

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 Telex: 625825-625853 FAO I E-mail: Codex@fao.org Facsimile: +39(06)5705.4593

Agenda item 5

CX/RVDF 00/4
February 2000

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

Twelfth Session

Washington, D.C., 28 - 31 March 2000

ANTIMICROBIAL RESISTANCE AND THE USE OF ANTIMICROBIALS IN ANIMAL PRODUCTION

BACKGROUND

1. The Codex Committee on Residues of Veterinary Drugs in Foods at its 11th Session received the reports of a WHO Meeting on the Medical Impact of the Use of Antimicrobial Drugs in Food Animals and a WHO Meeting on the Use of Quinolones in Food Animals and Potential Impact on Human Health. It also received a brief report on joint FAO/WHO activities concerning the non-human medical use of antimicrobials.¹

2. The Committee had a lengthy discussions on the use of antimicrobials in animal production.² While acknowledging the occurrence of some public health problems from antimicrobial resistant foodborne commensals and pathogens, some delegations noted that the majority of the current problems were caused by the overuse of antimicrobials in human medicine. However, these delegations expressed concern about the potential human health consequences if resistance in foodborne and animal pathogens were to further increase and spread.

3. Some delegations suggested that CCRVDF should address issues relating to antimicrobial resistance and the safety of food of animal origin and in this regard, suggested that the Codex Alimentarius Commission might wish to consider extending the terms of reference of the CCRVDF accordingly. Whilst supporting that the CCRVDF should address the assessment of health risks from the consumption of food contaminated with resistant bacteria, other delegates pointed out that such an extension would not be necessary as the current CCRVDF terms of reference would already cover the subject of antimicrobial resistance. It was noted that JECFA currently considered the impact of antimicrobial residues on the gut based on available information, but did not consider the transfer of antimicrobial resistance arising from the use of antimicrobials and their release into the environment, which was outside the terms of reference of JECFA.

4. In addition, the Committee noted that there might also be a lack of data on which to build consensus, and that other international organizations such as the OIE, EU and the World Veterinary Association (WVA) were also addressing the subject.

5. The representative of WHO stressed that there was sufficient evidence to cause concern. Addressing them would require a very close collaboration between human and veterinary medicine, agriculture, academia and national agencies. The aim of such collaboration would be, in view of human health, to assess the scope of the problems and to identify mitigation procedures. As food is involved, it would be inevitable that safety and trade related issues would be raised which needed to be resolved at both national and international levels.

¹ ALINORM 99/31, paras 12-25.

² ALINORM 99/31, paras 27-31.

6. *The Committee agreed to further consider this issue at its next meeting, taking into account the activities of other international bodies. This information would be presented to the Committee at its next session.*

7. This paper contains: a summary of discussions and/or decisions of Codex related to antimicrobial resistance since the last session of the CCRVDF; the reports of the activities of the International Office of Epizootics (OIE), World Health Organization (WHO), Food and Agriculture Organizations (FAO) and World Veterinary Association (WVA)/International Federation of Agricultural Producers (IFAP)/World Federation of the Animal Health Industry (COMISA) on antimicrobial resistance in Annex 1; and the extract of the report of the 32nd Session of the Codex Committee on Food Hygiene in Annex 2.

DISCUSSIONS AND/OR DECISIONS RELATED TO ANTIMICROBIAL RESISTANCE WITHIN CODEX SINCE THE 11TH SESSION OF THE CCRVDF

23rd Session of the Codex Alimentarius Commission³

8. The Commission noted the recommendation of the 46th Session of the Executive Committee concerning the urgent need for the Commission to develop international guidelines or recommendations which addressed all the issues relating to animal feeding and that the new mechanism of an ad hoc Intergovernmental Codex Task Force would be an appropriate means of achieving this goal. Several delegations supported the establishment of such a Task Force in view of the great importance attached to consumers' health and practices in international trade. The Commission agreed to establish an ad hoc Intergovernmental Codex Task Force on Good Animal Feeding and to designate the Government of Denmark to be responsible for appointing the Chairperson of the Task Force.

9. Its Terms of Reference include addressing those aspects important for food safety, such as problems related to toxic substances, pathogens, microbial resistance, new technologies, storage, control measures, traceability, etc.. It will work in collaboration with relevant Codex Committees and relevant international bodies, including FAO, WHO, OIE and IPPC⁴. Its First Session is scheduled for 12-14 June 2000.

