

DAIRY VETERINARY NEWSLETTER

January 2011

92% of U.S. Dairy Cows Live in 23 States, Including Utah

The percentage of U.S. dairy cattle that are housed in the 23 major dairy producing states continues to increase, and is now 92% of the nation's dairy cows. The list of 23 states includes Utah. The Livestock Marketing Information Center (LMIC) as reported in a story on Dairy Herd Network says that the 23 major dairy states actually gained 0.7% more cows, while the remaining 27 states continue to decrease in cow numbers. Alphabetically, the 23 major dairy states are: Arizona, California, Colorado, Florida, Idaho, Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, New Mexico, New York, Ohio, Oregon, Pennsylvania, Texas, Utah, Vermont, Virginia, Washington and Wisconsin.

The Change in Neo-Terramycin (Neomycin/Oxytetracycline) Milk Replacers

Since October 2, 2010, what had been the single most commonly fed type of milk replacer is no longer available (or at least is supposed to be – more on that below). This is because of a change in FDA regulations. Multiple sources suggest that before the change took effect, approximately 60% of milk replacers fed to dairy calves contained 400 grams per ton (200 mg per pound of milk replacer) of neomycin sulfate and 200 grams per ton (100 mg per pound of milk replacer) of oxytetracycline. This was commonly referred to as an NT (neo-terramycin) milk replacer with a 2:1 ratio of neomycin to oxytetracycline (terramycin).

It is difficult to find information directly from the FDA concerning the new milk replacer regulations. Most of the readily available written information is found in numerous dairy industry publications; most of it agrees but some is contradictory. The actual FDA information can be found in the Code of Federal Regulations (CFR) Title 21, Sec. 520.1484 and Sec. 520.1660d, revised April 1, 2010. Interestingly, the part of the CFR describing the new dosages and uses of oxytetracycline says, "Do not administer this product with milk or milk replacers". The neomycin section does not say that.

New standards for continuous feeding of NT milk replacers

Now milk replacers containing neomycin and oxytetracycline must have these antibiotics in a 1:1 ratio. For continuous feeding of a 1:1 ratio NT milk replacer, the new dose limit is 0.05 to 0.10 milligrams per pound of body weight. Some of the published information regarding the new milk replacers does not convert this to the dosage of NT in the milk replacer powder itself. An example conversion follows below.

Using a 100 pound calf as an example, the concentration of NT in the milk replacer powder to feed 0.10 milligrams per pound of body weight:

0.1 mg/lb body wt x 100 lb body wt = 10 mg of each antibiotic fed daily to the calf

The pounds of milk replacer powder fed usually equals the gallons of liquid replacer fed

If a 100 lb calf consumes 1.25 pounds of milk replacer powder (5 quarts of liquid replacer) each day, the dose of each antibiotic = 10 mg/1.25 lb milk replacer powder = 8 mg/lb milk replacer powder

2000 lb/ton x 8 mg/lb milk replacer powder = 16,000 mg/ton = 16 grams/ton of milk replacer powder of each antibiotic, neomycin and oxytetracycline, for continuous feeding of milk replacer to calves. There is apparently no body weight or age limit on feeding this to calves. The dosage above works for calves of any body weight, as long as the milk replacer feeding rate is 10% of body weight per day.

New standards for short term treatment feeding of higher dose NT milk replacers

Feeding a 100-fold higher dose of neomycin and oxytetracycline, 10 mg per pound of body weight, is now allowed “for treatment of bacterial enteritis caused by *Escherichia coli*, and to treat bacterial pneumonia caused by *Pasteurella multocida*” for 7 to 14 days. What is not clearly stated is whether a laboratory diagnosis of these specific bacteria is needed in order to feed the high-dose NT milk replacer. If so, whether the diagnosis in at least one calf allows the treatment feeding of other calves in the herd that also have diarrhea or respiratory disease signs is also not stated. In addition, the CFR states that for feeding the high-dose NT milk replacer, the bacterial enteritis is to be “caused by *Escherichia coli* susceptible to neomycin sulfate” and the bacterial pneumonia is to be “caused by *P. multocida* susceptible to oxytetracycline”. There is no mention of any methods of antimicrobial susceptibility testing, however.

