codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 8 **CX/RVDF 01/8-Add.1**
November 2001

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS
Thirteenth Session, 4-7 December 2001
Charleston, South Carolina, USA

COMMENTS ON THE CONTROL OF VETERINARY DRUG RESIDUES IN MILK AND MILK PRODUCTS

AUSTRALIA

1. Australia has the pleasure of submitting the following comments in relation to the Codex Committee on Residues of Veterinary Drugs in Foods request for the above issue.

2. Section 2.1. The first sentence should highlight that the use of 'dry-cow' intra-mammary treatments in non-lactating animals can lead to residues when lactation recommences.

3. Section 3.1. Third paragraph, last sentence should be amended to read "Compliance with label directions and preventing the milk from treated animals from commingling with the milk from the rest of the herd (as further outlined in section 3.5) are very important prevention practices".

4. Section 3.3. First paragraph, second sentence should be amended to read "Effective control of drug residues also includes regulatory measures such as the licensing of drugs and the provision to the user of acceptable and unambiguous conditions of use".

5. Section 4.2. At the end, or at the beginning of this section a statement should be included along the lines of: "Government/regulatory agencies and industry should work together to achieve an outcome of preventing milk with violative residue levels entering milk and milk products processing, and of preventing milk/milk products with violative residues reaching consumers. It should be industry's decision to determine whether it is economic to test milk at farm level (and therefore facing smaller scale losses if violative residues are detected), or before milk (from several farms) enters milk processing (and therefore facing larger losses is violative residues are detected). When making this decision the industry should consider limits of detection methods for some residues."

6. Section 4.5. Paragraph two, there is a sentence that reads: "Screening test values significantly less than the reference values could mean .....". Is it possible for a screening test result to equal fortified but not incurred residue concentrations (as quantified by the reference analytical method)? If so, this information should be included.

7. Section 4.7. The comments provided for 4.2 above are also valid here.

BRAZIL

8. Brazil supports the document and informs that it will take into account its recommendations in the implementation of its monitoring programs of veterinary drugs residues in milk.

CUBA

9. We believe the document contains the fundamental elements to design monitoring programs for veterinary drugs in raw milk from milk cows, and we agree that the prevention of said residues in raw milk and in related food products is based on the procedures and use of drugs at the farm level.

FINLAND

10. First of all we have some suggestions in the structure and form of the text. The text deals with the drug residues in milk in general, but the details and examples are only concerning antimicrobial residues which are the most common veterinary drug residue in milk. The screening tests available are only for testing the antimicrobials. Milk industry cannot be expected to screen for all other drug residues. Testing other residues is expensive and time consuming. We suggest that the heading and the text should only deal with the antimicrobials like "prevention and control of antimicrobial drug residues in milk and milk products". We also suggest that the text should be divided in three sections taking into consideration the different stakeholders: 1) prevention, 2) laboratory methods and 3) monitoring and control.

11. In the section 2 Introduction the misuse and the abuse are explained to be the main reason to the drug residues. We have an experience that the most common reason is a mistake on farm level. When the antibiotics are prescription only medicines the great responsibility lies on the user i.e. farmer. Thus we suggest that the first sentence in the section 3.1. should be: "The prevention of drug residues in the milk supply is the responsibility of the milk producer, veterinarians, the dairy industry and the regulatory authorities". It should also be emphasised that education on good medication practises and book keeping of medications are important factors in preventing drug residues in milk.

12. In the section 4.2 Factors Affecting Milk Residue Monitoring should be stressed that it is not acceptable to dilute milk in order to reach lower residue concentrations in milk. The antimicrobial residues have negative impact on those milk manufacturing processes where microbial flora is used. Furthermore sensitive persons can react even at low concentrations of residues.

13. In the section 4.3 The Effect of Milk Processing it should be stressed that processing is not an acceptable way of dealing with the residues known to exist in a milk consignment. Research on the effects of cooking temperatures on the potency of antimicrobial drugs is not sufficient. In heat treatment drugs can form new compounds even more toxic.