32nd Session of the Codex Committee on Food Hygiene⁵

10. The CCFH considered a discussion paper which addressed all sources of antimicrobial resistance and referred to the work currently underway in WHO, OIE and FAO in their respective areas of competence. The CCFH had a discussion on whether or not to proceed with the work on this issue. The CCFH agreed that this issue should be considered further at the next session, on the basis of a revised discussion paper in the form of a risk profile. Recognizing the importance of the issue, the Committee also agreed to ask the advice of the Executive Committee and the Commission on how to proceed in order to ensure coordination of work between concerned Committees.

OTHER RELEVANT ISSUES

11. The CCRVDF at its First Session⁶ considered the framework of the Committee. At that time, several delegations expressed concern at the consequences of adding antibiotics to feedstuffs in low doses to increase feed efficiency. It was noted that the joint FAO/WHO Expert Consultation on Residues of Veterinary Drugs in Foods (1984) had thoroughly considered the problems arising from such practices and had thus identified matters of public health concern. The CCRVDF agreed that it should deal only with problems related to the residues of veterinary drugs in foods and not to the possibility of transferring resistant strains to human beings. It was agreed that the latter was a matter of food hygiene which could be referred to the appropriate Codex Committee. The Committee noted that this subject had been the subject of several expert consultations in WHO. At several later sessions, the Committee agreed that it should focus on aspects relating to residues in foods and the control thereof.

12. Antimicrobials are used for therapeutic, prophylactic or growth promotional purposes. For the latter purposes, they are added to feed and/or water, which may fall in the Terms of Reference of the ad hoc Intergovernmental Codex Task Force on Good Animal Feeding. The Agreement on the Application of

³ ALINORM 99/37, paras 230, Appendix VI.

⁴ International Plant Protection Convention.

⁵ See Annex 2 of this document for details.

⁶ October 1986, ALINORM 87/31, paras 130-131

Sanitary and Phytosanitary Measures of the World Trade Organization makes reference to the standards, guidelines and recommendations developed under the auspices of the International Office of Epizootics for animal health and zoonoses, while for food safety it makes reference to the standards, guidelines and recommendations of Codex.

13. The concern on the use of antimicrobials in animal production, especially the use of those also used for humans, has been growing sharply recently. And work and activities of governments and international organizations on this issue have increased accordingly. If, as a result of the work and activities, there are changes in the use of antimicrobials including the ban of some or more of them, they will likely to have certain impact on the MRL setting by JECFA and CCRVDF.

14. As agreed at its last session, the 12th Session of the CCRVDF is expected to further consider issues of the use of antimicrobials in animal production and antimicrobial resistance, and to decide whether or not to proceed with new work on the issue and how. It is important to keep in mind that there is a need for information exchange, close collaboration and coordination with all relevant Codex Committees and international organizations and duplication of work of other bodies should be avoided.

REPORT OF ACTIVITIES OF INTERNATIONAL OFFICE OF EPIZOOTICS (OIE) ON ANTIMICROBIAL RESISTANCE

BACKGROUND:

Concern about the emergence of antimicrobial resistance in bacteria has grown significantly over the recent years, leading some countries to strive for stricter limitation of the use of antimicrobial substances.

The emergence of antimicrobial resistance in pathogenic bacteria raises in particular a problem in human medicine. The use of antimicrobials in livestock production has been suspected, among others, to be a possible cause contributing to the increase of resistance to which humans may be exposed.

Decision of the OIE Regional Commission for Europe, 26-30 May 1997:

Considering the importance of this matter and in relation to its missions, which are

- to inform governments on the existence of animal diseases changes in their distribution world-wide and means of controlling them,
- to coordinate research at an international level on animal disease surveillance and control, and
- to examine regulations on international trade in animals and animal products, with a view to their harmonisation between Member Countries,

considering the mandate of the OIE as one of the three international intergovernmental organisations solicited to provide internationally harmonised standards, guidelines and codes of practices to serve as reference for measures taken by Member Countries in relation to Agreement on Sanitary and Phytosanitary Measures under the World Trade Organisation,

the European OIE Member Countries, at the General Session of the International Committee in May 1997 [1], decided to launch an investigation on the two following subjects :

- The role of international trade of animals, animal products and feed in the spread of antimicrobial resistance
- The means to control the spread of resistance factors of infective agents.

