CHAPTER 6.3.

PRINCIPLES FOR RESPONSIBLE AND PRUDENT USE OF ANTIMICROBIAL AGENTS IN ~~VETERINARY MEDICINE~~ AQUATIC ANIMALS

Article 6.3.1.

Purpose

These principles ~~recommendations~~ provide guidance for the responsible and prudent use of antimicrobial agents in *aquatic animals*, with the aim of protecting both animal and human health. The *Competent Authorities* responsible for the registration and marketing authorisation of products ~~registration~~ and the control of all ~~groups~~ organisations involved in the production, distribution and use of ~~veterinary~~ antimicrobial~~s~~ agents have specific obligations.

Article 6.3.2.

Objectives of responsible and prudent use

Responsible and prudent use includes a set of practical measures and recommendations intended to reduce the risk associated with the selection and dissemination of antimicrobial resistant micro-organisms and antimicrobial resistance determinants in *aquatic animal* production to:

1. maintain the efficacy of *antimicrobial agents* both for veterinary and human medicine and to ensure the rational use of antimicrobials in *aquatic animals* with the purpose of optimising both their efficacy and safety*;*

2. comply with the ethical obligation and economic need to keep *aquatic animals* in good health;

3. prevent or reduce the transfer of both resistant micro-organisms and ~~or~~ resistance determinants from *aquatic animals* to humans and terrestrial animals;

~~4. maintain the efficacy of *antimicrobial agents* used in human medicine and prolong the usefulness of the antimicrobials;~~

5. prevent ~~the contamination of animal-derived food with~~ antimicrobial residues that exceed the established maximum residue limit (MRL) occurring in the food;

~~6. protect consumer health by ensuring the safety of food of *aquatic animal* origin.~~

Article 6.3.3.

Definitions

Antimicrobial agent: means a naturally occurring, semi-synthetic or synthetic substance that at in vivo concentrations exhibits antimicrobial activity (kill or inhibit the growth of micro-organisms). Anthelmintics and substances classed as disinfectants or antiseptics are excluded from this definition.

Pharmacovigilance of antimicrobial agent: means the detection and investigation of the effects of the use of these products, mainly aimed at safety and efficacy in animals and safety in people exposed to the products.

Article 6.3.4.

Responsibilities of the ~~regulatory~~ *Competent Authorities*

The ~~national~~ ~~Regulatory~~ *Competent Authorities*~~, which are~~ responsible for granting marketing authorization for antimicrobial~~s~~ agents~~,~~ have a significant role in specifying the terms of the authorization and in providing the appropriate information to the *veterinarian* or other *aquatic animal* health professional through product labeling and/or by other means, in support of prudent use of ~~veterinary~~ *antimicrobial agents* ~~drugs~~ in *aquatic animals*.

It is the responsibility of ~~regulatory~~ *Competent Authorities* to develop up-to-date guidelines on data requirements for evaluation of ~~veterinary~~ *antimicrobial ~~drug~~ agent* applications.

~~National governments~~ *Competent Authorities* in cooperation with animal and public health professionals should adopt a proactive approach to promote prudent use of *antimicrobial agents* in *aquatic animals* as an element of a comprehensive ~~national~~ strategy for the containment of antimicrobial resistance.

~~Other~~ Elements of ~~the national~~ a comprehensive strategy should include good animal husbandry practices, vaccination policies and development of animal health care at the farm level, and consultation with a *veterinarian* or other *aquatic animal* health professional, all of which should contribute to reduction of the prevalence of animal disease requiring antimicrobial treatment.

~~Regulatory~~ The *Competent Authorities* should expeditiously grant marketing authorizations when criteria of quality, efficacy, and safety are met.

The examination of ~~dossiers/drug~~ marketing authorization applications should include an assessment of the risks to ~~both~~ animals~~, and~~ humans and the environment resulting from the use of antimicrobial agents in *aquatic animals*. The evaluation should focus on each individual ~~veterinary~~ *antimicrobial agent* ~~drug~~ ~~veterinary medicinal product~~ ~~but~~ and take into consideration the class of antimicrobials to which the particular active ~~principle~~ substance belongs. The safety evaluation should include consideration of the potential impact of the proposed use in *aquatic animals* on human health, including the human health impact of antimicrobial resistance developing in ~~food-borne~~ micro-organisms found in *aquatic animals*. An assessment of the impact of the proposed use on the environment should be conducted.

~~The regulatory authority~~ *Competent Authorities* should aim to ensure that advertising of antimicrobial agents complies with ~~national~~ relevant legislation and marketing authorizations granted and discourage direct advertising ~~to *aquatic animal* producers~~ other than to those legally entitled to prescribe the antimicrobial agent.

Information collected through pharmacovigilance programmes, including on lack of efficacy, should form part of the *Competent Authority's* comprehensive strategy to minimize antimicrobial resistance.

~~Regulatory~~ *Competent Authorities* should disseminate, to *veterinarians* or other *aquatic animal* health professionals, information on trends in antimicrobial resistance collected during surveillance programmes and should monitor the performance of susceptibility testing laboratories.

~~The~~ *Competent Authorities* and stakeholders should work together to provide for ~~develop~~ effective procedures for the safe collection and destruction of unused or out-of-date *antimicrobial agents*.

Article 6.3.5.

Responsibilities of the veterinary pharmaceutical industry

The veterinary pharmaceutical industry has responsibilities for providing information requested by the ~~Regulatory~~ *Competent Authorities* on the quality, effectiveness and safety of *antimicrobial agents*. The responsibilities of the veterinary pharmaceutical industry covers pre- and post- marketing phases, including manufacturing, sale, importation, labeling, ~~and~~ advertising ~~issues~~ and pharmacovigilance.