NEW ZEALAND

General Comments

14. The paper is provided as an appendix to the existing Codex Guideline for the Establishment of a Regulatory Programme for Control of Veterinary Drug Residues in Foods (CAC/GL 16-1993). That 1993 Guideline gives principles that should be considered when developing a regulatory programme, a significant amount of detail on sampling for specific foods including milk, and some general considerations and attributes on the analytical methods for residues of veterinary drugs in foods. The 1993 Guideline establishes that platform for the Milk and Milk Products paper, which should provide further specific information on what may be considered in a regulatory programme for milk and milk products.

15. The objective of the paper is to present elements for consideration in the design of programmes for the monitoring of drug residues in raw milk of dairy animals. The paper has a very strong focus on preventative programme concepts, as well as discussing how to design a monitoring programme to confirm that the preventative programme is working. The objectives of the paper may need to be reconsidered in light of the preventative focus and also the progress made in the area of food safety, which is reflected in the Codex Code of Hygienic Practice for Milk and Milk products. This is currently under development, and also focuses on preventative measures.

16. The paper should explain more specifically the relationship between screening results found in raw milk and an MRL that applies in the raw milk or the final food. The goal of minimising or eliminating all residues from all milk (raw, for human consumption, ingredients, and milk products) is strongly supported, but the relationship of screening methodology to confirmatory tests that must meet MRL requirements in legislation may be more simply explained in a separate section. The paper does touch on this in several places, but a specific section would be useful.

17. The paper is specific to dairy cattle. If that is the intention, this should be specified in the title. If the intention is that the paper apply to the milk of other common dairy animals (e.g. goats, sheep, buffalo), then the text should be revised accordingly.

Specific Comments

18. Section 3.5 - Principal Characteristics of Milk Residue Control. This section focuses on what should be considered in designing a preventative programme. The paper does not recognise the system for setting veterinary drug label conditions and its impact on control of milk residues within the regulatory programme.

19. The level of residues in milk will decrease as distance from the animal increases (bulk farm milk > tanker > silo), due to dilution. There are many causes of residues in milk: mistakes by the farm operator (e.g. misreading the veterinary drug's label), changes in farm practice, changes in farming conditions such as seasonal conditions, an error in the withholding period assessment, or errors in data supplied to support the withholding period assessment. Violations of MRLs should be investigated to determine the origin of the violation. Where it is ascertained that a violation arose despite compliance with the withholding period, the Competent Authority responsible for withholding period assessment should be informed of the circumstances.

20. Similarly, changes in dairy animal management may impact on residue withholding periods to the extent that the practice proposed in original assessments may need to be reassessed as new information on farm and animal practices comes to hand. The paper should reflect this reassessment review process as a function of the Competent Authority's role in the licensing and approving of veterinary drugs.

21. Section 4.1 - Function of Residue Monitoring. The first sentence of the second paragraph states: "It is important to keep in mind that residue detection programmes are not intrinsically designed to prevent or remediate residue contamination problems." An effective residue monitoring programme can remedy contamination by identifying where the contamination has occurred, the cause of it and what steps could reasonably be taken to prevent recurrence in the future. Thus, the importance of traceback and remedial measures once a violation has been found should be further emphasised in the paper.

22. The ability to use data from a monitoring programme to track trends in residues, even if MRLs have not been violated, to indicate seasonal, farm practice or usage patterns, is also a valuable feedback tool to ensure that Competent Authorities have confidence in the preventative programme.

23. Section 4.3 - The Effect of Milk Prcoessing. The paper moves away from raw milk to the effects of processing into an ingredient or food. New Zealand agrees that validated methodology to relate milk residues in fluid milk with those residues that end up in processed products like butter and cheese is completely lacking. The

effect of fractionation and other technologies is also unknown and needs investigation to establish their impact on international trade.

24. Sections 4.4 to 4.7 - Monitoring Methodology Development and Validation. These sections provide a very detailed discussion on method development and validation. The integrity and robustness of sampling and methodology has already been discussed in some detail in the 1993 Guideline. The area is extremely technical and expertise is needed to have confidence in the decision-making processes to recognise methodology for a monitoring programme. Discussion in the paper should be focussed on dairy specific issues that are not managed by the 1993 Guideline.