Results of an investigation in European countries, 1998:

The edition of a report on these two subjects had been entrusted to the OIE Collaborating Centre for Veterinary Medicinal Products, ANMV, AFSSA, Fougères-France [2].

The report essentially represents an analysis of the information obtained from answers to the questionnaire that has been elaborated as to obtain, for the two subjects, the factual information necessary to establish an objective evaluation of the situation in Europe and to take positions which are based on reliable technical data.

To this end, the objective of the questions in relation to 'the role of international trade of animals, animal products and feed in the spread of antimicrobial resistance' was to establish a detailed inventory of the national programmes monitoring bacterial resistance against antimicrobial substances. In particular, it was important to determine for the region of Europe

- the number of national surveillance programmes for antimicrobial resistance in livestock production
- the characteristics of these programmes
- the resources made available
- the degree of standardisation of methodologies used.

In relation to the measures used to control the spread of resistance factors of infective agents at a national level, it was useful to review the legal and technical requirements applicable in relation to the granting of marketing authorisations and the administration to animals of antimicrobial substances, both in their use as veterinary medicinal products and as animal feed additives.

According to these answers, only 16 out of 35 European countries have official antimicrobial resistance monitoring programmes at their disposal, 9 include food of animal origin and 7 of which assure coordination between veterinary and human programmes.

Due to a great diversity in national concepts, goals and technical methodologies these programmes provide results which are not directly comparable. Coordination and harmonisation of national monitoring programmes appear therefore to be indispensable.

Research on antimicrobial resistance is undertaken by 9 countries, few of which provided details on their research. Further information should be obtained in order to enable OIE to contribute to the development and coordination of these research activities.

Two thirds of the countries concluded that international trade of animals can play a role in the transfer of resistance. One third considers animal products and animal feed as a possible vector in the transfer of resistance.

Only 4 countries use a risk analysis procedure in concluding their resistance monitoring programmes. Whereas, 15 out of 31 countries impose constraints on exporting countries with respect to the authorisation of veterinary medicinal products and/or feed additives and 4 countries with respect to resistance monitoring programmes. Sixteen countries indicate to plan or consider to do so in the future. In view of the Agreement on Sanitary and Phytosanitary Measures under the World Trade Organisation, the OIE should propose a practical adaptation of the risk analysis concept to this specific public health problem.

All countries appear to be aware of the necessity to strictly control the use of antimicrobials as veterinary medicinal products and feed additives. Administrative procedures for marketing authorisation of veterinary medicinal products exist in all countries. Specific information for risk assessment on the emergence of antimicrobial resistance is required by the large majority of the countries for the authorisation. In establishing the conditions of the marketing authorisation, special rules are imposed in particular for substances capable of inducing resistance, the combination of antimicrobials, the determination of therapeutically effective doses and duration of treatment. All countries apply restrictions to the use of antimicrobials in animals. However, resistance data requirements, authorisation rules and restrictions of use have not been sufficiently specified. Adminstrating veterinary medicinal products containing antimicrobials to animals requires a veterinary prescription in all countries.

Only a small number of countries does not have administrative procedures to authorise the marketing of feed additives, but imposes restrictions on its use. All countries, with the exception of Sweden and Iceland accept the use of antimicrobials as feed additives. Likewise, as for veterinary medicinal products, the majority of the countries require specific antimicrobial resistance data, apply special rules for authorisation and impose specific restrictions on the use of antimicrobials as feed additives. However, contrary to veterinary medicinal products, two thirds of the countries do not require veterinary prescription for the administration of antimicrobials as feed additives.

