Virginia Cooperative Extension

PUBLICATION 404-401

# On-farm Tests for Drug Residues in Milk

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## Introduction

The presence of drug or antibiotic residues in milk and meat is illegal. Milk supplies containing detectable concentrations are not acceptable. Unless drug residues are avoided to protect milk's reputation as a healthy, safe food, the market becomes jeopardized. Consumers want to be confident that their food supply is free of contamination by herbicides, pesticides, drugs, or antibiotics. Approximately 5-10 percent of the population is hypersensitive to penicillin or other antibiotics and suffers allergic reactions (skin rashes, hives, asthma, anaphylactic shock) at concentrations as low as 1 ppb penicillin. There is concern that small amounts of certain antimicrobial agents may significantly shift the resistance patterns in the microbial population in the human intestinal tract.

Antibiotics are known to interfere with the manufacture of several dairy products. Concentrations of 1 ppb delay starter activity for cheese, butter, and yogurt. Antibiotics also decrease the acid and flavor production associated with butter manufacture, and they reduce the curdling of milk and cause improper ripening of cheeses.

## SOURCE OF DRUG RESIDUES

Drugs are administered to dairy cows for treatment of mastitis through intramammary or intravenous infusions and for disease therapy by intramuscular or intravenous injections, oral administration, feed supplementation, or reproductive infusions. FDA surveys indicate that improper use of drugs in the control of mastitis is the major source of residues found in the milk supply. The beef industry claims that a great percentage of the drug residues found in beef carcasses are in those of culled dairy cows.

Many drugs are retained in the animal body for longer times than indicated by label discard times. Consequently, milk samples remain positive for residues. A good example is penicillin with a recommended milk discard time of 72 hours. However, penicillin residue has persisted in milk for as long as 18 days. Other drugs may cause residues. At the end of the label withholding time, we have detected drug residues in 35% of cows treated with cephapirin for mastitis and 27% of cows given intramuscular injections with penicillin (Table 1). Some of the cephapirin treated cows were still positive at 48 hours after the recommended milk discard time. Drugs administered for dry cow therapy do not appear to cause drug residues if milk is not shipped for the first four days after calving, if dry periods are l's recommendations are followed, dry cow therapy should not result in residues after calving. However, residues are possible and fresh cows should be tested, especially cows with short dry periods.

**Table 1. Adequacy of Recommended Milk Discard Times (Seymour et al., 1988)**

| Discard Time | Cephapirin | Penicillin |
|---|---|---|
| | - - % Cows Cleared - - | |
| **Recommended** | **65** | **73** |
| | - - - % Cows + - - - | - - - - |
| + 1 day | 35 | 27 |
| + 2 days | 21 | 20 |
| + 3 days | 12 | 13 |
| Number of cows | 34 | 15 |
| Route of administration | Intramammary | Intramuscular |

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Produced by Communications and Marketing, College of Agriculture and Life Sciences, Virginia Polytechnic Institute and State University, 2009

Cows were treated "extra-label." Similar results were found with Cephapirin when treated according to label.

Intrauterine infusions of drugs have caused detectable residues in milk. Studies have reported residues caused by intrauterine treatment with tetracycline, dihydrostreptomycin, benzyl penicillin, oxytetracycline, sulfamethazine, and penicillin streptomycin. Combiotic (procaine penicillin and dihydrostreptomycin) has been detected in milk for 24-48 hours after intrauterine infusion.

Suspected reasons for drug residues include:

- Extended usage or excessive dosage of approved drugs.
- Poor records of treatment.
- Milker or producer mistakes—accidental transfer into bulk tank.
- Failure to observe recommended label withdrawal time.
- Lack of advice on withdrawal period.
- Prolonged drug clearance.
- Treated-animal identification problems.
- Multiple dosing.
- Products not used according to label directions.
- Withholding milk from treated quarters only.
- Contaminated milking equipment.
- Early calving or short dry periods.
- Purchase of treated cows.
- Use of dry cow therapy to lactating cows.

