Department of Food Science

Milk Safety

FSE 99-21

Preventing Antibiotic Residues in Milk

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The occurrence and detection of antibiotic residues in milk continue to be concerns for the dairy industry. Several steps have been taken to assure the public that the milk supply is safe. Many dairy producers have voluntarily adopted the 10-point "Milk and Dairy Beef Residue Prevention Protocol." This relies on the HACCP concept to "manage out" the hazards by close attention to critical control points. On the regulatory front, increased surveillance and testing have been mandated.

Standard Test

For years, the standard for antibiotic testing has been the *Bacillus stearothermophilus* disc assay method. This was the official test for regulatory use. A few other tests which mimic the results of the disc assay were also approved. They were designed to detect residues of penicillin, the most commonly used antibiotic. Penicillin may still be the antibiotic of choice for treating selected diseases of lactating cows. However, other antibiotics are now being used. Many of these antibiotics are being used in an "extra label" fashion. That is, they are prescribed by veterinarians to be used in a way not indicated by the manufacturer's labeling information. Often, this means that the withholding times necessary before the milk can be used for food are not well established. Antibiotic residues above the FDA-established "safe" or tolerance levels could be present. The disc assay is not adequate to detect antibiotics at this level nor does it effectively detect the range of antibiotics currently used.

Random Testing

To detect milk with antibiotic residues above the legal limit, regulatory agencies have relied on random and regularly scheduled sampling of producer and market milk. Many plants have tested for penicillin residues on a regular or intermittent basis. In addition to the official tests,(i.e., the disc assay) and some screening tests designed to reproduce the results of the disc assay, additional screening tests appeared on the market. Some of these screening tests had the ability to detect penicillin-like beta lactam antibiotic residues at lower levels than could be tested by the official tests. New tests appearing on the market also detected antibiotics other than the beta lactams, prompting widespread reports of antibiotic residues in milk.

A Testing Dilemma

With the increasing sensitivity of new antibiotic tests, the question turned in two directions:

1. Of what significance are low level antibiotic residues?
2. How does one verify the presence of low level residues when official tests are not designed to operate in those low ranges?

The first point was addressed with the establishment by FDA of "safe levels" and tolerance levels of antibiotics in milk. Residues above these levels were considered to be violative, while those below were not considered to be of public health or regulatory significance. The practical difficulty of detecting these residues resides in the accuracy and precision of the newly developed tests. That leads to the second question.

Confirmatory analytical techniques had to be developed in order to verify the results of new screening tests. This was accomplished for most antibiotics.

Evaluation and standardization of these tests remained to be done. Since screening tests had been developed to detect many individual antibiotics and families of antibiotics, regulatory agencies began with the most common antibiotics. Screening tests which detect the beta lactam family of antibiotics were the first to be evaluated.

Evaluation of Screening Tests

Screening tests were evaluated by FDA for six antibiotics in the beta lactam family: penicillin, ampicillin, amoxicillin, cloxacillin, cephapirin, and ceftiofur. Only tests successfully completing FDA evaluation may be used for official testing. The

criterion was established that the test must detect four of the six antibiotics. An abbreviated summary of the results is shown in Table 1.

As we can see from the table, no test regularly detects all the target antibiotics at the "safe" or tolerance level. Some, such as the Delvo-X-Press with ceftiofur or the Charm II with cephapirin, detect residues well below the legal limit and could cause legal milk to be rejected or subjected to further regulatory action. The acceptance of these tests ends the industry option to use other non-evaluated screening tests, including the disc assay, to fulfill regulatory testing requirements.

Residue Monitoring and Surveillance

As of 1992, industry is required to 1) screen all bulk milk pickup tankers for beta lactam residues prior to processing, and 2) collect four random samples for FDA testing in separate months during every consecutive six months. Random sampling is at the discretion of the regulatory agency. Regular audit of the industry program by the regulatory agency requires samples of 10 percent of the tankers on site the day of inspection to be checked quarterly. When a positive tanker is found, the regulatory agency must be notified, the violative producer identified, and further pickups from that producer discontinued.

