

# Guide to Prudent Use of Antimicrobial Agents in Dairy Production

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## 2013



## International Dairy Federation

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Send any comments or inquiries to:  
International Dairy Federation (I.N.P.A.)

Boulevard Auguste Reyers 70/B

1030 Brussels

Belgium

Phone: + 32 2 325 67 40

Fax: + 32 2 325 67 41

E-mail: [info@fil-idf.org](mailto:info@fil-idf.org)

Web: [www.fil-idf.org](http://www.fil-idf.org)

# IDF Guide to Prudent Use of Antimicrobial Agents in Dairy Production

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## Foreword

Good practices at farm level are essential tools to ensure that both the needs of the food industry and the expectations of consumers are met.

The 'FAO/IDF Guide to Good Dairy Farming Practice' sets the tone and provides a generic framework for individual on-farm quality-assurance programmes, focusing on both consumer safety and the image of the dairy sector. In line with this guide, the current IDF Guide to Prudent Use of Antimicrobial Agents in Dairy Production aims at providing a framework to support the responsible use of antimicrobial agents on dairy farms. The guidelines stress the importance and need for a whole supply chain approach to ensure food safety.

The focus of this publication is on desired outcomes rather than on specific, prescriptive actions or processes. It provides examples of recommended practices for all participants in the regulation, supply and use of antimicrobial agents at farm level. Consultation across these sectors was undertaken throughout the development process, to ensure the guide is robust.

The Guide includes an overview of relevant Good Agricultural Practice (GAP) as well as fact sheets to enable the key participants in the dairy supply chain to effectively collaborate in producing high quality milk.

I encourage everyone in the industry to adopt and use this new Guide.

Nico van Belzen, PhD  
Director General  
International Dairy Federation  
March 2013

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Note: This guide does not have any legal status and does not supersede national requirements.

# About this guide

## 1. Background

Antimicrobial agents play an indispensable role in animal health and welfare management. At the same time, the need for prudent use is obvious to ensure good food safety outcomes and to manage the potential risk of antimicrobial resistance. The emergence of multi-resistant bacteria is posing challenges to health professionals and communities around the world for both human and animal health. These bacteria are not destroyed by the common antimicrobial agents and so pose a risk to people, particularly children, the elderly and those with poorly functioning immune systems, as well as to animals.

Throughout the years, the dairy sector has been very much aware of the need for responsible use and has, in many countries, implemented adequate measures throughout the dairy supply chain.

Integrated supply chain management approaches now adopted by the dairy industry require positive action and cooperation by all participants - dairy farmers, veterinarians, dairy and meat processing companies, pharmaceutical companies and regulators – to help prevent the creation and transmission of antimicrobial resistance.

The *IDF Guide to Prudent Use of Antimicrobial Agents* has been prepared to provide a generic framework to support the responsible use of antimicrobial agents on dairy farms. The guidelines recognize that dairy farms supply milk and meat for human consumption and that a coordinated, whole of supply chain approach is required to manage the food safety risks associated with modern food production.

This document focuses on desired outcomes, rather than on prescriptive actions or processes. It provides examples of recommended practices for all participants that are involved in the production, distribution, supply, use and regulation of antimicrobial agents used on dairy farms. These examples effectively manage the risks posed by using antimicrobial agents, are achievable and are currently being implemented in many parts of the world. It is, however, recognized that not all the recommended practices included in this Guide may be relevant/ implementable in all the circumstances and that relevant recommended practices may be identified from the Guide for implementation as appropriate to the production system being followed.

The guide highlights the role of:

- Dairy farmers in managing animal health and husbandry practices to minimize the occurrence and spread of disease
- Veterinarians providing expert advice to ensure that the most appropriate treatments are used correctly

- Food (dairy and meat) processing companies in setting clear specifications for the raw products they source and in verifying and monitoring farmer compliance
- Pharmaceutical companies in ensuring that antimicrobial agents are properly manufactured, assessed, labelled and then only sold through regulated distribution channels
- Competent authorities in effectively controlling the manufacture, registration, supply and use of antimicrobial agents, and in having effective systems in place to monitor for potential problems such as antimicrobial resistance

The term “antimicrobial agent” is used rather than “antibiotic” in this Guide. The term antimicrobial agent is as defined by the World Organisation for Animal Health (OIE) and means a naturally occurring, semi-synthetic or synthetic substance that exhibits antimicrobial activity (kills or inhibits growth of microorganisms) at concentrations attainable in vivo. Anthelmintics and substances classed as disinfectants or antiseptics are excluded from this definition.

## 2. Guiding objective for prudent use of antimicrobial agents on dairy farms

The guiding objective is that milk and meat should be produced from healthy animals under generally accepted agricultural conditions, with minimal and controlled use of antimicrobial agents. An integrated whole of supply chain approach is needed to achieve this.