Using a 200 pound calf as an example, the concentration of NT in the milk replacer powder to feed 10 mg per pound of body weight:

10 mg/lb body wt x 200 lb body wt = 2000 mg of each antibiotic fed daily to the calf

Again, the pounds of milk replacer powder fed usually equals the gallons of liquid replacer fed

If a 200 lb calf consumes 2.5 pounds of milk replacer powder (10 quarts of liquid replacer) each day, the dose of each antibiotic = 2000 mg/2.5 lb milk replacer powder = 800 mg/lb milk replacer powder

2000 lb/ton x 800 mg/lb milk replacer powder = 1,600,000 mg/ton = 1600 grams/ton of milk replacer powder of each antibiotic, neomycin and oxytetracycline, for treatment feeding of milk replacer to calves for 7 to 14 days. Note that this is 4 times higher than the old neomycin dose, but the duration of feeding is limited. Some dairy industry publications and product feeding instructions says that there is a 250 pound body weight limit for treated calves. However, in the CFR this is not mentioned. I could find no FDA information regarding a weight limit. The dosage above works for calves of any body weight, as long as the milk replacer feeding rate is 10% of body weight per day.

Product availability and potential confusion

The first announcements of the FDA rules said that existing stocks of the old 2:1 NT milk replacers would have to be used up by now and no longer available for sale. All dairy industry publications on the subject say that this was to take place by October 2, 2010. However, numerous NT 2:1 milk replacers with the “old” 400 grams neomycin:200 grams oxytetracycline per ton dosage still appear to be for sale on various supply company websites.

To comply with the new guidelines for continuously fed milk replacers, there are indeed NT milk replacers with 16 grams/ton of each antibiotic available. The feeding instructions explain how to feed 0.1 mg per pound of body weight of each antibiotic, in accordance with the new standards.

I found several of the new high-dose 1600 grams/ton NT milk replacers for sale, but they were often described as “to meet the needs of a newborn calf”, or “for optimum health and performance”, with no mention of only treating enteritis or pneumonia. Some instructions said to feed for 7 to 14 days, but did not say that feeding must be stopped after that time, instead advising to continue treatment for 24 to 48 hours beyond remission of disease symptoms. This is not meant to criticize milk replacer manufacturers; most people are probably just getting used to the new rules. However, it does point out the potential for calf feeding personnel to be confused and feed milk replacers with the new high levels of neomycin and oxytetracycline to calves for far longer than the new FDA regulations allow. When the pending FDA regulation changes were announced in 2009, Tom Earleywine, director of nutrition services for Land O’Lakes Animal Milk Products, was quoted in an article, “Medicated Milk Replacers Regs Take Effect In 2010” in the 12/15/09 issue of Bovine Veterinarian. “It is possible that calf-raisers might feed the (new high dose) medicated milk replacer for five to six weeks, if they only purchase one type of milk replacer.” The article points out that feeding it past 14 days means the calf-raiser would be feeding the medication off-label.

There are also some “add packs” for sale, which are often mentioned in dairy industry publications. These add packs are powdered NT concentrates for mixing with non-medicated milk replacer to make the new high-dose treatment NT milk replacer. Some of these add pack concentrates make a milk replacer with 2000 grams/ton of both neomycin sulfate and oxytetracycline. The manufacturers correctly point out that in order to feed the antibiotics at 10 mg/pound of body weight, the amount of medicated “add pack” powder that is to be mixed in milk replacer powder varies with the feeding rate of milk replacer per pound of body weight. This becomes complicated for anyone mixing and feeding milk replacer.

The new medicated NT concentrate products (add packs) for treatment state that they should be mixed only into non-medicated milk replacer. Technically, this means that a farm feeding the continuous feeding NT medicated milk replacer needs to also have non-medicated milk replacer on hand if they intend to mix an NT concentrate type of product into it. I am probably not the only veterinarian or member of the dairy industry who is wondering whether this will be practical reality on farms. The consequences of mixing the treatment NT product containing 100 times higher concentrations of the antibiotics (1600 grams/ton) into the continuous feeding NT milk replacer (16 grams/ton) instead of into non-medicated milk replacer (the former practice results in 1% more total antibiotic than the latter) are not clear. This is not a recommendation not to follow the new regulations, but is just meant to raise a question.

Will the change in medicated milk replacer increase calf death loss? How effective was the old NT formulation?

