codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

JOINT OFFICE: Viale delle Terme di Caracalla 00100 ROME Tel: 39 06 57051 www.codexalimentarius.net Email: codex@fao.org Facsimile: 39 06 5705 4593

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS
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PROPOSED DRAFT APPENDIX ON THE PREVENTION AND CONTROL OF VETERINARY DRUG RESIDUES IN MILK AND MILK PRODUCTS

Governments and international organizations wishing to submit comments on the following subject matter are invited to do so **no later than 3 February 2003** as follows: U.S. Codex Office, Food Safety and Inspection Service, US Department of Agriculture, Room 4861, South Building, 14th and Independence Avenue, S.W., Washington, DC 20250, USA (Fax No: +1.202.720.3157; e-mail: uscodex@usda.gov), with a copy to the Secretary, Codex Alimentarius Commission, Joint FAO/WHO Food Standards Programme, FAO, Viale delle Terme di Caracalla, 00100 Rome, Italy (Telefax: +39.06.5705.4593; E-mail: Codex@fao.org).

BACKGROUND

The 13th Session (December 2001) of the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF) considered a document presented by the United States concerning the control of veterinary drug residues in milk and milk products. The Committee noted that the *Guidelines for the Establishment of a Regulatory Programme for Control of Veterinary Drugs in Foods,* which was intended to apply to all foods when adopted in 1993, might require a total revision to reflect current Codex risk analysis guidelines and other recent developments related to the control of veterinary drug residues, especially since the proposed draft Appendix duplicated many aspects of and it was becoming as comprehensive as the Guidelines, while dealing only with milk and milk products. It was also noted that the proposed draft Appendix should more adequately reflect the prevention of drug residues at the farm level, including control, monitoring and detection of drug residues in raw milk.

The 13th CCRVDF agreed to return the draft Appendix on the Prevention and Control of Drug Residues in Milk and Milk Products to Step 2 for redrafting by the United States on the basis of the Committee's discussions as well as the Proposed Draft Code of Hygienic Practice for Milk and Milk Products and written comments submitted, for circulation, comments and further discussion at its 14th Session. It was also noted that this revision should take account of the review of the *Guidelines for the Establishment of a Regulatory Programme for the Control of Veterinary Drug Residues in Foods* (ALINORM 03/31, paras. 59-62).

As directed above, governments and international organizations are invited to comment on the attached proposed draft Appendix to the Guidelines for the Establishment of a Regulatory Programme for Control of Veterinary Drug Residues in Foods, concerning the prevention and control of veterinary drug residues in milk and milk products.

PREVENTION AND CONTROL OF DRUG RESIDUES IN MILK AND MILK PRODUCTS

(prepared by the United States)

INTRODUCTION

1. Milk and milk products are a rich and convenient source of nutrients for people in many countries. Of particular significance, milk and milk products form a large portion of the diet of sensitive subpopulations (e.g., infants, children, pregnant women, and lactating women) in some countries. The improper use of veterinary drugs in dairy animals may result in consumers being exposed to potentially harmful residues through milk and milk products. The purpose of this document is to provide guidance to countries so that their appropriate level of public health protection for milk and milk products may be achieved.

1 OBJECTIVE

2. The objective of this document is to apply the principles of the *Guidelines for the Establishment of a Regulatory Programme for Control of Veterinary Drug Residues in Foods* to the particular case of milk and milk products. In so doing, it provides guidance on an overall program for the prevention, control and monitoring of potentially harmful veterinary drug residues in milk and milk products.

2 NEED FOR MILK RESIDUE CONTROL - NATURE OF PROBLEM

3. The improper use of drugs in the treatment of lactating and nonlactating dairy animals can result in milk containing concentrations of drug residues in excess of established Maximum Residue Limits (MRLs), thereby rendering the milk unsuitable for human consumption and for food product manufacturing. In addition to being a human food itself, milk is often used in the manufacture of other human food products. This provides multiple paths for drug residues to occur in other human food products. The overall strategy for the prevention of potentially harmful, or violative, drug residues in milk and related food products, therefore, relies heavily on suitable procedures and drug use at the farm level.

