

**Appendix N Pilot Program
Question and Answer
Version 3.0
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DRAFT**

This Q&A document answers questions that have been submitted to the NCIMS Appendix N Modification Study Committee. The start date for the Pilot Program for the testing of the tetracycline class of drugs is subject to the NCIMS Board review and has yet to be determined.

Purpose of the Pilot Program

The Pilot Program is being developed by the Appendix N Modification Study Committee in response to NCIMS Proposal 2015 #211, and refers to the development of a Pilot Program, which will establish a regulatory framework by which testing raw milk for veterinary drugs would be required for drugs other than beta-lactams.

The purpose of the Pilot Program is to identify possible hurdles likely to be encountered by stakeholders in implementing this program, and to identify solutions to address these challenges through a potential future testing framework (i.e., through formalized requirements of the program into the PMO). Participation in the Pilot Program ensures that representative perspectives will be obtained, thus providing a strong foundation for a future program that meets the individual needs of all stakeholders.

1. Participation.

1.1. Who is expected to participate in the Pilot Program?

At the October 7-8, 2015 NCIMS Executive Board meeting, the Chair expressed the following in a consensus statement: "... we as a Board should look at participation by member States of the conference, as well as Grade "A" milk facilities, to be expected." Member States include all 50 States and Puerto Rico. Likewise, it's expected that those milk facilities in the International Certification Program (ICP) participate.

1.2. Are the following facilities expected to participate in the Pilot Program?	
Facility type	Participation
Dairy facilities	All IMS-listed milk plants (milk plants as defined in the PMO) are expected to participate.
Transfer stations and receiving stations	Participation by transfer stations and receiving stations (as defined in the PMO) is not expected at this time for purposes of the Pilot Program. However, if a transfer or receiving station is screening milk for tetracycline class of drugs (oxytetracycline, tetracycline and chlortetracycline) instead of that load being screened at the milk plant, the milk plant is responsible for maintaining the documentation to show that the load of milk received at that milk plant has been screened for tetracycline class of drugs and to ensure the required testing frequency of one out of every 15 loads is met
Facilities that receive Grade “A” raw milk and produce either non-Grade “A” dairy products or non-dairy products (e.g., milk is an ingredient in a formulated food) – but no Grade “A” dairy products	Participation is not expected at this time, however, should a non-IMS listed Grade “A” milk plant desire to participate in the Pilot Program, they should contact their State Regulatory Agency for guidance.
Facilities that receive Grade “A” raw milk but do not ship Grade “A” dairy products out of state	Participation is not expected at this time, however, should a non-IMS listed Grade “A” milk plant desire to participate in the Pilot Program, they should contact their State Regulatory Agency for guidance.
Facilities that receive Grade “A” non-cow raw milk	Expanded testing for drugs other than beta-lactams will initially be limited to Grade “A” cow raw milk only. Testing of non-cow milk for non-beta-lactam drugs will be discussed in the future.

1.3. How will industry be initially informed about the Pilot Program?

The Regulatory Agency will contact industry within their States with information concerning the Pilot Program.

1.4. How and when will industry know if a particular state is participating in the Pilot Program?

If a State plans to participate in the Pilot Program, it will contact industry before the implementation date. If a facility desires to participate in the Pilot Program and has not been contacted by their Regulatory Agency, they should express their interest, review the program materials on the NCIMS website and ask their Regulatory Agency for guidance.

1.5. Would it be permissible if a State chooses to support industry with an industry agreement and perform Tetracycline testing in the State lab on bulk milk pickup tankers to meet the Pilot Program requirements?

Nothing would prohibit this testing from occurring. Records shall be kept by Regulatory Agency and/or industry to demonstrate compliance with the frequency of testing. Care must be taken to ensure no confirmed positive tetracycline milk enters the human or animal food chain.

1.6. If a State and/or industry is/are experiencing hurdles with implementing the Pilot Program, what is the process for resolving those hurdles?

