
U. S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
July 23, 2001

Interpretation of Pasteurized Milk Ordinance (PMO) Appendix N Testing Program for Drug Residues (M-a- 86) (Revision 3)

TO: All Regional Food and Drug Directors
Attn: Regional Milk Specialists

FROM: Chief, Milk Safety Team (HFS-626)

SUBJECT: Appendix N Testing Program for Drug Residues

This interpretation was referred to the NCIMS delegates in accordance with the "Guidelines for Issuing Interpretations of the *Grade "A" Pasteurized Milk Ordinance* (PMO) and Related Documents" by the NCIMS Executive Board. After deliberation, the delegates accepted a modification to the definition of Presumptive Positive. Revision 3 has incorporated the modification into this memorandum.

This interpretation provides accountability, and assists States in their efforts to achieve uniformity. It further clarifies the industry responsibilities for testing bulk milk pickup tankers for drug residues and the States' responsibilities in the monitoring of industry programs in the implementation of Appendix N of the PMO.

For purposes of this interpretation the following definitions are to be used:

Presumptive Positive: A presumptive positive test is a positive result from an initial testing of a tanker using an M-a-85 (latest revision) approved test, which has been promptly repeated in duplicate with positive and negative controls, using the same test on the same sample, with one or both of these duplicate retests giving a positive result.

Screening Test Positive (Load Confirmation): A screening test positive result is obtained when the presumptive positive sample is tested in duplicate, using the same or equivalent tests (M-I-96-10, latest revision) as that used for the presumptive positive, with a positive and negative control, and either or both of

the duplicates are positive and the controls give the proper results. A screening test positive (load confirmation) is to be performed by an Official State Laboratory, Officially Designated Laboratory or Certified Industry Supervisor using the same or an equivalent test (M-I-96-10, latest revision).

Producer Trace Back/Permit Action: A producer trace back/permit action test is performed after a screening test positive load is identified by an Official State Laboratory, Officially Designated Laboratory or Certified Industry Supervisor, using the same or an equivalent (M-I-96-10, latest revision) test as was used to obtain the screening test positive (load confirmation). A confirmed producer test positive result is obtained in the same manner as a confirmation (screening test positive) for a load. After an initial positive result (producer presumptive positive) is obtained on a producer sample, that sample is then tested in duplicate using the same test as was used to obtain the producer presumptive positive result. This testing is performed with a positive and negative control, and if either or both of the duplicates are positive and the controls give the proper results, the producer sample is confirmed as positive.

Individual Producer Load: An individual producer bulk milk pickup tanker is a tanker (or a compartment of a tanker) that contains milk from only one dairy farm.

Industry Analyst: A person under the supervision of the Certified Industry Supervisor or Industry Supervisor who is assigned to conduct screening of bulk milk pickup tankers for Appendix N drug residue requirements.

Industry Supervisor/Certified Industry Supervisor: An individual trained by the State Laboratory Evaluation Officer (LEO) who is responsible for the supervision and training of Industry Analysts who test bulk milk pickup tankers for Appendix N drug residue requirements.

Certified Industry Supervisor: An Industry Supervisor who is evaluated and listed by a State LEO as certified to conduct drug residue screening tests at industry drug residue screening sites for PMO, Appendix N regulatory actions (confirmation of tankers, producer trace back and/or permit actions).

Certified Industry Supervisors; Evaluation and Records:

References: *Evaluation of Milk Laboratories* (EML) and IMS-a-30, Supplement 2

Certified Industry Supervisors/Industry Supervisors/Industry Analysts: Regulatory Agencies may choose to allow Industry Supervisors to be certified. Under this program, these Certified Industry Supervisors may officially confirm presumptive positive tanker loads and confirm producer milk for regulatory purposes (producer trace back/permit action). In the implementation of Appendix N of the PMO, the LEO will use the appropriate Appendix N 2400 series form when evaluating Official State Laboratories,

Officially Designated Laboratories or Certified Industry Supervisors, Industry Supervisors and Industry Analysts.

The Certified Industry Supervisor/Industry Supervisor shall report to the LEO the result of all competency evaluations performed on Industry Analysts. The names of all Certified Industry Supervisors, Industry Supervisors and Industry Analysts (as well as their training and evaluation status) shall be maintained by the State LEO and updated as replacement, additions and/or removals occur. The State LEO shall verify (document) that each Certified Industry Supervisor and/or Industry Supervisor has established a program that ensures the proficiency of the Industry Analysts they supervise. The State LEO shall also verify that each Industry Supervisor and Industry Analyst has demonstrated proficiency in performing drug residue analysis at least biennially. Verification may include an analysis of split samples and/or an on-site performance evaluation or another proficiency determination that the State LEO and the Laboratory Quality Assurance Branch (LQAB) agree is appropriate.