# RECOMMENDED USE OF ON-FARM DRUG RESIDUE TESTING

Dairy farmers should use a drug residue test regularly. Data collected from 160 herds in California, New York, Pennsylvania, Virginia, and Wisconsin indicate that 70% of Virginia dairy herds use drug screening tests, but only 38% of the 809 herds from the five states used these tests on the farm (Wilson et al., 1998). Certain situations have greater risks for residues. Withholding times on the label may have been established with healthy or high producing cows where the drug retention is less than occurs in sick or diseased cows. Consider using a drug residue screening test as follows:

1. Fresh cows, especially those dry treated and with dry periods of six weeks or less, cows that freshen early, cows which had been treated shortly before calving, or cows whose treatment status was unknown. Discard milk for the first three days after calving. This includes first lactation cows who had been treated with either a lactating or dry cow mastitis treatment prior to calving. Also, test cows that received intrauterine drug infusions.

2. At the end of the recommended milk discard time and after the milk becomes visually normal, test milk from any lactating cow treated for mastitis.

3. At the end of the veterinarian's recommended withholding time, which should be stated on the drug label, test any cows treated "extra-label." Also, test problem cows that have been treated longer than recommended, or with higher doses, or with combinations of drugs or special mixes.

4. All new additions to the herd including purchased cows or first lactation animals should be tested before their milk is added to the bulk tank.

5. Any cull cows that have been treated or baby calves that have been fed milk from treated cows should not be sold until the end of the withdrawal time for meat animals. Calves born to cows treated during the dry period may acquire tissue drug residues prior to birth or from drinking colostrum. Tests are available for use on urine or serum samples for certain drugs. Contact your veterinarian, VDACS milk inspector, dairy field rep, or Virginia Tech's Dairy Extension Office if you would like additional information.

Certain factors increase the reliability of using antibiotic residue screening tests. These include:

- What test is used on your farm? Will this test detect drugs used on your farm? Are other tests more appropriate for drugs in use on your farm? Choose a screening test that is appropriate for detecting the antibiotic administered.

- Do not treat cows who have little chance to respond, e.g., for example, cows chronically infected with Staphylococcus aureus.
- Test milk that is visually normal.
- Test composite milk rather than foremilk.
- If test result is negative, milk is acceptable to add to bulk tank.
- If test result is positive, continue to withhold milk from bulk tank and retest cow in 24 hr. plus conduct California Mastitis Test (CMT) to determine if somatic cell count is high. If cow continues to test positive, submit milk sample to milk coop or processor for confirmatory test (Andrew, 1997).

California studies have found high rates of false positive results when cows with clinical mastitis were tested prior to treatment, causing them to conclude that some of these test kits will "cause milk to be discarded unjustifiably far beyond current regulatory withdrawal times"(Cullor et al., 1993). False positive outcomes were reported with Delvotest P, Cite Probe, and Charm Farm, but not with LacTek or Bacillus stearothermophilus Disc Assay (BSDA). The last two tests are not on-farm tests. When we observed that a considerable number of cows treated with either penicillin or cephapirin remained drug positive at the end of the withholding period, we used the BSDA test. At that time, the Delvotest and Penzyme test were the only farm screening tests and they detected 17% false positive readings, which were due either to differences between sensitivities of tests or natural inhibitors in milk (Seymour et al., 1988). Subsequently, we tested composite milk samples taken from cows with clinical mastitis before any treatment and compared four farm screening tests to BSDA with the following percent positive tests: BSDA, 6.0%; LacTek, 10.0%; Penzyme, 11.4%; Delvotest, 17.2%; and Cite Probe, 40.0%. Some of the cows were treated intramammary with one of two antibiotics and some were positive at the end of the withholding period: BSDA, 0/12 cows; LacTek, 0/12; Penzyme, 4/12; Delvotest, 1/12; and Cite Probe, 8/12. With respect to antibiotic residue screening of individual cows, we must not lose sight of the fact that some cows do produce milk positive with antibiotic residues at the end of the recommended withholding period when treated according to label directions. Without screening individual cows, a dairy farm risks adding positive milk to the bulk tank. With screening individual cows, a dairy farm risks disposal of milk that might be antibiotic free. This author prefers the second risk to the first when he considers the cost of a contaminated bulk tank of milk. The safest approach is to add no milk from a positive cow to your bulk tank.