SPAIN

25. During the 11th Session of the Committee on Veterinary Drug Residues, it was agreed that the control program for residues in milk and milk products would be extended to include all species that produce milk for human consumption, not just milk from cows and its derived products.

26. Document CX/RVDF 00/12, presented by the United States during the 12th Session of the Committee, did not capture that recommendation, which had been approved in the prior session, a fact which caused the European Union, in document CRD 19, to reiterate that it should comply with what had been agreed upon. The delegation of Spain, supported by other delegations, also made a statement to that effect during the 12th Session.

27. In the English language version of CX/RVDF 01/8, which is presented for discussion during the 13th Session of the Committee, this agreement has been taken into account, although two errors have been missed. In paragraph 3 of Section 3.5 of the document, there are two times where only the word "cow" is mentioned, and we suggest substituting the expression "dairy animals" for "dairy cows," and, for the same reason, in paragraph 2 of Section 4.5 replacing the expression, "Lactating dairy cattle" with "Lactating dairy animals". Also, on page 2, section 1, the expression: "… of dairy animals", should be changed to: "… of all dairy animals species".

28. These changes should be included in the Spanish and French language versions.

SWITZERLAND

29. Switzerland would like to suggest that the title on page 2 "Prevention and control of drug residues in milk and milk products" should be changed into "Prevention and control of antimicrobial veterinary drugs in milk and milk products".

30. Switzerland supports the following comments made by the International Dairy Federation (IDF):

- The IDF is of the opinion that more emphasis should be placed on the prevention of drug residues at farm level, including control, monitoring and detection of drug residues in raw milk.

- The term "milk" and "milk product" should be used in compliance with the definitions as provided in Codex STAN 206-1997 (General Standard for the Use of Dairy Terms). The term "milk" is defined as the unprocessed (raw) milk; whereas processed milk, including pre-packed drinking milk, is considered as "milk product".

CONSUMERS INTERNATIONAL

31. Consumers International commends the United States for this excellent document. Consumers International notes the large role that milk and milk products play in the diet of infants and children and pregnant women, at least in some countries, and that the greater exposure by these sensitive subgroups underscores the need to

minimize and prevent residues as much as possible. To emphasize this, we suggest the following modification to section 2.1:

> The misuse and the abuse of drugs in the treatment of lactating dairy animals can result in the contamination of milk with levels of drug residues in excess of established Maximum Residue Limits (MRL's) thereby rendering the milk unsuitable for human consumption and for food product manufacturing. In addition to being a human food, milk is also a component that 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. Also, milk and milk products form a large portion of the diet of sensitive subpopulations (e.g., infants, children, pregnant women, lactating women) in some countries, and thus it is desireable to prevent and control drug residues in milk and milk products as much as possible. The overall strategy for the prevention of drug residues in milk and related food products is based on procedures and drug use at the farm level.

32. The report of the twelth session of the Committee noted the view of Consumers International that the recommendations of WHO concerning antimicrobial resistance be incorporated into the document (see. para 122). We continue to believe that the document should reflect these recommendations. It is not clear to what extent antimicrobials are used for non-therapeutic purposes in dairy cows and other milk-producing animals, but there is some indication that they may be used. Meanwhile, there are many efforts at the international level to ensure prudent use of antimicrobials, and it would seem appropriate to include something in this document. The WHO Meeting in Berlin in 1997 (The Medical Impact of the Use of Antimicrobials in Food Animals) recommended (in section III of the report) that:

> "The recommendation made by the previous WHO advisory group (1994) is reinforced: The use of any antimicrobial agent for growth promotion in animals should be terminated if it is: * used in human therapeutics; or * known to select for cross-resistance to antimicrobials used in human medicine.