Failure by the Industry Supervisor or Industry Analyst to demonstrate adequate proficiency to the LEO shall lead to their removal from the LEO list of Industry Supervisors and/or Industry Analysts. Reinstatement of their testing status shall only be possible by completing retraining and/or successfully analyzing split samples and/or passing an on-site evaluation or otherwise demonstrating proficiency to the LEO. (See IMS-a-30, Supplement 2, which describes the certification requirements for Certified Industry Supervisors and the training requirements for Industry Supervisors and Industry Analysts).

Sampling and Testing of Bulk Milk Pickup Tankers: The bulk milk pickup tanker shall be sampled after the last producer has been picked up and before any additional commingling. The sample must be representative. The sample analysis shall be completed before the milk is processed.

Tanker Unloaded Prior to Negative Test Result: If the bulk milk pickup tanker is unloaded and commingled prior to obtaining a negative test result and the screening test is positive, the State Regulatory Agency shall be immediately notified. The commingled milk is unacceptable for human consumption. The milk shall be disposed of under the supervision of the State Regulatory Agency.

Bulk Milk Pickup Tanker Screening Test Procedures (See Attachment):

Performance Tests/Controls: Each lot of test kits purchased shall be tested by positive (+) and negative (-) controls, as defined in the Attachment to this document, in each screening facility prior to its initial use and each testing day thereafter. Records of all positive (+) and negative (-) control performance tests shall be maintained.

Initial Drug Testing Procedures: The following procedures apply to testing bulk milk pickup tankers for drug residues following the provisions of Appendix N. Industry analysts may screen tankers and receive or reject milk. Milk plants, receiving stations,

transfer stations and other screening locations may choose to participate in the Industry Supervisor Certification Program.

Industry Presumptive Positive Options: There are two industry options for the milk represented by a presumptive positive sample:

1. The State Regulatory Authorities involved (origin and receipt) shall be notified. The appropriate State Regulatory Authority shall take control of the presumptive positive load. A written copy of the presumptive positive test results shall follow the initial Regulatory Agency notification. Testing for confirmation of that presumptive positive load shall be in an Official State Laboratory or Officially Designated Laboratory or by a Certified Industry Supervisor at a location acceptable to the State Regulatory Authority. Documentation of prior testing shall be provided to the analyst performing the load confirmation. The presumptive positive load may be re-sampled (at the direction of the State Regulatory Agency) prior to analysis with the same or equivalent test (M-I-96-10, latest revision), as was used to obtain the presumptive positive result. This analysis shall be done in duplicate with positive and negative controls. If either or both of the duplicate samples are positive and the positive and negative controls give the correct reactions, the sample is deemed a Screening Test Positive (Confirmed Load). A written copy of the test results shall be provided to the Regulatory Agency. The milk, which that sample represents, is no longer available for sale or processing into human food.
2. The owner of the presumptive positive milk may reject the load without further testing. At that time the milk represented by the presumptive positive test is not available for sale or processing into human food. The milk cannot be re-screened. The State Regulatory Authorities involved (origin and receipt) shall be notified. Under this option, producer trace backs shall be conducted.

Re-sampling:

(Presumptive Results)-Occasionally, an error in sampling or a suspicious test result is discovered after a presumptive result is initially obtained. When this happens, the State Regulatory Agency may allow the industry to re-sample the bulk milk pickup tanker. The reasons that made the re-sampling necessary shall be clearly documented in testing records and reported to the State Regulatory Agency. This written record shall be provided to the State Regulatory Agency and shall be maintained with the record of the testing for that load.

(Screening Test Results)-Re-sampling or additional analysis of screening test results should be discouraged. However, the State Milk Regulatory Agency may direct re-sampling and/or analysis, when it has determined that procedures for sampling and/or analysis did not adhere to accepted NCIMS practices (Standard Methods, 2400 Series Forms, Appendix N and the applicable FDA interpretative or informational memoranda). This decision by the State Regulatory Agency must be based on objective evidence. A State Regulatory Agency allowing re-sampling must plan a timely follow-up to identify the problem and initiate corrective action to ensure the problem that led to the need for

re-sampling is not repeated. If re-sampling and/or analysis is necessary, it shall include a review of the samplers, analysts, and/or laboratories to identify the problem(s) and initiate corrective action to ensure the problem(s) is not repeated. The reasons that made the re-sampling or analysis necessary shall be clearly documented in testing records maintained by the State Regulatory Agency, and shall be maintained with the record of the testing for that load.