4. As an example, a typical event that may result in the contamination of milk with drug residues exceeding the MRL is the failure to withhold the milk from treated animals for a time sufficient to allow drug residues in the milk to deplete below the MRL. The decisions associated with the administration of drugs to dairy animals occur at the farm level. Since the goal of a milk residue avoidance program is to prevent contamination of milk with potentially harmful drug residues, appropriate prevention and control practices must be employed at the farm level.

3 PREVENTION OF DRUG RESIDUES IN MILK

5. The prevention and control of potentially harmful residues of veterinary drugs in milk and milk products requires a collaborative effort from a number of parties, including milk producers and manufacturers, veterinarians, and governmental authorities. All parties need to fulfill their respective roles to prevent the contamination of milk and milk products with potentially harmful residues. It is important for the maintenance of a safe milk supply that clear communication and cooperative interaction exist among the parties to ensure that best practices are followed, that problems are identified and that resolutions are achieved.

6. An over-arching principle for the prevention and control of potentially harmful drug residues in milk is that good hygienic and veterinary practices should be applied throughout the production process, thereby reducing the likelihood of animal disease and, concomitantly, the need for the use of veterinary drugs. Thus, veterinary drugs should be used only when necessary and as a complement to, but not a replacement for, good management, vaccination and farm hygiene. As a result of complying with this principle, the occurrence of potentially harmful drug residues in milk will be minimized.

3.1 Responsibilities of the Milk Producer and Veterinarian

7. The primary responsibility for the prevention of potentially harmful drug residues in the milk resides with the dairy producer, who controls the hygienic conditions of the milk production facility, maintains the environment of the dairy animals and administers drugs to dairy animals. The dairy veterinarian who controls or recommends the selection, administration and the use conditions of drugs administered to dairy animals shares this responsibility. Both the milk producer and the veterinarian share the responsibility to use drugs judiciously, and they should keep a record of the products used, including the quantity, the date of administration and the identity of animals.

8. The cooperation and commitment of the milk producer and the veterinarian are critical to the success of any residue control program. A program to prevent violative residues requires proper management of animal health and drug use by the dairy producer and veterinarian at the farm level. This program may involve the application of disease prevention measures such as the separation and isolation of treated animals from the rest of the production herd, physical marking of the treated animals, record keeping, utilizing separate milking equipment or milking treated animals last. Compliance with drug label directions as well as compliance with any off label guidance or legislation, permitting only trained individuals to administer veterinary drugs and screening of the milk from treated animals prior to commingling with milk from the rest of the milking herd (as further outlined in Section 3.5) are very important drug residue control practices.

3.2 Responsibilities of the Milk Industry

9. Industry quality control personnel who educate dairy producers in proper milk handling practices and screen raw milk for drug residues also share the responsibility for assuring a milk supply free from violative drug residues. That responsibility extends to the processing plant quality control personnel who make the final evaluation and screening of the raw milk prior to processing. After the milk has left the farm for processing, industry is responsible for monitoring or screening programs to determine if the commingled raw milk is free of violative drug residues.

3.3 Responsibilities of the Government Authority

10. The government authority's role in the prevention and control of drug residues in milk spans a wide range of functions. First, the governmental authority, adhering to its laws and regulations, should approve or authorize all veterinary drugs for use in dairy animals on the basis of a comprehensive evaluation that includes a detailed safety assessment. From the assessment, the authority should establish the MRL (or its equivalent), identify the residue of a specific drug that will be used for monitoring purposes, select an analytical method for monitoring and enforcement purposes, set the milk withholding time, and ensure that drug product labeling provides clear and detailed direction for use, including the milk withholding time.

11. Government authorities should verify that the prevention systems established by the dairy industry to comply with regulatory requirements are adequate, valid and effective in maintaining a safe milk supply. In addition, government authorities should establish adequate sanctions and enforcement procedures to ensure that milk remains in compliance with MRL requirements. Government authority verification of the industry program may include screening of commingled milk at the farm level, screening of commingled milk at the transport tanker level and testing of finished dairy products for drug residues.