Recommendations of the 18th Conference of the OIE Regional Commission for Europe, Prague, 22-25 September 1998 [3]:

Appreciating the information provided on the currently existing limited resistance monitoring capacities and on existing control measures put in place in European countries, and

Considering

- the responsibility of the OIE in informing governments of the existence and evolution of animal diseases of the measures to be taken in control of these diseases,
- that European countries have recognised that antimicrobial resistance is a major and complex problem
- the necessity to better understand the mechanisms responsible for the emergence and spread of antimicrobial resistance, as well as the potential of antimicrobial resistant bacteria of animal origin to be transmitted to humans causing diseases for which formerly effective antimicrobials may no longer be available
- the possible role of international trade in animals, animal products and feed in the spread of transferable antimicrobial resistance and possible methods for the control of the spread of infectious agents and resistance factors
- the need for more information on the emergence and spread of antimicrobial resistance, and on existing resistance monitoring programmes in veterinary medicine, control methods and research programmes in this field in order to obtain scientifically based data for further decisions,
- the possibility that in the future regulations are adopted, at a national or international level, with respect to the use of antimicrobials as veterinary drugs or feed additives,

- the recommendations of two recent World Health Organisation Reports on the use of antimicrobials in animal production and their potential impact on human health which recognised the necessity for collaboration with the OIE in developing a Code of practice for the use of antimicrobials in food animal production,

THE OIE REGIONAL COMMISSION FOR EUROPE

Recommended that

1. Veterinary authorities of the Member Countries in the region:
 - implement appropriate antimicrobial resistance monitoring programs for animals and animal derived products
 - encourage coordination between human and animal antimicrobial resistance monitoring programmes
 - work towards the prudent use of antimicrobial products, for example by improving preventive veterinary measures in animal husbandry and aquaculture
 - support research programmes on antimicrobial resistance mechanisms and on the impact of different methods of using antibiotics
2. The OIE study the possibility of establishing an ad hoc group, taking into account the scientific work carried by the Food and Agriculture Organisation of the United Nations and the World Health Organisation, which would consider as its highest priorities:
 - the development of technical guidelines on the prudent use of antimicrobial agents and on monitoring of the quantities of antibiotics used in animal husbandry
 - after collection of the necessary data, the harmonisation of national resistance monitoring programmes in animals and animal derived products
 - the development of an appropriate risk assessment methodology for the potential impact on public health of antimicrobial resistance in bacteria of animal origin
 - drafting a priority list of relevant bacteria and antimicrobial agents to be included on monitoring programmes.

OIE European Scientific Conference, Paris, 24-26 March 1999

The use of Antibiotics – Ensuring the protection of Public Health [4]:

Following the OIE Prague recommendations, the OIE and FAO Collaborating Centre for Veterinary Medicinal Products, ANMV, AFSSA, France, in close collaboration with the OIE and the FAO, organised a European scientific conference, which was held from 24 – 26 March at the OIE main offices in Paris.

This conference focussed on implementing strategies and actions for the control and reduction of antimicrobial resistance originating from the use of antimicrobials in animals.

To this end the specific objectives were to discuss and advance recommendations on

- a model for risk assessment of
 - the possible impact of the use of antibiotics in animals of the development of antimicrobial resistance in animals,
 - the potential transfer of antibiotic resistant bacteria from animals to humans and
 - the potential of reduced efficacy of antimicrobial in animals and humans
- the implementation of prudent use of antimicrobials in animals
- antimicrobial resistance monitoring in Europe.

Three working groups met well in advance of the conference in order to elaborate substantiated documents on these topics which were presented for consideration to the conference.

The Conference being attended by a 280 participants from 29 countries, representing scientific academia, regulatory authorities of human and animal health, ministries of health and agriculture, veterinary, agricultural producer and veterinary pharmaceutical industry associations, discussed and agreed on recommendations on these three topics.

Decision of the OIE International Committee, Paris, 17-21 May 1999:

At its 67th session of 17-21 May 1999 the OIE International Committee fully endorsed all recommendations forwarded by its Regional Commission for Europe in September 1998 in Prague, which in particular proposed to the establishment of an OIE ad hoc expert group on antimicrobial resistance [5].

Moreover, following the support and an additional recommendation of the OIE Standards Commission, the OIE International Committee decided that additionally to the previously identified mandates the OIE ad hoc expert group should deal specifically with the standardisation and harmonisation of laboratory methodologies for the detection and quantification of antimicrobial resistance.