Many articles in the dairy industry press suggest that there will obviously be a challenge to dairy calf health or less effectiveness when feeding the new lower dose continuously fed NT milk replacer. This is a central issue regarding this regulation change – will it increase disease or death in dairy calves?

From the article in Bovine Veterinarian, again: “Over the last 10 years, we have run 11 different research trials, where we compared non-medicated milk replacer to the 2:1 medicated milk replacer,” Earleywine said. Seven of the 11 total trials showed a response of weight gain with neomycin and oxytetracycline in the milk. There was no effect on scours which is the expected response when feeding neomycin and oxytetracycline. But, upon further evaluation, the studies show that calves fed at a higher plane of nutrition responded only one-third of the time to the medicated milk replacer. Calves fed at the lower level of nutrition, responded

100 percent of the time to the medicated milk replacer. ‘Our research doesn’t show a big benefit to medicated milk replacer, if you’re feeding adequate nutrition,’ notes Earleywine. ‘Nutrition trumps medication every day.’”

Don Sockett, veterinarian at the Wisconsin Veterinary Diagnostic Laboratory, was also quoted. “‘The most common agents that cause neonatal diarrhea are *Cryptosporidium parvum*, rotavirus and coronavirus which are resistant to antimicrobial drugs. *E. coli* and *Salmonella* account for less than 10 percent of all the neonatal calf diarrhea cases submitted to our lab.’ There is a lack of peer-reviewed studies demonstrating the efficacy of neomycin and oxytetracycline when used for the prevention and treatment of neonatal calf diarrhea caused by *E. coli* and *Salmonella*, Sockett says.”

As we have detailed in this newsletter before (January 2009), efficacy data for antibiotics vs. calf enteric pathogens that cause diarrhea is limited, and this is especially true for the last 10 years. D. White et al. in J Clin Microbiol, December 2000 tested 48 *E. coli* strains from diarrhea cases of calves less than 2 weeks old for antimicrobial susceptibility. The proportion found resistant to antibiotics included: florfenicol 92%, ampicillin 88%, amoxicillin-clavulanic acid 69%, cephalothin 77%, ceftiofur 69%, tetracycline 100%, kanamycin 92%, streptomycin 100%, sulfamethoxazole 100%, trimethoprim-sulfamethoxazole 69%.

P.D. Constable reported in J Vet Internal Med, Jan-Feb 2004, that among the U.S. - labeled calf diarrhea treatments amoxicillin, chlortetracycline, neomycin, oxytetracycline, streptomycin, sulfachloropyridazine, sulfamethazine, and tetracycline, “On the basis of published evidence for the oral administration of these antimicrobial agents, only amoxicillin can be recommended for the treatment of diarrhea.”

D.C. Donovan et al. reported in J Dairy Sci, April 2002 on a study where 22 Holstein calves were fed a milk replacer with 250 grams neomycin:125 grams oxytetracycline per ton and 23 calves were fed a milk replacer with fructooligosaccharides, allicin, and probiotics. (More information on these substances is in the paper.) Fecal severity scores, serum protein concentration, and weight gain during 35 days on milk replacer were the same between the 2 groups. The paper concludes that, “These functional foods for preweaned calves may be viable substitutes for antibiotic use without decreasing overall performance”.

A.C. Berge et al. published an interesting paper in J Dairy Sci, Sept 2009. 358 dairy calves were divided into 4 groups (2 x 2): a conventional therapy (CT) group treated with several different antibiotics if they showed diarrhea or a targeted therapy (TT) group treated with antibiotics for diarrhea only if they had fever ($> 103^{\circ}$ F) or attitude classed as Depressed or Non-responsive, and then within each of those 2 groups, equally divided into a group fed 2:1 NT milk replacer and a group fed non-medicated milk replacer. Each calf was studied for 60 days. It should be noted that this was on only one farm, and there was a *possible bias in the study*. The farm management must have wanted this; the TT group (82 with NT milk replacer, 84 with non-medicated) had 160 bulls and 6 heifers. The CT group (95 with NT milk replacer, 97 with non-medicated) had 174 heifers and 18 bulls. Having bulls dominate the targeted therapy group might affect average daily gain, but also result in less attentiveness to disease in that group. *However, the comparison within each treatment group between NT and non-medicated milk replacer was not affected.* Only 4 calves (1%) died during the study. PCV, serum IgG, TP, hydration, difficult birth (0.5%) respiratory score and attitude score were not different between groups. Days with diarrhea was 10.1% for the 177 calves fed NT milk replacer, 8.1% for the 181 fed non-medicated (P < 0.0001). There were also more days with joint disease in NT fed calves (P = 0.0001). Average daily gain turned out to be the same among all groups correcting for birth weight (it was higher among low birth weight calves). Estimated medication and treatment labor costs were \$12.40 for the CT calves fed NT milk replacer, \$11.70 for CT calves fed non-medicated, \$4.50 for TT calves fed NT milk replacer, and \$2.10 for TT calves fed non-medicated.