## DRUG SCREENING TESTS FOR ON-FARM USE

Many drug residue tests are shown in Table 2 (see following page). Included is the claimed minimum detection limit for different drugs as well as the ability of the test to detect the recommended violative level in 15 spiked milk samples in studies at Virginia Tech (Bishop et al., 1992). For example, penicillin has a "safe" level of 10 ppb and a recommended violative level at 4.8 ppb. In the study by Bishop et al. (1992), all 15 milk samples spiked with 10 ppb were positive by all tests. With amoxicillin and cephapirin, all tests detected 15 of 15 positive samples at 10 and 20 ppb, respectively. For cloxacillin, only the Delvo Express could detect 15 out of 15 samples spiked with 10 ppb. LacTek, which is not an on-farm test, detected 14 of 15 positive samples or 93 percent, but this test is not very sensitive for ceftiofur. Although the "safe" concentration for ceftiofur has been established at 1,000 ppb, results in Table 2 were reported for concentrations of 50 ppb, which most tests are capable of detecting. Determine which tests are useful for the drugs administered on your farm. For example, Delvotest P detects oxytetracycline but not at the recommended violative levels. Other tests are more appropriate. Dairy producers may be testing milk from cows treated with either of these drugs and the test will not detect levels near the recommended violative level, whereas the milk plant may be using a more sensitive test. Dairy farmers should know which drugs have been used on the farm and discuss with their veterinarians which drug residue test(s) are appropriate, especially if such drugs as dihydrostreptomycin, novobiocin, spectinomycin or streptomycin were used.

## USE OF DRUGS ON VIRGINIA DAIRY FARMS

Shown in Table 3 are the percentages of 347 dairy herds that indicated which drugs were used on their farm. The most commonly used were penicillin, oxytetracycline, cephapirin, amoxicillin, cloxacillin, and gentamicin. Of these herds, 53 percent used an on-farm drug residue test, mostly Delvotest P. However, Delvotest P is