Mandate of the OIE ad hoc expert group on antimicrobial resistance:

- Development of an appropriate risk assessment methodology for the potential impact on public health of antimicrobial resistant bacteria of animal origin
- Harmonisation of national antimicrobial resistance monitoring programmes in animals and animal derived products
- Drafting of a priority list of relevant bacteria and antimicrobial agents to be included in monitoring programmes
- Development of technical guidelines on prudent use of antimicrobials
- Monitoring of quantities of antimicrobials used in animal husbandry
- Standardisation and harmonisation of laboratory methodologies used for the detection and quantification of antimicrobial resistance

REFERENCES:

1. 65th General Session of the OIE International Committee, 1997 : Final report, Paris - France, 26-30 May 1997
2. J.BOISSEAU and B. ROSTEL (1998) 'The role of international trade in animals, animal products and feed in the spread of transferable antibiotic resistance and possible methods for control of the spread of infectious agent resistance factors' Rapport présenté lors de la 18^{ème} conférence de la Commission régionale de l'OIE pour l'Europe, Prague - 22-25 septembre 1998
3. OIE - 18th Conference of the OIE Regional Commission for Europe, 1998: Final report, Prague, Czech Republic, 22-25 September 1998
4. OIE European Scientific Conference, The use of Antibiotics – Ensuring the protection of Public Health, Paris, France, 24-26 March 1999. <http://www.anmv.afssa.fr/ccois>
5. 67th General Session of the OIE International Committee, 1999: Final report, Paris - France, 17-21 May 1999

REPORT OF ACTIVITIES OF WORLD HEALTH ORGANIZATION (WHO) ON ANTIMICROBIAL RESISTANCE

Only about 50% of antimicrobials produced are applied in human medicine. Most of the remainder is used in food animals for growth promotion and disease therapy and also in aquaculture, plant protection and various branches of the industry (e.g. for oil pipeline flushing). Use in food animals includes all classes of antimicrobials used in human medicine. Even first-line antimicrobials (e.g. Glycopeptides) are being used as feed additives for growth promotion in e.g. pigs and poultry. Therefore, the World Health Organization (WHO) considers the assessment and containment of the public health implications of the non-human use of antimicrobials and as a matter of priority.

Several WHO consultations and other expert bodies have identified links between antimicrobial use in livestock and the emergence of mainly foodborne bacteria which have reduced susceptibility to important antimicrobials which are used in treating infectious diseases in humans. There are an increasing number of reports of both outbreaks and individual cases of antimicrobial resistant foodborne pathogens, which have resulted not only in a human disease which is more difficult to treat, but also in death. Recently, a risk assessment of fluoroquinolone resistant *Campylobacter* in the USA has been published estimating, e.g. that 1 in 32 persons with Campylobacteriosis will seek care and is prescribed an antibiotic. Other publications from the USA show that licensing of fluoroquinolones for use in poultry resulted in a higher incidence of resistant *Campylobacter* in culture confirmed patients.

There is a need to clearly differentiate between the different types of uses of antimicrobials in livestock. For growth promoters, WHO recommends the termination of their use in livestock if similar products are also licensed in human medicine. A EU resolution to this effect was put into place in 1999. Since then studies from Denmark, Germany and Italy have shown a significant reduction in Vancomycin-resistant *Enterococci* isolations from poultry and poultry-derived food products. Some European member states have, with insignificant or no consequence either on disease rates in animals or on meat market prices, voluntarily suspended the use of all growth promoters irrespective of their human health importance. As a consequence, antimicrobial use in agriculture in e.g. Denmark was reduced by more than 60%.

The major challenge for therapeutic antimicrobials remains the development and implementation of guidelines and methods for their prudent use (see below for WHO activities) including the development of mechanisms for safety assessments of antimicrobials intended for food animal use. There is a significant difference between the "traditional" chemical residue-based determination of the safety of animal drugs and the determination of safety in the context of antimicrobial resistance. Proposals exist on how to address this non-traditional risk by establishing that the risk to be assessed is the potential loss of effective therapy for human microbial disease. WHO, jointly with FAO and OIE, could potentially play a facilitating role in the development of guidelines for the safety assessment of antimicrobials intended for food animal use, in the context of antimicrobial resistance.