Dairy farmers should apply Good Agricultural Practices (GAP) when using antimicrobial agents in the following areas:

- Animal health
- Milking techniques and hygiene
- Nutrition
- Animal welfare
- Environment

Veterinarians (or appropriate authorized technical advisors) should assist dairy farmers to apply GAP by providing:

- Advice on the management of animal health, especially preventive measures that can preclude the need to use antimicrobial agents
- Diagnostic services including advice on suitable and effective treatment regimes
- Appropriate administration and/or supply of antimicrobial agents
- Advice on the appropriate use of antimicrobial agents, including dose rates, recording of treatments, marking treated animals and withholding periods

Food (dairy and meat) processing companies should provide support to dairy farmers through:

- Establishing and promoting specifications for acceptable product
- Advising suppliers about preventive control measures
- Monitoring of incoming milk and meat supplies using screening tests to prevent food safety concerns and ensure that farm products are suitable for processing into food
- Undertaking follow-up investigative and corrective actions if farm products do not meet specifications and reporting relevant information and advice to farmers
- Applying control measures for microbiological hazards

Pharmaceutical companies should reduce the risks from antimicrobial agents by:

- Developing, manufacturing and supplying products of high quality with low risk for residues and antimicrobial resistance
- Generating the data to support a scientific risk assessment prior to product registration
- Providing relevant and appropriate information on labels and data sheets
- Ensuring that products are packaged in appropriate quantities for treatments
- Providing clear identification of medicated feed

Competent authorities should underpin the prudent use of antimicrobial agents on dairy farms by:

- Assessing the risks and regulating the types of antimicrobial treatments available for supply and use
- Ensuring all antimicrobial drugs/medicinal products are registered according to transparent criteria before being placed on the market
- Determining and approving the appropriate dose rate and withholding period for various classes of dairy livestock
- Approving information on the labels of treatment and data sheets
- Licensing appropriately qualified and experienced veterinarians to prescribe antimicrobial agents
- Monitoring data on milk and meat products for antimicrobial residues
- Reviewing data from the agricultural and medical fields for adverse outcomes from antimicrobial use
- Taking action to minimize the inappropriate supply and use of antimicrobial agents

### 3. Presentation of the guide

The Guide includes tables of GAP and suggested measures for each key supply chain participant – dairy farmers, veterinarians, food (milk and meat) processing companies, pharmaceutical companies and competent authorities.

Individual fact sheets provide examples of the actions that should be undertaken by each participant in the dairy supply chain.

In developing individual, company or country-specific guidelines for the prudent use of antimicrobial agents for dairy animals, reference should be made to the following (some references apply to more than one part of the supply chain) as well as relevant legislation for each country:

For	References
<b>Dairy farmers</b>	FAO and IDF Guide to Good Dairy Farming Practice. Animal Production and Health Guidelines. No. 8 (2011) [1]
	IDF Guide to Good Animal Welfare in Dairy Production – 2008 [2]
	Codex Alimentarius Code of Hygienic Practice for Milk and Milk Products CAC/RCP 57-2004 [3]
	FAO Good Agricultural Practices – a working concept (2007) [4]
	FAO and OIE Guide to Good Farming Practices for Animal Production Food Safety (2010) [5]
<b>Veterinarians</b>	OIE Terrestrial Animal Health Code. Chapters 6.6 to 6.10 on the recommendations for controlling antimicrobial resistance, in particular Chapter 6.9 on Responsible and Prudent Use of Antimicrobial agents in Veterinary Medicine. <a href="http://www.oie.int/en/international-standard-setting/terrestrial-code/access-online/">http://www.oie.int/en/international-standard-setting/terrestrial-code/access-online/</a> [6]
	EU list of banned drugs: Annex IV of CR 2377/90/EC (1990) [7]
	OIE List of Antimicrobial Agents of Veterinary Importance <a href="http://web.oie.int/download/Antimicrobials/OIE_list_antimicrobials.pdf">http://web.oie.int/download/Antimicrobials/OIE_list_antimicrobials.pdf</a> [8]
<b>Food processing companies</b>	Bulletin of the IDF No. 449/2011: Integrated Supply Chain Management (2011) [9]
	IDF Strategies for Detecting Antibiotic Residues in Milk: Guidance on the application of screening and confirmatory methods in integrated dairy chain management. IDF SCAMAC (in preparation) [10]
	Bulletin of the IDF No. 442/2010: Special Bulletin on Screening Methods: Current situation and compilation of commercially available screening methods for the detection of inhibitors/antibiotic residues in milk (2010) [11]
	Bulletin of the IDF No. 319/1997 includes an article by Heeschen, W.H. on Codex regulations and food safety (1997) [12]
	Heeschen, W.H. and Suhren, G. IDF integrated detection system for antimicrobials: introductory statement and practical experiences in Germany. In: Proceedings of IDF symposium on residues of antimicrobial drugs and other inhibitors in milk (1995) [13]
	EU Guidelines for the Validation of Screening Methods for Residues of Veterinary Medicines [14]
<b>Pharmaceutical companies</b>	Codex Alimentarius Code of Practice to Minimize and Contain Antimicrobial Resistance CAC/RCP 61-2005 [15]