12. Government authorities should review the results of milk monitoring, with particular emphasis on reports of violative residues in milk, investigate for causes of violative residues and take remedial action as warranted. When it is ascertained that a violation arose despite compliance with label directions, including observation of the specified withholding time, the authority should reassess the conditions of use.

13. Government authorities should also encourage concerned parties, as well as the pharmaceutical industry, to contribute to the development of educational programs for dairy producers. Such programs should aim at promoting good husbandry practices including appropriate and prudent use of veterinary drugs.

14. Lastly, all parties responsible for the maintenance of a milk supply compliant with MRLs, including government authorities, should periodically critique their residue control procedures to assure continued adequate performance.

3.4 Audit of Dairy Farm Management and role of HACCP

15. The development of a practical and effective residue prevention program at the dairy production level should begin by identifying those herd management practices which may contribute to the occurrence of violative drug residues. This involves a review of herd management procedures and other milk production techniques for the purpose of identifying critical points in the milk production process where controls and intervention practices are essential to minimize violative drug residues in milk. In reality this strategy is the application of the concepts of prevention and control compatible with the Hazard Analysis Critical Control Points (HACCP) process. The information derived from a HACCP-type risk assessment of milk production operations can be very helpful in developing an effective and efficient drug residue control strategy for milk. Thus, the use of control measures should be based on HACCP principles, wherever practicable. Hazard analysis and design of a HACCP plan by the processor so that milk products are safe may identify the need for additional measures to be taken for hazard control at the production level.

3.5 Principal Characteristics of Milk Residue Control

16. The first step in preventing the occurrence of potentially harmful drug residues in milk is to maintain a healthy herd and employ herd health practices that will minimize the need to use animal drugs. Proper management of the animal's environment by the dairy producer can improve the health of the dairy animal and thereby reduce drug use on the dairy farm. Maintaining hygienic practices that assure cleanliness of the milk production facility and a clean dairy animal environment can have a major impact in preventing the development of disease in the herd, thereby minimizing drug use.

17. There is no single program for the prevention of potentially harmful drug residues in milk that can be utilized for all dairy farms. Dairy farms vary in size, location, environmental conditions, economics and level of management skills. Specific techniques will vary to meet the specific needs of the dairy farm. To be effective, programs need to be practical and effective for the individual dairy producer responsible for the prevention of potentially harmful drug residues in milk.

18. However, regardless of the size of the farm or other variable management practices, it is important that veterinarians and milk producers use drugs according to the approved labeled specifications and observe proper withholding times. These two specifications are critical elements in prevention and control programs. Specific consideration should be given to these critical elements as well as the general standards of good veterinary practice. However, it is recognized that the scope of labeled indications of approved drugs may be insufficient to address the diverse medical needs encountered on the farm, necessitating off label drug use by veterinarians. Any off label use should ensure food safety and comply with off label guidance or legislation.

19. Animal drugs and syringes used for drug administration should be located and stored in an area that will exclude accidental contamination of milk, the storage vessel and the milking equipment with drugs or drug residues. In addition, all drugs should be labeled with information pertinent to the proper and safe use of the drug. This information should include the identity of the drug, including any batch or production numbers, the directions for use including milk withholding times, any special precautions, storage conditions, expiry date and the name and address of the manufacturer.

20. Because the information on the label of the drug is designed to prevent the occurrence of violative drug residues in milk, milk producers should follow the label instructions carefully and keep accurate records of drug use on each treated dairy animal. These records should capture such information as the date, time, identity, dosage, and route of administration of the drug and appropriate milk withholding times. In the case where the drug is prescribed for use in a manner different from what is approved on the label, the name and address of the veterinarian who prescribed it, the specific conditions of use and the milk withholding and slaughter withdrawal intervals should appear on the label.