33. The WHO Global Strategy for the Containment of Antimicrobial Resistance also took up this recommendation, it states:

> "Use of antimicrobial growth promoters that belong to classes of antimicrobial agents used (or submitted for approval) in humans and animals should be terminated or rapidly phased-out in the absence of risk-based evaluations. The termination or phasing-out should be accomplished preferably by volunterary programmes of food animal producers, but by legislation if necessary."

34. This is also taken up in CX/RVDF 01/10, in paragraph 5 and 15. CX/RVDF 01/10 identifies as a specific area for further action that CCRVDF should be involved in reducing the prevalence of bacteria resistant to antimicrobials in animal-derived food (para. 34). And para. 12 of that document states that prudent use of antibiotics seems to be the main tool for preserving the effectiveness of antimicrobials. Therefore, we suggest the following modifications to section 3.1, Responsibilities of the Milk Producer and Veterinarian:

> The cooperation and commitment of the milk producer and the veterinarian are critical to the success of any residue control program. A prevention program 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 animal, record keeping, utilizing separate milking equipment or milking treated animals last. Compliance with drug label directions and screening of the milk from treated animals prior to commingling with the rest of the milking herd are very important prevention practices. Veterinary drugs should be used only when necessary and as a complement to and not a replacement for good management, vaccination and farm hygiene. Non-theraputic use of antimicrobial drugs (e.g., for growth promotion) should be terminated if the antimicrobials are used in human theraputics or known to select for cross resistance to antimicrobials used in human medicine.

EUROPEAN COMMUNITY

35. The European Community would like to thank the United States for redrafting this paper and supports the proposed draft Appendix to the Guidelines for the Establishment of a Regulatory Programme for Control of Veterinary Drug Residues in Foods. However, the European Community would like to present the following comments.

36. Point 2.2. The European Community supports this point and would like to underline the fact that milk controls could be done either at the farm level from the collection tank or it is also possible at the dairy plant level before the bulk tank coming from the farm is discharged, in such a way that it is possible to trace back to the farm of origin.

37. Point 3.5. The European Community believes that the frequency and the groups of substances to be tested in the national residue monitoring plan, should be established with a view to priorities.

38. The control strategy should be decided by the Competent Authorities considering the situation of the country and the risk analysis principles, and the farms should follow the instructions given by the national competent authorities.

39. Point 4.3. The European Community believes that testing for residues should be done on raw milk as it is mentioned in point 4.7. and not on processed milk. The European Community supports the development of pharmacokinetics and metabolism studies about the distribution of drugs in milk.

INTERNATIONAL DAIRY FEDERATION (IDF)

40. The International Dairy Federation welcomes the decision of the Codex Committee on Residues of Veterinary Drugs in Foods to develop guidelines on Control of Veterinary Drugs in Milk and Milk Products and would like to congratulate the United States and its drafting partners on the excellent paper they have prepared.

General Comments

41. The IDF is of the opinion that more emphasis should be placed on the prevention of drug residues at farm level, including control, monitoring and detection of drug residues in raw milk.

42. In this respect, the IDF would like to recall that the modern approach to food safety, which is already reflected in the Draft Codex Code of Hygienic Practice for Milk and Milk Products (currently at Codex Step 3), relies on preventive measures rather than on intermediate and end products testing. In this framework, the testing of milk is intended to make sure that good practices are applied at farm level but not to 'screen' the milk systematically prior to processing.

43. Thus, the IDF would like to stress that the prevention of drug residues in milk is first of all an issue arising at the level of primary production of milk.

44. Finally, the term “milk” and “milk product” should be used in compliance with the definitions as provided in Codex STAN 206-1997 (General Standard for the Use of Dairy Terms). The term “milk” is defined as the unprocessed (raw) milk; whereas processed milk, including pre-packaged drinking milk, is considered as “milk product”.

Specific Comments

45. Section - 1 Objectives. In addition to monitoring, the objective of this document is to provide guidelines on the prevention and control to ensure food safety.