The NCIMS Executive Board Chair expressed in the consensus statement at the October 7-8, 2015 Executive Board meeting: “We recognize that States are going to have individual challenges, and we respect those; and we will work with those States and try to be of assistance as much as possible as they face those.” Industry is expected to discuss logistical details (e.g., on testing protocols, approval/certification by LEOs, facilities, reporting, etc.) with their State(s) and ideally come to agreement in advance of testing. If industry and a State(s) are unable to implement the Pilot Program, then that issue shall be brought forward to the Appendix N Modification Committee to identify a potential solution. If a consensus cannot be reached, the issue shall be communicated to the NCIMS Executive Board for resolution.

1.7. May a company with multiple milk plants decide on a milk plant-by-milk plant basis whether or not to participate in the Pilot Program, or must all milk plants within a given State or part of the same company have the same participation status?

All IMS listed milk plants are expected to participate after coming to agreement on logistical details with their State(s) in advance of testing. Refer to 1.2 and 1.3.

2. Drug Residue Selection.

2.1. What drug residue has been chosen as the first residue for the Pilot Program?

The tetracycline class of drugs, oxytetracycline, tetracycline and chlortetracycline, was chosen as the first drug residue for the Pilot Program.

2.2. Why was the tetracycline class of drugs selected?

There were 8 drug families recommended by FDA based on the *Multicriteria-based Ranking Model for Risk Management of Animal Drug Residues in Milk and Milk Products*. The tetracycline class of drugs was selected based on use on dairy farms, availability of test methods, and speed of implementation.

3. Frequency of Testing.

3.1. How many Grade “A” raw milk samples are required to be tested for tetracyclines by a milk plant as part of the Pilot Program?

The Pilot Program requires no less than 1 out of 15 (~6.7%) bulk milk pickup tankers and/or all raw milk supplies that have not been transported in bulk milk pickup tankers of Grade “A” raw milk to be tested for tetracyclines calculated on a quarterly basis. However, this would not prohibit testing at a greater frequency if a milk plant desires to do so.

3.2. How are the 1 out of 15 (~6.7%) bulk milk pickup tankers and/or all raw milk supplies that have not been transported in bulk milk pickup tankers of Grade “A” raw milk to be selected for tetracycline testing?

It is up to each individual milk plant or company, in consultation with the Regulatory Agency, to determine how to best comply with the overall requirements of testing 1 out of 15 (~6.7%) bulk milk pickup tankers and/or all raw milk supplies that have not been transported in bulk milk pickup tankers calculated on a quarterly basis.

To meet the overall requirement of 1 out of 15 (~6.7%) bulk milk pickup tankers and/or all raw milk supplies that have not been transported in bulk milk pickup tankers, calculated on a quarterly basis, a milk plant could, for example:

- Select two days each month to perform tetracycline testing (e.g., the first and third Wednesdays of each month) within a quarter,
- Select a week(s) within a quarter to test every bulk milk pickup tanker,
- Implement a random sampling program within the quarter, or
- Select other means to meet the requirements.

A milk plant is allowed to change their testing program in consultation and agreement with the Regulatory Agency.

Providing for testing during each quarter will minimize data gaps when determining tetracycline drug residues in the milk supply (for example, accounting for any usage patterns of tetracycline drugs related to seasonal animal health issues). Allowing each milk plant to best determine how to meet testing requirements, while taking into consideration limitations and logistics of testing equipment, lab personnel, budgets, etc., will minimize disruption and cost to operations (for example, a company may purchase new testing equipment and test at one milk plant, and then transfer the equipment to another milk plant to test). Assuming that every milk plant will not follow the exact same testing schedule, we expect there to be an inherent randomness to testing as it is implemented across the industry.

3.3. When a milk plant tests 1 out of 15 (~6.7%) bulk milk pickup tankers and/or all raw milk supplies that have not been transported in bulk milk pickup tankers of Grade "A" raw milk for tetracyclines, is there a corresponding reduction in the number of beta-lactam tests that are required to be performed?