<b>Competent authorities</b>	Codex Alimentarius Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance CAC/GL 77-2011	[16]
	Codex Alimentarius Guidelines for the Design and Implementation of National Regulatory Food Safety Assurance Programmes Associated with the Use of Veterinary Drugs in Food Producing Animals CAC/GL 71-2009.	[17]
	Codex Alimentarius Code of Practice to Minimize and Contain Antimicrobial Resistance CAC/RCP 61-2005	[18]
	WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food (2000)	[19]
	OIE Terrestrial Animal Health Code 2012. Standards on the recommendations for controlling antimicrobial resistance. Chapters 6.7 to 6.10 in particular Chapter 6.7 and 6.8 on the monitoring of the use of antimicrobial agents and antimicrobial resistance <a href="http://www.oie.int/en/international-standard-setting/terrestrial-code/access-online/">http://www.oie.int/en/international-standard-setting/terrestrial-code/access-online/</a>	[6]

## Definitions

**Antimicrobial agent:** mean naturally occurring, semi-synthetic or synthetic substance that exhibits antimicrobial activity (kills or inhibits the growth of micro-organisms) at concentrations attainable in vivo. Anthelmintics and substances classed as disinfectants or antiseptics are excluded from this definition (OIE Definition). This document is primarily focussed on the antimicrobial agents used for veterinary purposes, although many of the antimicrobial agents used in human medicine are the same compounds as those used for veterinary purposes. Antimicrobial agents are inclusive of anti-bacterials, anti-virals, anti-fungals and anti-protozoals. The term antibiotic means the same as anti-bacterial.

**Antimicrobial residues:** Small quantities of the antimicrobial agent(s) and/or their metabolites in any edible portion of animal products, including residues of associated impurities of the veterinary treatments concerned.

**Competent authority:** The veterinary authority or other government authority of a country having the responsibility and competence for ensuring or supervising the implementation of animal health and welfare measures, international veterinary certification and other standards and recommendations relating to veterinary medicines and/or food safety.

**Contaminant:** Any biological or antimicrobial agent, foreign matter or other substance not intentionally added to food that may compromise food safety or suitability.

**Micro-organism:** Microscopic, single-celled organisms, some types of which cause disease. Some species of bacteria have the ability to acquire and/or transfer antimicrobial agent resistance to other micro-organisms.

**Maximum residue limit (MRL):** The maximum concentration of an antimicrobial residue that is recommended by the Codex Alimentarius Commission to be permitted legally or recognized as acceptable in or on a food (expressed in mg/kg or µg/kg on a fresh weight basis). The MRL is based on the type and amount of residue (antimicrobial agent or its metabolite) considered to be without toxicological hazard for human health, while taking into account other relevant public health risks as well as food technological aspects. The MRL for antimicrobial agents may be reduced to be consistent with good practice in the use of antimicrobial agents.

**Off-label use:** The use of antimicrobial agents not strictly in accordance with the manufacturer's approved label directions. In many countries, this is only legal when the off-label use is in accordance with instructions from the prescribing veterinarian.

**Pathogen:** A micro-organism that can cause infection, illness or disease.

**Unregistered antimicrobial agent:** An antimicrobial agent that has not been approved by the competent authority for veterinary supply and use. Human antimicrobial medications that have not been registered for veterinary use are considered to be unregistered. In many countries, the supply and use of unregistered antimicrobial agents for use on dairy farms is illegal, although limited supply may be available under prescription by a licensed veterinarian.

**Withholding period (WHP):** The minimum period of time that must elapse between the last administration or application of a veterinary treatment and the collection of edible tissue or products from a treated animal to ensure that the content of residues in food complies with the maximum residue limit (MRL). MRLs should be established for each antimicrobial agent. Note: WHPs often relate to situations in which only one drug is used. Seek advice if using multiple agents.

**Veterinary medicines:** antimicrobial agents and biological products sold for the treatment of animals where evidence of proven efficacy and safety have been examined by competent authorities to ensure that the products are suitable for their purpose. These medicines may require a prescription from a veterinarian to allow purchase and application, and to confirm that their use is appropriate.

## Good practices

### 1. Dairy farmers

Ultimately, dairy farmers are responsible for the health and welfare of their livestock. Applying Good Agricultural Practice (GAP) on dairy farms can greatly reduce the need to use antimicrobial agents.