46. Section 2.1 - Need for Milk Monitoring. A more appropriate title could be “Need for Milk Residue Control”.

47. Section (2.3) - Application of MRLs. The IDF would like to point out that established MRLs are applicable to “milk” unqualified. This is often interpreted as the MRLs being applicable for milk from individual teats/animals through to the ready-to-drink/eat milk product. However,

48. MRLs are applied as maximum/target/critical levels in risk management throughout the food chain as follows:

- Milk from individual animals/teats: The MRLs are applied for *determining withholding periods* of individual drugs. From a safety point of view, due to subsequent dilution of the milk (with milk from other teats/animals and other herds during collection/at the plant), the use of MRLs implies the building in of a large safety factor

- Milk from farm bulk tanks: The MRLs are applied for *verification of* whether *good farming practices* have been implemented at the individual farm. Exceeding the MRLs is often combined with penalties. The *objective is preventive* (to assure the farmers focus/commitment). From a safety point of view, due to subsequent dilution of the milk (with milk from other herds during collection/at the plant), the use of MRLs implies the building in of a significant safety factor

- Milk delivered to the plant collection tankers: The MRLs are applied for *verification of* whether the milk is *suitable for processing*, i.e. whether fermentation could be affected. Such verification is not needed for safety purposes.

- Milk products for consumption: The MRLs are applied for *food safety purposes*, i.e. residue levels above the MRLs imply food safety problems

49. The IDF recommends that the various applications of the MRLs, as indicated above, be included in the document, for instance, as a new section 2.3. This location will enable making references to the four levels of verification throughout the document.

50. Sections 3.1/ 3.2 /3.3 – Responsibilities. Although all parties involved in the milk chain have a responsibility and must work together to prevent the occurrence of excessive levels of drugs residues in milk products, it should be emphasized that:

- the responsibility for prevention of drug residues in the milk supply lies mainly with dairy producers and, to some extent, their veterinarians. Other suppliers, including the pharmaceutical and the feed industry, also share this responsibility under the supervision of governmental authorities.

- the dairy industry shares this responsibility when violating levels of residues are found in processed products. In order to avoid this, the dairy industry should apply monitoring and screening programs. Whenever the dairy industry buys semi-processed dairy products, traceability information on the raw material used as well as control data with respect to residues of veterinary drugs, must be provided.

51. Not all veterinary drug users are necessarily aware of 'Good Veterinary Practices', which are referred to twice in the document. This raises the issue of the availability of potentially hazardous drugs to people who are not properly trained. Antibiotics for instance are generally not available for human use without medical prescription, but they may be accessible for use in animals to persons without adequate knowledge.

52. On the other hand, the prescription of antibiotics in human medicine does not prevent misuse of these drugs. Nevertheless, the impact of free access to antibiotics on the magnitude of the problem of residues in milk may not be negligible and may justify more stringent regulatory frameworks in certain countries.

53. The responsibility of government authorities should not be limited to verifying the prevention systems established by the dairy industry. Besides, the paper states that 'residue detection programs are not intrinsically designed to prevent or remediate residue contamination problems'.

54. More emphasis should be placed on the elaboration and enforcement of a prevention program at primary production level, in line with the modern 'farm to fork' approach to food safety.
55. The first step for governments is to implement regulatory frameworks based on both the Codex Recommended International Code of Practice for Control of the Use of Veterinary Drugs (CAC/RCP 38-1993) and the Codex Guidelines for the Establishment of Regulatory Programme for Control of Veterinary Drug Residues in Foods (CAC/GL 16-1993).

56. In line with this, government authorities should encourage all concerned parties, including the pharmaceutical industry, to contribute to the development of educational programmes for dairy farmers. Such programmes should aim at promoting good husbandry practices including appropriate and prudent application of veterinary drugs. The objective should be to decrease and prevent cases of misuse of veterinary drugs in general and, as a consequence, to limit and avoid the presence of hazardous residues in milk and, in the particular case of antibiotics, to limit the development of antimicrobial resistance.

57. Government authorities should also control the implementation of these programmes and verify that they are adequate and effective in preventing misuse of drugs and avoiding violating levels in milk and finished products.