**Table 2. Drug Screening Tests and Detection Levels (Boeckman and Carlson, 1998)**

| Test | Drug (Claimed Levels/Tested) | | | | |
|---|---|---|---|---|---|
| | **AMOXI** | **AMPI** | **CEFT** | **CEPH** | **CLOX** |
| Rec. Viol. Level[a] | 10 | 10 | 1,000(50)c | 20 | 10 |
| Charm II | 8 bb | 6 b | 7 b | 4 b | 10 (23) |
| Charm Cowside | 10 b | 10 b | 16 b | 6 b | 30 ( 7) |
| Charm Farm | 10 b | 10 b | 25 b | 20 b | 45 ( 7) |
| Delvo Express | 9 b | 7 b | 12 b | 4 b | 50 b |
| Delvotest P | 5 b | 4 b | 50 b | 8 b | 25 ( 0) |
| Delvotest SP | 6 b | 8 b | 70 (80) | 8 b | 20 ( 0) |
| Lactek | 7 b | 5 b | 44 ( 7) | 19 b | 8 (93) |
| Penzyme | 6 b | 6 (93) | 80 (93) | 12 b> | 80 (13) |
| Penzyme II | 5 b | 7 b | 80 b | 14 b | 80 ( 0) |
| Cite Snap | 9 | 8 | 10 | 3 | 50 |
| | **DIHYSTR** | **ERYTH** | **HETA** | **NEOMY** | **NOVOB** |
| Rec. Viol. Level[a] | 125 | 50 | 0 | 150 | 100 |
| Charm II | 50 | 25 (87) | 10 | 20 (13) | 100 b |
| Charm Cowside | | 50 | 10 | | |
| Charm Farm | | 200 ( 7) | 10 | 150 b | |
| Delvo Express | | | 10 | | |
| Delvotest P | 5,000 | 500 ( 0) | 8 | 150 b | 500 ( 0) |
| Delvotest SP | | 250 ( 0) | 8 | | 500 ( 0) |
| Lactek | | | 10 | | |
| Penzyme | | | 7 | | |
| Penzyme II | | | 6 | | |
| Cite Snap | | | 10 | | |
| Neomycin | | | | 10 b | |
| | **OXYTET** | **PEN** | **PIRSU** | **SULDF** | |
| Rec. Viol. Level[a] | 30 | 4.8 | 400 | 10 | |
| Charm II | 19 b | 3 b | 100 | 4 b | |
| Charm Cowside | | 4 b | 100 | 10 b | |
| Charm Farm | 100 (33) | 5 b | 100 | 10 (93) | |
| Delvo Express | | 5 b | | | |
| Delvotest P | 300 ( 0) | 3 b | 80 | 10 ( 0) | |
| Delvotest SP | 400 ( 0) | 3 b | 50 | ( 0) | |
| Lactek | 30 | 4 b | | | |
| Penzyme | | 5 b | | | |
| Penzyme II | | 4 b | | | |
| Cite Snap | 30 Tetr | 4 | | | |
| Cite Sulfa | | | | 10 | |

[a]*"Recommended violative" level at which regulatory action will be taken. This also may be a "safe" level or concentration or tolerance.*

[b]*Percent Sensitivity or percent positive samples out of 15 spiked milk samples (Bishop et al., 1991). Those designated "b" had a sensitivity of 100%.*

[c]*Level at which test was conducted.*

*Abbreviations for Drugs: AMOXI = Amoxicillin, AMPI = Ampicillin, CEFT = Ceftiofur, CEPH = Cephapirin, CLOX = Cloxacillin, DIHYSTR = Dihydrostreptomycin, ERYTH = Erythromycin, HETA = Hetacillin, NEOMY = Neomycin, NOVOB = Novobiocin, OXYTET = Oxytetracycline, PEN = Penicillin, PIRSU = Pirsue, SULDF = Sulfadimethoxine,.*

not dependable for detecting cloxacillin, dihydrostreptomycin, erythromycin, gentamicin, novobiocin, or oxytetracycline. Of the herds that used oxytetracycline, 44-60 percent used the Delvotest to test for a possible residue. A higher percentage of high producing herds used penicillin (90 percent), oxytetracycline (68 percent), and gentamicin (32 percent), and a higher percentage used on-farm residue tests for all three drugs.

**Table 3. The use of specific drugs by 347 Virginia dairy farms reported in a 1991 mail survey.**

| Drug | % of Herds Using | &Using On-Farm Test[a] |
|---|---|---|
| Amoxicillin | 27 | 50 |
| Ampicillin | 15 | 62 |
| Cephapirin | 35 | 56 |
| Cloxacillin | 24 | 48 |
| Dihydrostreptomycin | 10 | 47 |
| Erythromycin | 16 | 49 |
| Gentamicin | 22 | 45 |
| Hetacillin | 5 | 44 |
| Novobiocin | 12 | 48 |
| Oxytetracycline | 44 | 55 |
| Penicillin | 79 | 57 |

apercent of herds that used this drug that tested milk with an on-farm residue test sensitive to that drug.

## Summary for Safe Drug Use

1. Read and follow label directions.

2. Administer drugs properly including teat end preparation.

3. Mark and identify all treated cows.

4. Keep a written record of all treatments and communicate this to all milkers.

5. Milk all treated cows last using special precautions such as separate milking units and remove fill pipe from bulk tank.

6. Discard milk from all 4 quarters of all treated cows.

7. Avoid "home-brews."

8. Test every cow with appropriate screening test.

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