Good dairy farming practices have been described in the *FAO and IDF Guide to Good Dairy Farming Practice* [1] and the key practices that support the prudent use of antimicrobial agents on farms are collated in the table below.

Good dairy farming practices to ensure prudent use of antimicrobial agents	Examples of suggested measures that underpin the prudent use of antimicrobial agents on dairy farms	Objective of measures
1.1 Establish the herd with resistance to disease	1.1.1 Choose breeds and animals well suited to the local environment and farming system 1.1.2 Determine herd size and stocking rate based on management skills, local conditions and the availability of land, infrastructure, feed and other inputs 1.1.3 Vaccinate all animals as recommended or required by local animal health authorities	Enhance herd disease resistance and reduce stress
1.2 Prevent entry of disease onto the farm	1.2.1 Only buy animals of known health status (both herd and individual animals) and control their introduction to the farm, using quarantine if indicated 1.2.2 Ensure that animal transportation on and off the farm does not introduce disease 1.2.3 Monitor risks from adjoining land and neighbours and have secure boundaries 1.2.4 Where possible, limit access of people and wildlife to the farm 1.2.5 Have a vermin or pest control program in place 1.2.6 Only use clean equipment from a known source	Maintain farm biosecurity Keep animals healthy Comply with international, national and regional animal movement and disease controls

Good dairy farming practices to ensure prudent use of antimicrobial agents	Examples of suggested measures that underpin the prudent use of antimicrobial agents on dairy farms	Objective of measures
<p><b>1.3 Have an effective herd health management program in place</b></p>	<p>1.3.1 Use an identification system that allows all animals to be identified individually from birth to death</p> <p>1.3.2 Develop an effective farm herd health management program focused on prevention that meets farm needs as well as regional and national requirements</p> <p>1.3.3 Regularly check animals for signs of disease</p> <p>1.3.4 Establish diagnosis and recommended treatment (consult veterinarian if necessary)</p> <p>1.3.5 Sick animals should be attended to quickly and in an appropriate way</p> <p>1.3.6 Keep sick animals isolated</p> <p>1.3.7 Separate milk from sick animals and animals under treatment and dispose of the milk appropriately</p> <p>1.3.8 Keep written records of all treatments and identify treated animals appropriately</p> <p>1.3.9 Manage animal diseases that can affect public health (zoonoses)</p>	<p>Detect animal diseases early</p> <p>Prevent spread of disease among animals</p> <p>Ensure food safety</p> <p>Ensure traceability</p>
<p><b>1.4 Use all antimicrobial agents and veterinary medicines as directed</b></p>	<p>1.4.1 Only use antimicrobial agents and veterinary medicines approved for supply and use under relevant legislation</p> <p>1.4.2 Use antimicrobial agents and veterinary medicines according to directions, calculate dosages carefully and observe appropriate withholding periods as determined by the manufacturer and approved by the competent authority</p> <p>1.4.3 Only use veterinary medicines as prescribed by veterinarians</p> <p>1.4.4 Store antimicrobial agents and veterinary medicines securely and properly, and dispose of them responsibly – do not use out of date products</p> <p>1.4.5 Maintain records of all treatments with veterinary medicines – do not use out of date products</p>	<p>Most effective treatment of animal disease</p> <p>Prevent occurrence of antimicrobial residues in milk and meat</p>

Good dairy farming practices to ensure prudent use of antimicrobial agents	Examples of suggested measures that underpin the prudent use of antimicrobial agents on dairy farms	Objective of measures
1.5 Ensure milking routines do not injure the animals or introduce contaminants into milk	1.5.1 Identify individual animals that require special milking management 1.5.2 Segregate milk harvested from sick or treated animals for appropriate disposal	Prepare animals for hygienic milking  Avoid contaminants in milk
1.6 Ensure animal feed and water are of suitable quantity and quality	1.6.1 Ensure the nutritional needs of animals are met 1.6.2 Only use approved antimicrobial agents for treatment of animal feeds or components of animal feeds and observe withholding periods	Keep animals healthy with good quality feed  Avoid contamination with antimicrobial agents due to farming practices
1.7 Ensure animals are free from discomfort	1.7.1 Design and construct buildings and handling facilities to be free of obstructions and hazards 1.7.2 Provide adequate space allowances and clean bedding 1.7.3 Protect animals from adverse weather conditions and the consequences thereof 1.7.4 Provide housed animals with adequate ventilation 1.7.5 Provide suitable flooring and footing in housing and animal traffic areas	Protection of animals against adverse climatic conditions and risk of disease  Provide a safe environment
1.8 Ensure animals are free from pain, injury and disease	1.8.1 Follow appropriate birthing and weaning practices 1.8.2 Protect against lameness 1.8.3 Milk lactating animals regularly 1.8.4 Avoid poor milking practices as they may injure dairy animals	Prevention of pain, injury and disease  Prompt treatment of pain, injury and disease
1.9 Ensure farm tasks are carried out safely and competently	1.9.1 Have appropriate procedures and equipment in place for undertaking dairy farming tasks 1.9.2 Induct and train/educate staff appropriately for their work 1.9.3 Ensure staff carry out their tasks competently 1.9.4 Choose competent people for training, advice and interventions	Limit risks to staff, livestock and infrastructure