21. In addition, all treated animals should be physically identified and isolated when practical. To assure that milk from treated animals is not accidentally commingled prior to the end of the recommended withholding time with milk offered for sale, separate equipment must be used to collect this milk or these treated animals should be milked after the equipment has been isolated from the milk storage vessel. The milk from treated animals should be discarded or diverted to other permitted uses that have been approved to protect the human food chain. Milk from treated animals may be offered for sale if the withholding time as well as other labeled instructions have been followed.

4 MONITORING FOR DRUG RESIDUES IN MILK

22. The prevention of violative drug residues in milk is a proactive undertaking which depends primarily upon suitable procedures, practices and drug use being exercised at the farm level. Prevention of conditions that may result in residues in milk above the MRL is always the best and most cost effective public health policy.

23. Nevertheless, an effective residue monitoring program can play a major role in the prevention and control of potentially harmful residues of veterinary drugs in milk by identifying where and when violations have occurred, the causes of the violations, and what steps could reasonably be taken to prevent recurrence in the future. Moreover, the ability to analyze data from a monitoring program to track trends in residues and to assess seasonal, farm practice or usage patterns, is a valuable feedback tool to ensure that regulatory agencies have confidence in the overall prevention and control program.

4.1 Functions of Residue Monitoring

24. Residue monitoring programs are intended to ensure compliance with prescribed veterinary drug use and assure the safety of the milk supply. These programs can involve the screening of raw commingled milk at the farm or during transport, the diversion and disposal of milk found to contain potentially harmful drug residues, and an investigation to determine the cause of the residue. Remedial actions can be educational in nature to promote and ensure proper use of animal drugs or involve legal action by government authorities against the producer causing the violative drug residue. Thus, the monitoring program can, through trace back, yield residue prevention benefits.

25. Monitoring programs can also serve as an important tool for the control of milk containing violative residues. They can identify the existence of violative residues, thereby indicating that milk should not be consumed or be used for the production and processing in a human food product; as a result, the safety and wholesomeness of milk and milk products are maintained.

4.2 Components of a Monitoring Program

26. The two main components of a milk monitoring program are sampling and analytical testing.

27. In designing a sampling program, consideration should be given to where samples are collected. The concentration of residues in milk decreases, as does the ability to trace back violations, as the distance from the animal increases (farm bulk milk>tanker>silo); concomitantly, economic penalties, should milk be found to contain violative residues, increase as the distance of the milk from the farm increases. From a practical standpoint, therefore, sampling at the dairy farm or the milk transport tanker level is recommended.

28. At the milk processing plant, the testing for residues should be done prior to the processing of the raw fluid milk. This allows intervention to occur prior to the use of the milk in the manufacture of milk and milk-based products. Focusing at this level will also reduce the volume of contaminated commingled raw milk, the potential contamination of processing equipment and finished dairy products. This strategy also prevents unnecessary delays that can result in the loss of a safe and wholesome milk supply.

29. With respect to analytical testing, rapid screening tests and validated methods to quantitate and confirm the identity of detected drugs form the cornerstone of a successful monitoring program.

30. Ideally, screening tests would be available for the entire spectrum of drugs used in dairy animals. Presently, international organizations have certified commercially available rapid screening methods for drug residues in milk, primarily beta-lactams. The availability of rapid screening methods for drug residues in milk allows monitoring programs to systematically test large numbers of raw commingled milk samples for residues, thereby decreasing the probability that milk containing violative residues would reach consumers or be used to manufacture milk based products.

31. Government authorities usually require both quantitative and qualitative data that will allow identification of the suspected violative drug residue in milk because this information is typically used to enforce laws or other regulations. Because screening tests generally are not sufficiently quantitative and specific, it is recommended that suitably validated laboratory methods of analysis for measurement and confirmation of a drug residue be available (confirmation further outlined in Section 4.4). These methods are normally more sophisticated than the screening assays and require more time to complete.

4.3 Factors Affecting Milk Residue Monitoring

32. The procedures used in the collection and manufacture of milk usually involve the commingling of milk from individual animals. In practice, this means the milk intended for human consumption is considered to originate at the farm bulk tank and not directly from individual animals. Monitoring of residues in the farm bulk milk holding tank offers the practical advantages of clear identification of the farm that caused a violative drug residue and allows effective remedial or regulatory action by producers and authorities.