In the wider context of non-human use WHO is focusing on the following subjects in the next WHO biennium:

1. Supporting Members States in strengthening antimicrobial resistance surveillance in foodborne bacteria by

- Conducting external quality assurance programmes with 60 laboratories on Salmonella typing and antimicrobial susceptibility testing (Feb-Dec 2000)
- Conducting international training courses on Salmonellosis and Antimicrobial Resistance Surveillance (First training course: Thailand Nov 1999; upcoming in 2000: South America; Mediterranean, China, Thailand; Eastern Europe)
- Expanding the Global Salm-Surv, a web-based, online databank on national and regional Salmonellosis and antimicrobial resistance surveillance laboratories (<http://www.gss.who.int>)
- Establishing a network of electronically linked national Salmonellosis reference laboratories: 65 countries participating; shortly expanding to *Campylobacter*
- Establishing international centres of excellence for surveillance and containment of antimicrobial resistance from antimicrobial use in agriculture (First Centre established in Thailand, Bangkok)

2. Developing and implementing global recommendations for the containment of antimicrobial resistance due to agricultural use.

As part of the WHO Strategy for containment of antimicrobial resistance, WHO has developed draft guidelines for the containment of antimicrobial resistance from antimicrobial use in livestock ". It will be discussed during an international electronic discussion group in April/May 2000 as the foundation for a planned WHO Consultation (with participation of FAO and OIE) on the same subject in June 2000.

3. Assessing the public health risks from antimicrobial use in aquaculture.

This was already planned for 1999 but did not materialize because of lack of partnership. New approach in 2000.

4. Development of Recommendations on the Procedures/Methods for the Surveillance of Antimicrobial Use in Agriculture and the Assessment of National Non-human Antimicrobial Use Patterns (2001)

5. WHO Scientific Meeting on the Consequences of Reducing the Use of Antimicrobials in Agriculture, October 2001

REPORT OF ACTIVITIES OF FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS (FAO) ON ANTIMICROBIAL RESISTANCE

FAO has been collaborating with OIE and WHO in this area. A tripartite OIE/FAO/WHO meeting was held on antimicrobial resistance in September 1999 in Geneva on the request of the OIE which wished to exchange information with these other organizations.

FAO's divisions and services, such as Animal Production and Health Service, Plant Production and Protection Division, Food and Nutrition Division, Fisheries Department have been commenting on the documents or activities of WHO. FAO will continue to participate in the OIE ad hoc expert groups as an observer.

The Animal Production and Health Division has provided technical assistance to developing countries in the areas of animal health and production. There will be activities on the use of antimicrobials in animal feedingstuffs (benefits and risk of development of resistance) depending on availability of resources.

In collaboration with WHO, the Fisheries Department is conducting a review to assess the potential for development of antimicrobial resistance in human pathogens associated with products from Aquaculture due to the use (and misuse) of antibiotics in aquaculture. The review is now being planned and will probably be undertaken in the first half of 2000. The outcome of this exercise will assist us in defining an appropriate course of action for the coming years in this area. The background for this review is that antimicrobials are used (and misused) in aquaculture production. Similar practices in other form of animal production have raised concerns regarding their contribution to the increase in the prevalence of multiple drug resistant human pathogens. It is therefore important to assess whether certain aquaculture systems or certain aquaculture practices could lead to similar concerns and whether there is a need for a detailed risk assessment.

**REPORT OF ACTIVITIES OF WORLD VETERINARY ASSOCIATION (WVA),
INTERNATIONAL FEDERATION OF AGRICULTURAL PRODUCERS (IFAP) AND
WORLD FEDERATION OF THE ANIMAL HEALTH INDUSTRY (COMISA) ON
ANTIMICROBIAL RESISTANCE**

PRUDENT USE OF ANTIBIOTICS: GLOBAL BASIC PRINCIPLES

This paper presents a set of principles governing the prudent use of antibiotics in animals, elaborated jointly by the international representative organisations of veterinarians, farmers, and the animal health industry. It may form the backbone of and/or guide in the elaboration of more specific guidelines.

The recommendations below concentrate on the use and not on government measures such as licensing and controls. However, the three organisations 1) fully pledged to use antibiotics within the jurisdiction of each country; 2) support that each country should have an appropriate regulatory system for the licensing and control of veterinary drugs in general and antibiotics in particular; 3) and recommend that counterfeit and other unregistered products should not be used and that such use be combated.