The veterinary pharmaceutical industry has the responsibility to provide the ~~regulatory~~ *Competent Authority* with the information necessary to evaluate the amount of *antimicrobial agents* marketed. The veterinary pharmaceutical industry should ensure that the advertising of *antimicrobial agents* directly to the *aquatic animal* producer is discouraged.

Article 6.3.6.

Responsibilities of wholesale and retail distributors

Distributors should ensure that their activities are in compliance with the relevant ~~national or regional~~ legislation.

Distributors should ensure that information for the appropriate use and disposal of the *antimicrobial agent* ~~preparation should~~ accompany all distributed products and should also be responsible for maintaining and disposing of the product ~~under~~ according to the manufacturer recommendations.

~~Distributors should have responsibilities in collection and destruction of antimicrobial agents that have passed their expiry date.~~

Article 6.3.7.

Responsibilities of veterinarians and other aquatic animal health professionals

Responsibilities of *veterinarians* or other *aquatic animal* health professionals include identifying, preventing and treating *aquatic animal diseases*, as well as the promotion of sound animal husbandry methods, hygiene procedures, vaccination and other alternative strategies to minimise the need for *antimicrobial* use in *aquatic animals*.

Veterinarians or other *aquatic animal* health professionals should only prescribe, dispense, administer or recommend ~~antimicrobial~~ a specific course of treatment with an antimicrobial agent for *aquatic animals* under their care.

The responsibilities of *veterinarians* or other *aquatic animal* health professionals are to carry out a ~~proper~~ thorough clinical ~~examination~~ assessment of the *aquatic animal(s)*, including as appropriate: ~~and make a diagnosis, based on the~~ clinical examination, post-mortem examination, bacteriology with culture and sensitivity, and other laboratory tests to arrive at the most definitive diagnosis possible before initiating a specific course of treatment with an antimicrobial agent. ~~the results of laboratory tests and~~. Evaluation of environmental factors and husbandry at the production site (e.g. water quality) should be considered as potential primary factors leading to infection and should be addressed prior to recommending a course of *antimicrobial agent* treatment.

If therapy with an *antimicrobial agent* is deemed ~~appropriate~~ necessary it should be initiated as soon as possible. The selection of the agent should be based on the knowledge and experience of the *veterinarian* or other *aquatic animal* health professional.

As soon as possible, susceptibility testing of the target micro-organism should be used to confirm the choice of treatment. Results of all susceptibility tests should be ~~communicated~~ retained and should be available to the ~~national~~ *Competent Authority*.

The *veterinarian* or other *aquatic animal* health professional should indicate precisely to the *aquatic animal* producer the treatment regime, including the dose, the treatment intervals, the duration of the treatment, the withdrawal period and the amount of *antimicrobial agents* ~~drug~~ to be delivered, depending on the dosage and the number of *aquatic animals* to be treated.

~~The *veterinarian* or other *aquatic animal* health professional may prescribe or recommend in appropriate circumstances~~ The use of *antimicrobial agents* extra-label/off-label~~,~~ may be permitted in appropriate circumstances in conformity with the relevant ~~national~~ legislation. For products destined for export, the ~~and~~ ~~any~~ requirements of importing countries should be considered.

Records on the use of *antimicrobial agents* should be kept in conformity with the relevant ~~national~~ legislation. *Veterinarians* or *aquatic animal* health professionals should also periodically review farm records on the use of the *antimicrobial agents* to ensure compliance with their directions and use these records to evaluate the effectiveness of treatment regimens. Suspected adverse reactions, ~~as well as~~ including a lack of effectiveness, should be reported to the *Competent Authority*. ~~The~~ Associated susceptibility data should accompany the report of lack of effectiveness.

~~*Veterinarians* or other *aquatic animal* health professionals should periodically review farm records on the use of *antimicrobial agents* to ensure compliance with their directions and use these records to evaluate the efficacy of treatment regimens.~~

Article 6.3.8.

Responsibilities of aquatic animal producers

Aquatic animal producers should implement health programmes on their farms in order to promote *aquatic animal* health and food safety. This can be done through adequate planning of culture strategies to maintain *aquatic animal* health through biosecurity programmes, husbandry, nutrition, vaccination ~~strategies~~, maintenance of good water quality, etc.

Aquatic animal producers should use antimicrobial agents only on the prescription or recommendation of a *veterinarian* or other *aquatic animal* health professional, and follow directions on the dosage, method of application, and withdrawal period.

Aquatic animal producers should ensure that *antimicrobial agents* are properly stored, handled, and disposed.

Aquatic animal producers should keep adequate records of *antimicrobial agents* used, bacteriological and susceptibility tests, and ~~to~~ make such records available to the *veterinarian* or other *aquatic animal* health professional.

Aquatic animal producers should inform the *veterinarian* or other *aquatic animal* health professional of recurrent disease problems and lack of efficacy of *antimicrobial agent* treatment regimes.

Article 6.3.9.

Training of ~~antimicrobial~~ users of antimicrobial agents

The training of users of *antimicrobial agents* should involve all the relevant organisations, such as ~~Competent~~ relevant regulatory ~~regulatory~~ authorities, pharmaceutical industry, veterinary schools, research institutes, and veterinary professional organisations and other approved users such as *aquatic animal* owners.

Article 6.3.10.

Research

To address the significant lack of information for numerous species of *aquatic animals*, ~~relevant~~ ~~Competent~~ the relevant regulatory authorities and other stakeholders should encourage public-funded and industry-funded research.