Alternative milk replacer formulations

There are other substances added to milk replacers, and they are getting more publicity/advertising with the loss of 2:1 NT. A literature search for refereed publications regarding evidence of effectiveness found:

Mannan oligosaccharide (MOS) – A. J. Heinrichs et al., J Dy Sci, December 2003. 72 Holstein calves were fed either non-medicated, 2:1 NT or MOS 4 grams/calf/day treated milk replacer, studied until 42 days old. None died, 10 diarrhea treated calves: 5 non-medicated, 3 NT, 2 MOS fed calves, not different. Normal fecal scores were more likely in NT or MOS fed calves than non-medicated ($P < 0.01$). However, severe diarrhea scores were not different among any treatments. TP, BUN, average daily gain, and beginning and ending height and heart girth were not different among the milk replacer groups. Possible antibacterial mechanisms of MOS are also discussed. The authors concluded, “Under the circumstances of this study, addition of MOS to milk replacer appeared to benefit calf health and reduce scours, indicating that MOS could effectively replace antibiotics in milk replacer”.

Oregano - A paper in J Vet Med A Physiol Pathol Clin Med, April 2006 by V.A. Bampidis et al. reports a comparative study of 30 dairy calves treated at onset of diarrhea signs (most were 7 to 20 days old), 14 calves with 4.5 mg neomycin sulfate/lb body weight and 16 calves with dried oregano leaves providing 4.5 mg oregano essential oil/lb body weight. One calf in each group died (7%), fecal scores and days of diarrhea (6.4 days mean) were not different between neomycin and oregano treated calves. The paper includes a discussion of the antimicrobial properties of oregano essential oil.

Garlic extract – 2 papers by S. Ghosh et al. from India, on PubMed. Garlic extract fed at 115 mg/lb body weight daily was associated with increased daily gain, feed efficiency, and reduced fecal diarrhea severity scores in Holstein cross calves from 5 to 60 days old, compared with whole milk. They describe making extract from garlic bulbs also.

Anise - no publications regarding calf disease or performance.

Rosemary – several refereed publications regarding beef carcass quality and feeding rosemary, no publications regarding calf disease or performance.

Cinnamon – some refereed publications suggest efficacy of cinnamon oil as a diarrhea treatment in other species, no publications regarding calf disease or performance.

Conclusions

Altogether, the few refereed publications on the subject suggest that neomycin or oxytetracycline are not necessarily essential treatments or preventatives against dairy calf diarrhea.

Feeding rates affect the grams per ton concentrations of the antibiotics in milk replacer. If farms feed at a rate other than 10% of body weight per day, the concentrations of NT needed to achieve the daily doses of 0.10 mg per pound for continuous feeding or 10 mg per pound for treatment for 7 to 14 days change also.

Feeding the “add pack” powdered NT concentrates for mixing with non-medicated milk replacer to make the new high-dose treatment NT milk replacer is somewhat complicated. In addition to the effect of milk replacer feeding rates, the potential for mixing errors, especially if milk replacer is not weighed, but mixed by volume such as that of a plastic cup, etc. can result in mistakes. (Continued)

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Dairy veterinarians should advise clients regarding the new regulations and varying levels of NT in milk replacers, and clients should consider alternatives to NT medicated milk replacers. If possible, help provide training and written instructions to all farm personnel mixing and feeding milk replacer to calves.

Please let us know your comments and also suggestions for future topics. I can be reached at (435) 760-3731 (Cell), (435) 797-1899 M-W, (435) 797-7120 Th-F or David.Wilson@usu.edu.



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