Good dairy farming practices to ensure prudent use of antimicrobial agents	Examples of suggested measures that underpin the prudent use of antimicrobial agents on dairy farms	Objective of measures
1.10 Ensure dairy farming practices do not have the potential to increase the frequency of antimicrobial resistance in animals and the environment	1.10.1 Contain dairy run off on the farm 1.10.2 Use veterinary treatments appropriately to avoid contamination of the local environment	Limit the impact of dairy farming practices on the environment and the pool of antimicrobial resistant microorganisms

## 2. Veterinarians

Veterinarians provide an important role in ensuring the prudent supply of antimicrobial agents for dairy farms. They are responsible for promoting animal health and welfare, as well as identifying, preventing and treating animal diseases. The promotion of sound animal husbandry practices, hygienic procedures, biosecurity and vaccination strategies, where relevant, can help to minimise the need for antimicrobial use in food-producing animals. The prescribing veterinarian should be familiar with the health status of the livestock being treated to ensure that the antimicrobial agents used are appropriate. The veterinarian must also ensure that clear directions are given to the people administering the treatments and managing the livestock, with particular reference to the required dose rate, route of administration and withholding periods.

Good practices to ensure the prudent use of antimicrobial agents on dairy farms	Examples of suggested measures to support dairy farmers in the prudent use of antimicrobial agents	Objective of measures
2.1 Assess the requirements for antimicrobial treatment	2.1.1 Be knowledgeable in the health status of the animals being treated 2.1.2 Diagnose the condition requiring antimicrobial treatment by considering the animal's history, signs and results of a clinical examination and/or by carrying out further diagnostic tests 2.1.3 Consider preventive and other measures that may help with accurate diagnoses and that may eliminate or reduce the need to use antimicrobial agents	Only supply antimicrobial agents when and where necessary  Ensure the antimicrobial agents prescribed will be effective for the condition being treated

Good practices to ensure the prudent use of antimicrobial agents on dairy farms	Examples of suggested measures to support dairy farmers in the prudent use of antimicrobial agents	Objective of measures
<p><b>2.2 Select an appropriate antimicrobial product for the circumstances</b></p>	<p>2.2.1 Select antimicrobial products that have good efficacy for the disease being treated whilst minimizing risks to the animal, product and user</p> <p>2.2.2 Use reliable, accurate and validated diagnostic tests to inform antimicrobial selection, especially for complicated or non-responsive diseases</p> <p>2.2.3 Only use combinations of antimicrobial agents that are complementary and possibly synergistic, and approved by the competent authority for use together</p> <p>2.2.4 Prescribing or using antimicrobial agents off-label must only be undertaken if permitted under national legislation and if the risks can be adequately managed</p> <p>2.2.5 Prescribing or using unregistered antimicrobial agents must only be undertaken if permitted under national legislation and if the risks can be adequately managed</p>	<p>Most effective treatment is used and spread of infection minimized</p> <p>Antimicrobial agent use is minimized</p> <p>Antimicrobial resistance is reduced</p> <p>Take account of the OIE list of antimicrobial agents of veterinary importance [8]</p>
<p><b>2.3 Give clear advice on the appropriate use of the antimicrobial agent</b></p>	<p>2.3.1 Consider advice from the manufacturer and on the product label when prescribing and/or administering antimicrobial agents</p> <p>2.3.2 Give clear instructions to persons that are responsible for administering antimicrobial agents about dose rates, method of administration and withholding periods</p> <p>2.3.3 Label all medicines supplied according to national legislation</p> <p>2.3.4 Record details of treatments administered and antimicrobial agents supplied in line with national legislation</p>	<p>Antimicrobial agents are used appropriately with minimal risks to people, livestock or food safety</p>
<p><b>2.4 Review treatments</b></p>	<p>2.4.1 Periodically review the health status of livestock being treated and the appropriateness of antimicrobial agent therapies</p> <p>2.4.2 Report unexpected outcomes of antimicrobial use to the competent authority</p>	<p>Problems with antimicrobial use are identified and investigated</p>

### 3. Food processing companies

Food (dairy and meat) processing companies play an important part in encouraging farmers to use antimicrobial agents in accordance with the veterinarian's instructions. Setting clear specifications for suppliers and checking the supplies against these criteria, with penalties for non-compliance motivates farmers to use prescribed treatments responsibly. Systems must also be in place to exclude supplies from processing that do not meet compliance criteria.