33. Rapid test kits for drug residues in milk have been developed for use on raw milk. Milk added to the bulk tank should come from animals that are healthy or from animals that have been judged healthy by a veterinarian for milking purposes if they had been under treatment. This allows for a relatively consistent milk matrix for use with the test kits thereby permitting good analytical performance.

34. Although the use of the more sophisticated methods for measurement and confirmation of drug residues in milk would obviate the matrix variability, these tests would likely take a longer time to perform, be too expensive for most dairies and, consequently, require shipping of a milk sample to a laboratory. Because fresh milk has a limited shelf life, the use of these sophisticated tests for manufacturing acceptance decisions could be an impediment to the provision of a wholesome product to consumers. However, if government authorities are considering legal action in a milk residue monitoring situation, the use of the more sophisticated methods would likely be necessary.

35. Although commingling of milk is an inherent part of the collection and processing of milk, the dilution effect has an impact in the analytical testing aspects of residue monitoring. For example, if the raw milk collected at the dairy farm is diluted by a factor of 100 when the farm milk is added to the milk holding tank at the milk processing facility, then the occurrence of a residue of a drug (e.g., ampicillin) of 100 micrograms/kg in the farm bulk tank would result in a fluid milk product of 1 microgram/kg.

36. Dilution via commingling also results in a progressively more difficult drug residue monitoring problem. Analytical methods exist that can detect ampicillin in the bulk tank at concentrations as low as 5 to 10 micrograms/kg. The limit of detection of the methods available for ampicillin provides a high probability that violative residues in the non-commingled milk in the above example would be detected. However, after further commingling of the milk in the milk processing facilities holding tank, the probability of detecting residues is significantly reduced.

37. The above discussion draws attention to the fact that while drug residue analytical monitoring programs can provide many advantages in detecting and correcting drug residue occurrences, the analytical methods also have limitations wherein potentially harmful drug residues in milk could escape detection and remediation.

38. Apart from the effect on analytical determinations, commingling has additional significant consequences. Antibiotic residues in milk can have a negative impact on those milk manufacturing processes where microflora are used. Furthermore, sensitive individuals can react, for example in an allergic manner, to very low drug residue concentrations. Therefore, it must be emphasized that it is not permissible to commingle milk containing potentially harmful residues in order to attain lower drug residue concentrations in milk.

4.4 Necessity for Screening Test Confirmation

39. The need for confirmation of screening test results prior to initiation of regulatory action cannot be overemphasized. Although it would be desirable for screening assays not to give false positives, to avoid false negatives screening assays sometimes do yield false positives. Thus, many screening tests do not give a positive response at one unique drug concentration; rather they give a positive response over a range of drug residue concentrations. This characteristic of some screening tests is not a deficiency or malfunction of the test but results from the way in which the screening test was technically developed. This results in a situation where a screening test positive result may be a true analytical positive but occurs at a concentration below the MRL. A confirmation procedure can determine whether a screening test positive result is an actual violative result.

40. There is no single scientific strategy for confirming analytical results. The configuration of a confirmatory procedure depends on the intended use of the confirmatory data. Government authorities generally require both quantitative information and data that will allow identification of the drug or chemical residue in milk because this information is typically used to enforce laws or other regulations. In all cases, however, it is essential that the confirmatory procedure be validated, i.e., be demonstrated to be fit for the intended use. Government authorities may require that the confirmatory methods meet internationally recognized and accepted performance criteria.

41. Verification of the initial test results with alternative test methods can provide greater confidence in the residue status of the milk. This is based on the premise that the function of a screening test is to give a highly reliable indication when the milk may contain drug residues above the MRL. A positive screening test result provides evidence or suspicion of the presence of a violative drug residue and that further investigation or action is warranted. Stated in another way, a negative result with a properly validated screening test means that no further testing is necessary for drug residues that are capable of being detected by the screening test.

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