All screening test positive (confirmed) loads must be broken down (producer trace back) using the same or an equivalent test method (M-I-96-10, latest revision).

Confirmation tests (load and producer trace back/permit action) shall be performed by an Official or Officially Designated Laboratory or Certified Industry Supervisor. Positive producers shall be handled in accordance with Appendix N of the PMO.

Assuring representative samples from individual-producer loads and multiple-farm tank loads from an individual producer. Representative samples shall be secured from each farm storage tank(s) of milk prior to loading onto a bulk milk pickup tanker at the dairy farm. The representative sample(s) shall travel with the bulk milk pickup tanker to a designated location acceptable to the State Regulatory Agency.

Record Requirements: Results of all testing may be recorded in any format acceptable to the State Regulatory Agency that includes at least the following information:

- Identity of the person doing the test,
- Identity of the bulk milk pickup tanker being tested* ,
- Date/time test was performed (Time, Day, Month & Year),
- Identity of the test performed/lot #/any & all controls,
- Results of test,
- Follow-up testing if initial test was positive/any & all controls,
- Site where test performed, and
- Prior test documentation shall be provided for a presumptive positive load.

*Include the BTU number(s) of the farms present on the bulk milk pickup tanker with the above information.

Copies of this memorandum are enclosed for your distribution to Regional Milk Specialists, State Milk Regulatory Agencies, State Laboratory Evaluation Officers and State Milk Rating Officers in your region. This memorandum is also available on the CFSAN World Wide Web site at <http://www.cfsan.fda.gov>. This memorandum should be widely distributed to representatives of the milk industry and all other interested parties.

Steven T. Sims, Acting Chief
Milk Safety Team

ATTACHMENT

Screening Tests Necessary to Implement the Provisions of Appendix N for Bulk Milk Pickup Tankers

A. Performance Tests/Controls:

1. Each lot of kits purchased is tested by positive (+) and negative (-) controls.
2. Each screening facility runs a positive (+) and negative (-) control performance test each testing day.
3. All NCIMS approved bulk milk pickup tanker screening tests include the following format: All presumptive positive test results are to be repeated in duplicate as soon as possible at the direction of the State Regulatory Agency on the same sample with single positive (+) and negative (-) controls by a certified analyst (Official State Laboratory or Officially Designated Laboratory or Certified Industry Supervisor) using the same or equivalent test (M-I-96-10, latest revision).

If the duplicate tests, with appropriate control results are negative (-), the tanker is reported as negative. If one or both duplicate test(s) is positive (+), the test result is reported to the State Regulatory Agency as a screening positive.

4. All positive (+) controls used for drug residue testing kits are labeled to indicate a specific drug and concentration level for that drug.
 - For tests that only detect Penicillin, Ampicillin, Amoxicillin & Cephapirin, the positive (+) control is Pen G @ 5 ± 0.5 ppb.
 - For test kits validated for the detection of Cloxacillin, the positive (+) control may be Cloxacillin @ 10 ± 1 ppb.
 - For test kits validated for one drug residue only, the positive (+) control is $\pm 10\%$ of the safe level/tolerance of the drug residue detected.

B. Work Area:

1. Temperature within specifications of the test kit manufacturer's labeling.
2. Adequate lighting for test kit procedure.

C. Test Kit Thermometers:

1. Thermometer traceable to a National Institute of Standards and Technology (NIST) Certified Thermometer.
2. Graduation interval not greater than 1°C .
3. Dial thermometers are not used to determine temperatures of samples, reagents, refrigerators, or incubators in milk laboratories.

D. Refrigeration:

1. Test kit reagent storage temperature specified by manufacturer.
- E. Balance (Electronic):
1. 0.01 g for preparation of positive (+) controls.
 2. Balance with appropriate sensitivity for calibration of pipetting devices within a tolerance of $\pm 5\%$. These devices may be calibrated at another location acceptable to the State LEO.
- F. Screening Test Sampling Requirements:
1. Temperature of milk in the bulk milk pickup tanker determined and recorded.
 2. Representative bulk milk pickup tanker sample for drug residue testing collected.
 3. Samples tested within 72 hours of collection.
- G. Screening Test Volumetric Measuring Devices:
1. Single use devices provided by kit manufacturers are acceptable for Appendix N screening analysts.
 2. NCIMS Certified Laboratories require calibrated pipetting/dispensing devices. These devices may be calibrated at another location acceptable to the State LEO.
 3. Measuring devices with tips bearing calibration lines provided by test kit manufacturers are acceptable for Appendix N screening.