Good practices to ensure the prudent use of antimicrobial agents on dairy farms	Examples of suggested measures to support dairy farmers in the prudent use of antimicrobial agents	Objective of measures
<b>3.1 Provide clear specifications for raw materials and the quality management systems to help farmers meet them</b>	3.1.1 Implement a documented and auditable food safety/Quality assurance (QA) system for all suppliers 3.1.2 Provide clear specifications for purchasing raw materials from suppliers and consider having an incentive and/or penalty system to foster compliance 3.1.3 Audit/assess the effectiveness of on-farm food safety/quality assurance systems regularly 3.1.4 Work with farmers to improve performance	Farmers are aware of buying/accepting specifications and the consequences or penalties for non-conformance
<b>3.2 Detection and exclusion of contaminated supplies</b>	3.2.1 Provide guidance for on-farm milk testing 3.2.2 Provide screening of farm supplies 3.2.3 Screen incoming supplies at processing facilities 3.2.4 Testing of product	Residues are detected quickly Causes of failures identified Minimize the risks of carryover to the bulk milk supplies at the factory level
<b>3.3 Adopt HACCP management for micro-biological hazards</b>	3.3.1 Assess microbiological hazards and apply relevant control measures, e.g. hygiene, heat treatment and temperature control	Minimize microorganisms in food Foodborne transfer of antimicrobial resistance is minimized

### 4. Pharmaceutical companies

All of the antimicrobial agents used for veterinary purposes on dairy farms are sourced from pharmaceutical companies. These companies are in the best position to ensure that the antimicrobial agents that are used on farm are of high quality and packaged with clear instructions for the user. They need to work with regulators to ensure that each antimicrobial product is subject

to a comprehensive risk assessment prior to being approved for supply and use on farms, and then provide appropriate aftermarket support for their products. Antimicrobial agents must be manufactured in accordance with Good Manufacturing Practice (GMP).

Good practices to ensure the prudent use of antimicrobial agents on dairy farms	Examples of suggested measures to support dairy farmers in the prudent use of antimicrobial agents	Objective of measures
<b>4.1 Provide the necessary information to allow the scientific assessment of antimicrobial products for efficacy and safety</b>	4.1.1 Generate and provide the required information/data to allow antimicrobial products to be assessed by the competent authority  4.1.2 Provide competent authorities with data on the type and amount of antimicrobial agents being manufactured and/or marketed	Antimicrobial agents available for use on farms are efficacious and safe to use
<b>4.2 Only supply approved antimicrobial agents through regulated channels</b>	4.2.1 Ensure antimicrobial agents are appropriately registered and approved by the competent authority before being marketed and supplied  4.2.2 Use GMP in the manufacture of antimicrobial agents  4.2.3 Supply antimicrobial agents through authorized and regulated channels  4.2.4 Information on antimicrobial agent use for dairy farmers should not be of an advertorial nature	Antimicrobial agents are judiciously dispensed to farmers by competent professionals
<b>4.3 Monitor aftermarket product performance</b>	4.3.1 Have systems in place to monitor for and receive feedback from product users  4.3.2 Actively investigate problems reported with antimicrobial agent use  4.3.3 Implement a pharmaco-vigilance program and, on request, a specific surveillance program for bacterial susceptibility and resistance	Issues with antimicrobial use are actively monitored and investigated  Emerging antimicrobial resistance issues are promptly identified and reported

## 5. Competent authorities

The prudent use of antimicrobial agents on dairy farms is underpinned by competent authorities approving the manufacture of antimicrobial agents, treatments and their supply and use on dairy farms. Assessing and monitoring the accuracy of information supplied to farmers and veterinarians is also important. Other actions to enforce appropriate controls on the supply and use of antimicrobial agents, as well as monitoring for adverse outcomes, including for antimicrobial resistance, also underpin prudent use.