58. Section 3.4 - Role of HACCP. This section should be further elaborated. While it is generally admitted that HACCP systems cannot be fully implemented at farm level, HACCP principles should be used to develop codes of practice or other useful guidelines for the management of dairy herds, which will help dairy farmers in the prevention of drug residues in milk.

59. Section 3.5 - Milk residues control. This section justifiably emphasises the need for proper and complete labelling of veterinary drugs. This is all the more important since these drugs may be used by people with little knowledge of their possible adverse effects on public health. The labelling should provide detailed direction for use, including milk withholding times.

60. The section also emphasises the importance of recording at farm level all information relating to the husbandry of food producing animals which may have an impact on food safety. The information is recorded for each individual animal in the case of milk production, but it may be recorded for flock/herd in the case of other animal productions. It includes in particular animal identification, occurrence of diseases, information relating to the drugs used for treatment: date, time, identity, route of administration, withholding time, as well as any other pertinent observations during the breeding period.

61. While recorded information is part of traceability requirements, it may also be very useful to dairy farmers and veterinarians for improving herd management procedures.

62. Section 4 - Factors Affecting Milk Residues Monitoring. The objective of any monitoring programme should be specified, e.g. prevention of misuse, verification of good farming practice. (see comments in the above proposed paragraphe 2.3 : 'Application of MRLs').

63. After further dilution of milk in the milk holding silo for manufacturing purposes, the probability of detecting residues is significantly reduced.

64. As a general measure of importance to the residue level at all other stages of the food chain, the level of drug residues in milk of each individual cow should be kept under the respective MRLs.

65. Section 4.1 - Method Validation. Determination of antibiotic residues in milk with a chemical reference method (usually HPLC, GC-MS or HPLC-MS) requires a well-equipped laboratory and well-trained staff. It is too expensive for most dairies to have such facilities. The time needed to analyse milk samples using chemical methods could be too long for fresh milk. It may require processing of the milk before obtaining the results of the analyses to avoid loss due to storage of possibly contaminated fresh milk for too long.

66. Analytical methods with detection limits below the MRLs should be used whenever available and, when necessary in case of positive results, confirmation methods should be used for identification and quantification.
67. Section 4.2 - Necessity for Screening Test Confirmation. 2nd paragraph, 1st line, delete the words 'bulk tank', to read: 'Rapid test kits for milk residues have been developed for use on raw milk'. In the same paragraph 3rd and 4th lines, delete the sentence beginning 'This allows for a relatively consistent milk matrix...' up to 'good analytical performance', whose meaning is unclear.

68. All suppliers' milk should be properly sampled before loading onto lorry or truck. If the bulk milk is found to be contaminated, it is then possible to find the responsible milk supplier upon analysing the samples corresponding to the contaminated load.

69. Section 4.3 - The Effect of Milk Processing. The document seems to focus on milk used for drinking (with or without a reconstitution step). This chapter should be further developed. For instance, microbiological fermentation “uses up” any residues. Consequently, control of antibiotic residues in raw milk intended for fermentation, is not a food safety issue, but is related to the processing quality of the milk.

70. No general recommendations can be given by which technological process the residue concentration can be reduced. Processing should not be used under any circumstance to reduce or mask drug residues.

71. Section 4.4 - Data Needed for Monitoring Method Development. For the newer drugs for which MRLs are fixed it is indicated whether the MRL is valid for the mother compound only or for the mother compound and its metabolites. Methods applied in monitoring programs have to be adjusted accordingly.

72. Microbiological screening methods detect microbiologically active compounds, providing positive/negative results.

73. Section 4.5 - Screening Method Validation. What is said in the first part of this section does not reflect the actual situation: unfortunately, reference methods for the validation of screening methods are not always available.

74. Screening methods should have a quantitation limit at least equivalent to the MRLs and must be validated either by comparing their results with the results obtained with chemical methods, or by analysing milks containing known amounts of residues, or by performing recovery analyses with known amounts of determined drugs. It is very important that samples of 'incurred milk', i.e. milk from cows to which the drug has been administered, are included in the validation study.

75. The 2nd sentence of the last paragraph should be changed to: 'Screening tests, if employed, should avoid false negatives'.