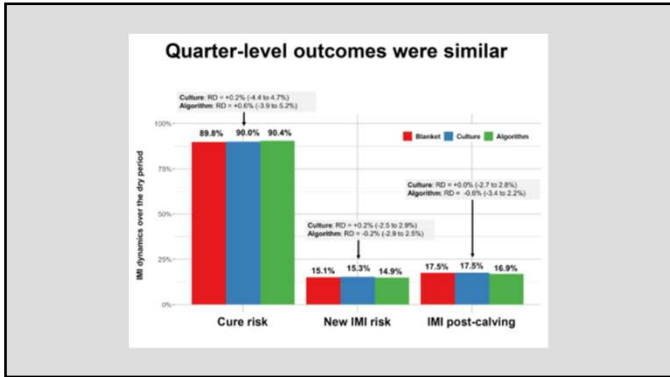
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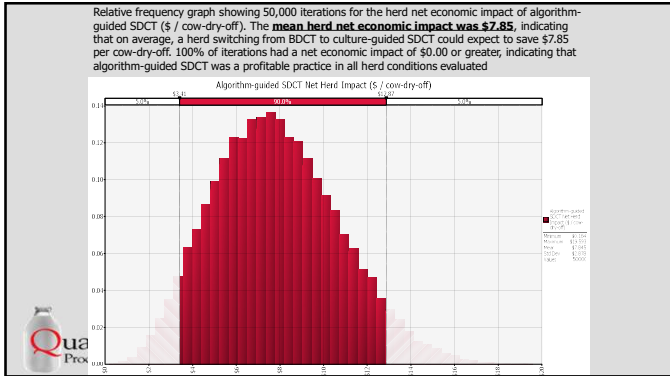
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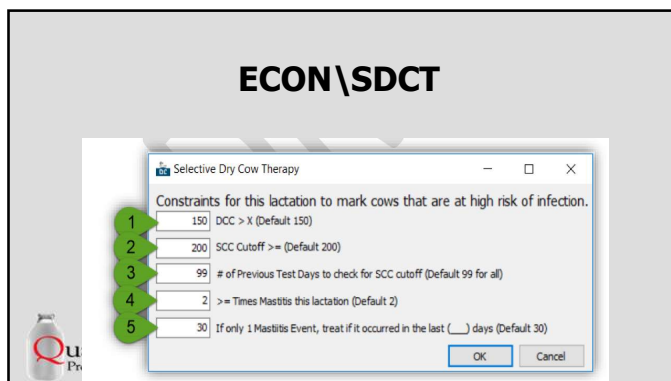
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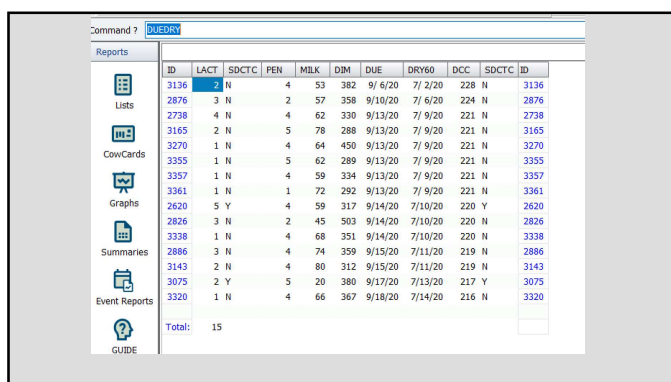
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Pathogen Based Treatment Decisions for Clinical Mastitis

Why do this?

Make More Money
while not compromising animal health

- Save money on tubes and labor
- Hospital pen density
- Decrease risk of residues in the tank
- Bogey man
 - Someone tells you that you have to
 - Mitigate risk of antimicrobial resistance
- Sell more milk

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On Farm Culturing

- Supplies and training for on-farm milk cultures

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- Selective treatment of clinical mastitis based on on-farm culture resulted in no differences in bio-economic outcomes

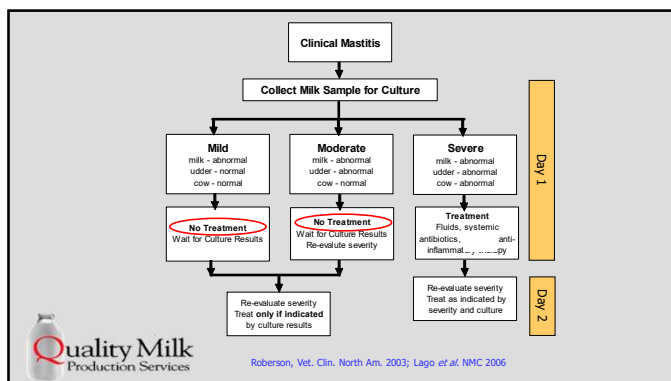
Recurrence of CM in the same quarter	SCC
Milk Production	Cow survival for the rest of the lactation after CM

Lago, et al, J. Dairy Sci, 2011
Lago et al, AABP 2016

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Data and Sample Flow for External Lab Diagnostics

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Clinical outcome comparison of immediate blanket treatment versus a delayed pathogen-based treatment protocol for clinical mastitis in a New York dairy herd

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Local Dairy Results
 Pathogen-based Treatment

>75,000 cows supported by QMPS in NY with pathogen based treatment

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Summary: PB treatment...

Decreased milk withholding time by approximately 3d

No significant differences in:

- ❖ Days to clinical cure
- ❖ Post MAST milk yield >\$32,000 per 1000 cows
- ❖ Post MAST LS
- ❖ Risk of cull in 1-2mo following MAST


Over 65% of mild/moderate mastitis will NOT be treated with antimicrobials if this protocol is employed.

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Conclusion


- Prevention is most important:
Efficiently milk clean dry teats with properly functioning equipment...
... on cows that have comfortable beds and are nutritionally supported



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Conclusion

- Occasionally we fail and mastitis happens
 - Pick a tube based on science and cost
 - Stay on label dosage; observe withholding
 - Get accurate diagnosis
 - Build implementable SOP
 - “Each extra line = 10% decrease in compliance”
 - Execute SOP
 - Monitor compliance and execution



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Goals in the dairy supply chain

- Work with producers who have been improving animal health
- Work with producers who have a plan for AMU with their Vet of Record
- Work with producers who keep records of AMU and have a VCPR
- Work with producers who have a mindset of continuous improvement

- It's a win-win-win-win
 - Farmers – animals – processors – public

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