Good practices to ensure the prudent use of antimicrobial agents on dairy farms	Examples of suggested measures to support dairy farmers in the prudent use of antimicrobial agents	Objective of measures
5.1 Assess the suitability of antimicrobial agents for use on dairy animals prior to registration	5.1.1 Conduct a risk assessment prior to registration 5.1.2 Establish maximum residue limits in food products (use Codex whenever possible) 5.1.3 Establish withholding periods for milk and meat after treatments 5.1.4 Approve product label information 5.1.5 Review product registration in the light of adverse reports of the antimicrobial's use	Approved treatments are registered for use Relevant information is on product labels and data sheets for farmers, veterinarians and sellers Registration of treatments is reviewed after field use of animal treatments or reported concerns from human medicine
5.2 Implement controls over the supply of antimicrobial agents	5.2.1 Restrict the supply of antimicrobial agents to licensed distributors 5.2.2 Register and regulate veterinarians and suitably qualified people (SQP) as appropriate 5.2.3 Advise veterinarians of trends in resistance	The supply of antimicrobial agents to farmers is managed by veterinarians or other suitably trained persons in accordance with national legislation and/or under the supervision of a veterinarian Veterinarians are knowledgeable about the current trends in antimicrobial resistance
5.3 Implement controls over the use of antimicrobial agents on dairy farms	5.3.1 Check the labelling and distribution of antimicrobial agents used on dairy farms 5.3.2 Verify on-farm quality assurance programs and farm practices with regard to the use of antimicrobial agents 5.3.3 Conduct surveys of or monitor milk, dairy products and meat for the presence of antimicrobial residues	Ensure compliance with regulatory requirements that effectively manage the risks of antimicrobial use on dairy farms
5.4 Monitor for adverse outcomes of antimicrobial use, including antimicrobial resistance	5.4.1 Monitor for changes in antimicrobial agent susceptibility of selected microorganisms from food, animals and clinical samples	Information on antimicrobial resistance is collated and disseminated

## Fact sheets

### Fact sheet 1: Dairy farmers

Animals producing milk and meat for human consumption need to be healthy. An effective animal husbandry program including health care and animal welfare should be in operation on all dairy farms. The health care program should emphasise the prevention of disease to reduce the need to use antimicrobial agents. An effective program includes appropriate record keeping.

#### General principles include:

##### 1.1 Establish a herd with resistance to disease

###### *1.1.1 Choose breeds and animals well suited to the local environment and farming system*

Different dairy species and breeds have different requirements. Selecting dairy animals that are suited to the local environment and farming system will greatly reduce disease risks and therefore the need to use antimicrobial agents. Animals introduced from different locations may be vulnerable to endemic diseases in the new location due to lack of previous exposure and the development of immunity.

###### *1.1.2 Determine herd size and stocking rate based on management skills, local conditions and the availability of land, infrastructure, feed and other inputs*

Larger herds and higher stocking rates generally require a higher level of organization, infrastructure and skill to manage them. The risks are magnified in more intensive dairy farming systems. Disease burdens can be higher and individual animals requiring intervention can be more difficult to identify and treat. Good planning and management skills are required to minimize the use of antimicrobial agents.

###### *1.1.3 Vaccinate all animals as recommended or required by local animal health authorities*

Vaccination is a useful tool for limiting the impact of disease by increasing the immunity of the animal population to specific pathogens, and so reduce or avoid the use of antimicrobial agents altogether. Animal health authorities can provide dairy farmers with information about the specific vaccines that are recommended for their area. In some dairying regions, dairy farmers are required by law to vaccinate their stock against serious contagious diseases.

## 1.2 Prevent entry of disease onto the farm

### 1.2.1 *Only buy animals of known health status (both herd and individual animals) and control their introduction to the farm, using quarantine if indicated*

The most effective way to prevent the introduction of infectious diseases is to keep a closed herd and maintain an effective biosecurity program that excludes all pathogens and pests. This means that no new animals enter the herd and that previously resident animals do not re-enter after they have left the herd. This is difficult to achieve in practice, so strict control of all animal introductions is essential. Increased risk of disease could also occur when animals share grazing or other facilities.

Prior to being introduced to the farm, all dairy herds and animals should be screened for diseases that are significant to their area of origin and new location. Sick animals should be rejected before transportation. All animals should have:

- An identification system to enable trace-back to their source (a birth to death identification system)
- Some form of vendor declaration or certification that details the health/disease status of animals and any appropriate tests, treatments, vaccinations or other procedures that have been or are being carried out. Potential sellers of dairy livestock must keep appropriate permanent animal health records for their animals. The health status of the vendor herd should also be verified. This is particularly important for diseases with long incubation periods like paratuberculosis etc.

Where the introduced animals' health status is unknown, they should be kept under quarantine or separate from the existing animals for an appropriate length of time.

Introduced animals should be inspected on arrival and should be free of external parasites such as ticks. Sick animals should be rejected. It is good practice to consider treating all introduced animals for internal parasites on arrival.

Keep records of all animal movements to and from the farm.

### 1.2.2 *Ensure that animal transportation on and off the farm does not introduce disease*

Potential buyers of live animals should always ask and be told if the animals are sick or diseased. Preferably, no sick or infirm animals should be transported alive. A suitably trained operative or a veterinarian should carry out any euthanizing required on-farm.