Notes:

1) for convenience the word “antibiotic” is used throughout this document; it is intended to convey all antimicrobial products administered orally or parenterally to animals, i.e. antibiotics (produced by fermentation of live micro-organisms) but also chemically-synthesised compounds with antibiotic activity such as sulphonamides and quinolones; it does not include disinfectants.

2) the basic principles are in bold typeface; where required to facilitate the interpretation of the principle or to add a specific recommendation, language in italics has been added.

THE BASIC PRINCIPLES

1. Antibiotics are health management tools that are licensed to be used to enhance good husbandry practices for the purpose of

- 1) disease prevention**
- 2) disease treatment**
- 3) production enhancement**

It is a fact that certain antibiotics may be used in food animals for performance enhancement, which leads to benefits in terms of animal welfare, reduction of environmental waste, and supply of economical high quality source of protein. Future conditions of use of antibiotics for this indication is pending the outcome of on-going investigations and international meetings expected to take place within the near future.

Antibiotics are a complement to good husbandry practices and should never be used to compensate for or mask bad farm and veterinary practices.

2. Codes of good practices, Quality assurance programmes, Herd Health Surveillance Programmes (HHSP), and education programmes should promote the responsible and prudent use of antibiotics.

3. Antibiotics shall be used under the supervision of a veterinarian.

Regular, close veterinary involvement is essential for informed advice concerning the use of antibiotics. Regardless of the distribution system available, the use of antibiotics should be subject to appropriate professional advice, including by a veterinarian.

4. Therapeutic antibiotics should be used when it is known or suspected that an infectious agent is present which will be susceptible to therapy. It is the responsibility of the veterinarian to choose the antibiotic product, based on his/her informed professional judgement balancing the risks and benefits for humans and animals.

The veterinarian shall have due regard to the public health risks of using veterinary medicines. Specifically for antibiotics, the veterinarian shall have due consideration for the potential for decreased antibiotic susceptibility in zoonotic bacteria and target pathogens in animals, and for the antibiotic

residues of toxicological and microbiological significance. At the same time, benefits such as promoting the health and welfare of animals, assuring safe, wholesome, and affordable food from healthy animals, while reducing human exposure to bacteria of animal origin, shall be taken into account.

Whenever bacteria are exposed to antibiotics, there will probably be some degree of selection for resistant populations. Therefore, it is vital to prudent use to limit therapeutic antibiotic use to those situations where they are warranted.

5. When antibiotics need to be used for therapy, bacteriological diagnosis with sensitivity testing should, whenever possible, be part of the informed professional clinical judgement.

When treating a disease, the sensitivity of the causal organism should ideally be ascertained before therapy is started. In disease outbreaks involving high mortality or where there are signs of rapid spread of disease among contact animals, treatment may be started on the basis of clinical diagnosis. Even so, the sensitivity of the suspected causal organism should, where possible, be determined so that if treatment fails it can be changed in the light of the results of sensitivity testing. Antibiotic sensitivity trends should be monitored over time, and such monitoring used to guide clinical judgement on antibiotic usage.

6. Label instructions should be carefully followed and due attention paid to species and disease indications and contra-indications, dosage regimen, withdrawal periods, and storage instructions. Off-label use of antibiotics should be exceptional and always be under the professional responsibility of a veterinarian.

Off-label use should be carefully justified, for instance as part of the written prescription. Where legal provisions exist, they should serve as a basis for guiding the conditions of off-label use.

7. Antibiotics used for therapy should be used for as long as needed, over as short a dosage period as possible, and at the appropriate dosage regimen.

***Dosage regimen:** It is essential to administer the antibiotic in accordance with the recommended dosage regimen. This will minimise therapy failures, exploit fully the efficacy potential of the product, and comply with the regulated withdrawal times. Each class of antibiotics has its own unique pharmacodynamic properties which are expressed fully when the recommended dosage regimen is applied.*

***As long as necessary:** Insufficient duration of administration can lead to recrudescence of the infection. This may lead to increased likelihood of selecting microorganisms with reduced sensitivity.*

***As short as possible:** Limiting the duration of use to only that required for therapeutic effect will minimise the exposure of the bacterial population to the antibiotic. The adverse effects on the surviving commensal microflora are minimised and the medical impact of the remaining zoonotic organisms is minimised/reduced. Theoretically, antibiotic use should be stopped as soon as the animal's own host defence system can control the infection itself.*

8. Records should be kept of all antibiotic administrations.

The implementation of record-keeping (ways and means, responsible professions) should be left to the national/local level. However, in order to ensure compatibility and usability of recorded data, some harmonisation of the principles and of the format is needed.