No. At this time, this Pilot Program does not affect the current Appendix N beta-lactam testing program. Individual milk plants will still be required to test every bulk milk pickup tanker and/or all raw milk supplies that have not been transported in bulk milk pickup tankers of Grade "A" raw milk received for beta-lactams; and States will continue to conduct finished product testing for beta-lactams. The Pilot Program to test 1 out of 15 (~6.7%) bulk milk pickup tankers and/or all raw milk supplies that have not been transported in bulk milk pickup tankers for tetracyclines is in addition to current regulatory obligations.

Proposal 211 states that the Pilot Program shall consider the potential for reducing beta-lactam testing of raw milk in future Conference actions in a manner consistent with FDA's recommendations.

3.4. Will the Pilot Program impact the residue testing requirements for finished product?

No. Finished product testing for drugs other than beta-lactams is not included in the Pilot Program.

3.5.a. Would each compartment of a multi-compartment milk tanker be considered a separate unit such that if tetracycline testing was conducted on each compartment, each test would count as an individual test?

Yes.

3.5.b. How would compliance be calculated (1 out of 15 (~6.7%)) when multiple-compartment tankers are received?

Each compartment/unit would be considered a separate bulk milk pickup tanker for the purposes of calculating 1 out of 15 (~6.7%) of tests to be performed. As long as at least 1 out of 15 (~6.7%) tankers are tested each quarter, a milk plant may decide to test all, some or none of the individual compartments/units of a multi-compartment milk tanker.

4. Test Methodology.

4.1. What tetracycline class of drugs test methods will be used as part of the Pilot Program?

The Pilot Program will utilize FDA evaluated and NCIMS Appendix N Modification Committee accepted or previously NCIMS approved/accepted (M-a-85, latest revision) test methods for screening, confirmation, producer trace back and reinstatement.

In conjunction with the NCIMS Laboratory Committee, Tetracycline Pilot Program Forms for the Pilot Program only will be developed for use with new test methods through the Pilot Program.

4.2. May a milk plant refuse or reject a load of milk based on an initial positive tetracyclines test result?

A milk plant can refuse or reject a load of milk, but must complete the test. Refer to the 2015 NCIMS Proposal 211 Pilot Program Accepted Tetracycline Test Kit Using Both Undiluted and Diluted Steps Flow Chart. An Initial Positive does not represent a completed test; the testing must continue through the Presumptive Positive Determination (to the dotted line on the flowchart).

This would be handled in the same way as for beta-lactams. M-I-03-13, question 82, states that a plant may not just run one test from a tanker for beta-lactams, get a positive result and reject the load. The plant laboratory must test the milk in accordance with Appendix N guidelines and confirm the Presumptive Positive sample by promptly running this initial sample in duplicate with positive and negative controls prior to rejection.

In addition, M-I-12-9, question 71, states that industry and the Regulatory Agency are required to follow the testing protocol, reporting, trace back, etc. as cited in Appendix N when tests other than beta-lactams that have been evaluated by FDA and accepted by NCIMS, such as the Charm II Tetracycline (Competitive Assay), are being utilized.

4.3. What does it mean on the 2015 NCIMS Proposal 211 Pilot Program Accepted Tetracycline Test Kit Using Both Undiluted and Diluted Steps Flow Chart that after an Initial Positive at the same facility the same test kit must be used? Does it mean the same test method or does it mean the same test kit from the same lot?

The statement "At the same facility utilizing the same test kit..." refers to the same test method (type of test kit), and does not refer to the same lot numbers.

4.4. Are dairy plants allowed to share their equipment and reagents with other dairy plants?

This would be allowable under the Pilot Program in consultation with the Regulatory Agency (ies). However, this would require properly trained industry analysts for that method at each site. Refer to Question 3.2 for industry's responsibilities responsibility concerning the Pilot Program.

4.5. How would the Charm II Tetracycline test kit work with the pilot program?

The Charm II is an M-a-85 approved test for tetracyclines. It can currently be used for initial screening, confirmation, trace back and reinstatement.