A producer's Grade "A" permit will be suspended when the regulatory agency is notified of a positive drug residue. After completion of at least one milking (or one milking plus two days for the second violation in a 12 month period), the producer may be reinstated if an official milk sample tests negative. This is provided the Milk and Dairy Beef Residue Prevention Protocol is in place on the farm. Should the protocol not have been instituted, it shall be in place within 30 days from the date of the reinstatement. The third occurrence in a 12-month period requires the two-day suspension and initiation of procedures to revoke the producer's permit.

The Screening Program

The effectiveness and fairness of the residue monitoring and surveillance program hinges on the proper choice of the antibiotic screening test to be used and its proper application by the analyst. In order that the industry might meet the requirements to screen every bulk milk pickup tanker prior to its being processed, FDA hasestablished training and certification procedures for industry analysts. As of July 19, 1994, all bulk milk tanker drug screening tests must be performed by either an Industry Supervisor, or an Industry Analyst. In order to understand these procedures, the following terms are defined:

Industry Supervisors (IS) are designated industry representatives who are trained by state LEO's to perform specific official drug screening tests. They and their "backup supervisors" are to supervise their company's screening program and train IA's.

Industry Analysts (IA) are analysts designated and trained by Industry Supervisors to perform drug residue screening tests. The IA's certification is only valid for the time his Industry Supervisor's certification is valid.

State Laboratory Evaluation Officers (LEO) have attended FDA's test kit workshops are eligible to train Industry Supervisors. They have the responsibility to train and certify industry personnel and laboratories.

Certified Industry Supervisors (CIS) are analysts in an official NCIMS certified laboratory who are certified to perform various tests for regulatory action.

Industry Supervisors, or their designated IA, may screen bulk milk pickup tankers. They may not open a regulatory sample to identify a positive producer. However, a certified analyst or a CIS may split the sample in an NCIMS Certified Laboratory. In order for regulatory action to be taken for or against a producer, it must be based on the results from an NCIMS Certified Laboratory. Laboratories can be certified to do drug testing only.

An Analysis of the Program

The milk industry hasmade excellent progress in a relatively short time. It has gone from random screening for penicillin and a few other residues to screening of every load of milk for at least four beta lactam antibiotics. In addition, random sampling of bulk milk pickup tankers provide for the testing of other residues by regulatory agencies. The validation of new screening kits and the training of analysts leaves some questions unanswered. Some of these are:

What about the other antibiotics? The newly approved tests detect only four, or at most, five beta lactams. What about the several other families of antibiotics currently available for use?

What about the problem of overly sensitive tests? All of the approved tests will detect at least one antibiotic at levels below the legal limit. This could cause legal milk to be rejected resulting in severe economic losses for the producer.

What about testing individual cow samples? The new kits were tested and approved for commingled milk samples. The producer does not have at his disposal tests which have been shown to be satisfactory for testing the milk from an individual cow prior to reintroducing her to the milking string.

Testing is Not the Answer

Above are just a few of the problems associated with efforts to ensure quality and safety by testing. The rest of the food industry and the manufacturing industries are rapidly becoming less dependent on testing as the mainstay of their quality programs. In its place, the principles of HACCP or TQM are being employed. The 10-point Milk and Dairy Beef Residue Prevention Protocol has been designed to return the residue prevention activity to where it belongs — to the producer level.

Antibiotic therapy takes place at the producer level. Nothing the processor or the regulatory agency can do will prevent antibiotic residues from occurring in bulk tank milk, though they may be able to screen out some violative loads. The prevention of antibiotic residues sits squarely on the shoulders of the producer and his veterinarian. It is the producers' management practices and their exercise of control in antibiotic therapy programs which can prevent residues in the milk supply. The penalties for violations are severe. A producer may lose his permit to ship milk and with it his livelihood. Consumers, the industry, and the government are speaking with one voice: "Antibiotic residues are not acceptable in the milk supply and the responsibility lies with the producer — the producer alone."

Abbreviations

CIS	Certified Industry Supervisors
FDA	Food and Drug Administration
HACCP	Hazard Analysis, Critical Control Points
IA	Industry Analysts
IS	Industry Supervisors
LEO	Laboratory Evaluation Officer
NCIMS	National Conference of Interstate Milk Shippers
PMO	Grade "A" Pasteurized Milk Ordinance
TQM	Total Quality Management

In Memorium
Dr. Donald P. Wesen passed away on July 25, 1994. His work will be sorely missed by his friends in the dairy industry of North Carolina.