9. Co-ordinated susceptibility surveillance should be conducted and the results be provided to the prescriber, supervising veterinarians and other relevant parties.

Surveillance should target microorganisms of both veterinary and public health importance. Data from diagnostic laboratories (with collection of samples from pathologic specimens) have an inherent bias towards a higher percentage of resistant strains than pre-treatment specimens. Therefore, it is encouraged to also gather data from samples collected at random from farm, slaughterhouses, or food in order to investigate the prevalence of resistance in veterinary pathogens, zoonotic pathogens, and sentinel organisms.

Data should be provided to prescribers, supervising veterinarians and other relevant parties; which will allow the modification of antimicrobial usage to balance the benefits with the risks. Accessibility to the data will vary from programme to programme and should normally be determined beforehand.

10. Efficacious, scientifically proven alternatives to antibiotics are needed as an important part of good husbandry practices.

Among the research needs, it is suggested to look into the development of economical and efficacious alternatives to the use of antibiotics and to evaluate the impact that these alternatives (e.g. vaccines, probiotics, competitive exclusion principles and products, nutrition, and new health technologies and strategies, including improved livestock management) might have on selection for resistance.

**EXTRACT OF THE REPORT OF THE 32ND SESSION OF THE
CODEX COMMITTEE ON FOOD HYGIENE**

- ANTIMICROBIAL RESISTANT BACTERIA IN FOOD ⁷ -

127 The Delegation of Denmark presented the discussion paper which had been prepared (with the assistance of other countries) as agreed by the last session of the Committee. The document considered all sources of antimicrobial resistance and referred to the work currently underway in WHO, OIE and FAO in their respective areas of competence. The Delegation highlighted the public health concerns related to the higher pathogenicity of resistant strains of Salmonella and Campylobacter in food, and proposed that a risk profile and risk assessment policy should be defined.

128 The Secretariat noted that consideration of this issue required a multidisciplinary approach and recalled that the 23rd Session of the Commission had established an intergovernmental Task Force on Animal Feeding, the Terms of Reference of which included addressing “*aspects which are important for food safety, such as problems related to toxic substances, pathogens, microbial resistance, new technologies, storage, control, traceability, etc.*”.

129 The Representative of WHO informed the Committee of the work of WHO on antimicrobial resistance in livestock, including the organization of an expert Consultation on Global Principles for Containment of Antimicrobial Resistance in Foodborne Bacteria (in collaboration with OIE and FAO) scheduled for March 2000, and stressed the importance of establishing a risk profile within the Codex framework, including consideration of the factors which contribute to an increase in antimicrobial resistance.

130 The Delegation of the United States expressed the view that antimicrobial resistance was one of the factors taken into account in risk assessment and there was no need for additional work in this Committee in terms of hygienic control measures. The Delegation therefore proposed to discontinue work on this issue, as it was adequately addressed in the framework of WHO, OIE and FAO, while matters related to residues of pesticides and veterinary drugs in food were addressed in the relevant Codex Committees.

131 The Delegation of Denmark pointed out that the Task Force would consider only some limited aspects of antimicrobial resistance and that a multidisciplinary approach was essential. Some delegations pointed out that antimicrobial resistance was a matter for consideration by the Committee on Residues of Veterinary Drugs in Foods. Other delegations and the Observer from IDF stressed that the expertise on microbiological hazards rested with the CCFH and that it would be appropriate to consider this issue further insofar as it related to the microbiological safety of foods.

132 The Committee agreed that this issue should be considered further at the next session, on the basis of a revised discussion paper in the form of a risk profile, to be prepared by the Delegation of Denmark, with the assistance of interested countries. Recognizing the importance of the issue, the Committee also agreed to ask the advice of the Executive Committee and the Commission on how to proceed in order to ensure coordination of work between concerned Committees.

⁷ December 1999, ALINORM 01/13, paras 127-132