4.6. Would it be acceptable to use the same sample for both beta-lactam and tetracycline testing?

Yes.

4.7. When running the "diluted sample" protocol, are the controls to be diluted as well?

Please refer to the Tetracycline Pilot Program Forms for the accepted/approved Tetracycline Pilot Program test methods.

4.8. How much will the testing platforms cost? What is the cost of the test strips?

Contact test kit manufacturers for this information.

5. Reporting Test Results.

5.1. Are tetracycline testing results to be reported to the 3rd Party Database (National Milk Drug Residue Database, (NMDRD))? If so, how often?

Tetracycline testing performed to meet the requirements of the Pilot Program is expected to be reported to the NMDRD. For the purpose of the Pilot Program, Regulatory Agencies are expected to report their data on a monthly basis to aid the Appendix N Modification Committee and NCIMS Executive Board in evaluating the Pilot Program.

To obtain a more representative view of the rate of violative milk samples, milk plants are expected to report the total number of tests performed and screening test positive (confirmation) results to the Regulatory Agency on a monthly basis.

5.2. What test results will be reported to the third party database?

Test results will be reported the same way as with the current beta-lactams program; number of tests performed and number of confirmed positive test results. An Initial Positive does not represent a completed test and therefore can't be reported.

5.3. What type of reporting form will be used by the industry to report results to the Regulatory Agency?

Industry will use the same form currently used in the beta-lactam program for reporting tetracycline results. (Drug Residue Report Form).

6. Pilot Program Duration.

6.1. When will the Pilot Program for testing of the tetracycline class of drugs start?

The effective date for the implementation of the 2015 NCIMS Proposal 211 Pilot Program has not been finalized. It is dependent on FDA CVM evaluation of test methods for acceptance in the Pilot, and the completion of the "Tetracycline Pilot Program" laboratory forms based on FDA CVM acceptance of submitted methods. The Appendix N Committee's best estimate of the effective date pending the completion of the tasks mentioned will probably be in the second quarter of 2017.

6.2. How long will the Pilot Program continue testing for the tetracycline class of drugs?

The Pilot Program will continue testing for the tetracycline class of drugs until a minimum of 18 months of data are generated by each Regulatory Agency for the Appendix N Modification Committee to review testing results and make recommendations.

6.3. At the conclusion of the Pilot Program, will tetracycline testing continue? Will another drug be added for testing?

This is yet to be determined. The Appendix N Modification Committee will be sharing a current status report of the Pilot Program at the 2017 NCIMS Conference.

7. Enforcement Actions for Violative Results

7.1. Will the producer be charged for violative loads of milk under the Pilot Program?

A goal of the Pilot Program is to assure that milk testing positive for tetracyclines does not enter the human or animal food chain. Costs associated with disposal of a violative load of milk will be handled between the producer and the milk supplier.

7.2. What regulatory actions are expected to occur specific to the dairy producer(s) found to

be responsible for a confirmed tetracycline positive test which led to raw milk being removed from the human or animal food chain?

What must occur is upon official notification to the Regulatory Agency and milk producer of a violative individual producer's milk for tetracycline, suspension of permit or equally effective measures shall be taken to prevent the sale of milk containing drug residues and further farm pickups by bulk milk pickup tankers and/or farm use of the violative individual producer's milk shall be immediately discontinued, until such a time, that subsequent tests are no longer positive for drug residues. Producers that test Positive shall have a Negative sample utilizing the diluted protocol for the NCIMS Proposal 211 Pilot Program Accepted Tetracycline Test Kit Using Both Undiluted and Diluted Steps (Flowchart), or an M-a-85 approved test method for tetracycline (currently only the Charm II).

7.3. Will a violative load of milk (for tetracyclines) count against a producer's permit as in counting as a violation toward permit revocation if repeated three times in a twelve-month period?

Unless an individual Regulatory Agency's statutory authority dictates otherwise, in consideration of the fact that this testing regimen is a Pilot Program and not currently incorporated in the PMO, then the answer is no.