The disposal of diseased and dead animals should be done in a way that minimizes the risk of disease spread and in line with the guidelines in the OIE Terrestrial Animal Code [6] and/or local regulations. For example, transport vehicles should not move dead or diseased animals from one farm to another farm without taking appropriate actions to minimize the risk of spreading disease.

### *1.2.3 Monitor risks from adjoining land and neighbours and have secure boundaries*

Be aware of local (endemic) diseases and/or exotic diseases that have the potential to affect the health of the herd or flock, especially from neighbouring farms. Contain animals appropriately to manage any potential risk of disease spread between farms and within farms.

### *1.2.4 Where possible, limit access of people and wildlife to the farm*

People (and vehicles) visiting a number of farms can spread disease between the farms. Keep tanker/milk pick up access and public tracks clear of faecal contamination. Restrict access to an “as needs” basis and put in place appropriate processes to minimize disease spread. If entering areas that pose a high risk of transferring disease onto or from the farm, visitors to the farm should wear clean protective clothing and clean, disinfected footwear. Disease can be spread both from and to humans and wildlife. Avoid visitor contact with animals unless necessary and keep records of all visitors as appropriate.

### *1.2.5 Have a vermin or pest control program in place*

Ensure that appropriate vermin controls are in place in all areas where vermin could breed, introduce disease and/or affect milk safety and quality. Vermin breeding sites should be eliminated, especially if those sites also harbour disease pathogens, such as manure heaps, livestock disposal sites etc. Vermin control measures may also be required in the milking shed, feed and water storages and animal housing areas. Vermin species vary geographically but can include indigenous animals, rodents, birds and insects.

### *1.2.6 Only use clean equipment from a known source*

Ensure that all agricultural and veterinary equipment introduced on to the farm is clean and that steps have been taken to prevent the introduction of disease. This may include asking questions about the history of where the equipment comes from and how it has been used. Take extra care with shared or borrowed equipment.

## **1.3 Have an effective herd health management program in place**

### *1.3.1 Use an identification system that allows all animals to be identified individually from birth to death*

All dairy animals should be easily identifiable by all people who come in contact with them. The systems used should be permanent, allowing individual animals to be uniquely identified from birth to death. Examples of identification systems include ear tagging, tattooing, freeze branding and radio frequency identification (RFID) measures such as microchips. Permanent cow identification is needed when recording the details of antimicrobial agent use.

*1.3.2 Develop an effective farm herd health management program focused on prevention that meets farm needs as well as regional and national requirements*

Herd health programs aim to keep all livestock healthy and productive, without the on-going prophylactic use of antimicrobial agents. They should include the farm's practices for the diagnosis, treatment, prevention and control of relevant animal diseases, including internal and external parasites. It is important to ensure a consistent approach to herd health, so all staff should be aware of and understand the farm's herd health program.

The program should cover all aspects of animal husbandry and handling, milk harvesting as well as other dairy farm management practices relevant to animal health. This may include disease screening, vaccination and/or control measures being required by animal health authorities or supply contracts. General cleaning routines and good hygiene levels on the farm also support herd health programs.

Where effective vaccines are available, they may be used to increase resistance to disease. Prophylactic treatments may be used as protective measures when no viable alternative strategy exists.

Effective herd health programs should be developed in consultation with appropriately skilled people such as veterinarians.

*1.3.3 Regularly check animals for signs of disease*

Antimicrobial therapies are most effective when given early in the course of the disease. Observe all animals regularly and use proven methods to aid in detection and accurate diagnosis of infectious disease. Some useful tools include monitoring body temperature, observing animal behaviour and body condition, and examining foremilk. Laboratory or other tests may be necessary to screen animals for disease. Herd and/or animal-level disease testing may also be available through statutory disease control programs or communal milk collection or herd improvement centres.

Detailed breeding and reproductive records should be kept and animals observed at appropriate stages as many diseases are associated with reproduction.

*1.3.4 Establish diagnosis and recommend treatment (consult veterinarian if necessary)*

Clinical diseases should be investigated to determine the underlying cause(s) so that animals can be treated with the most appropriate medicines and further cases prevented. Regular management practices such as hoof care programs can reduce the incidence of lameness.

*1.3.5 Sick animals should be attended to quickly and in an appropriate way*

Treat all disease, injury and poor health by proven methods after accurate diagnosis. Treat diseased animals appropriately to minimize the prevalence of

infection and the source of pathogens. Seek veterinary advice on the selection of appropriate antimicrobial therapies.

#### *1.3.6 Keep sick animals isolated*

Where possible and if indicated, keep sick animals isolated on the farm to minimize the spread of contagious disease. Provide separate facilities and/or milk sick animals last. Prompt treatment helps to limit the spread of infectious agents. Clean and disinfect equipment after it has been in contact with contagious animals and ensure that people coming into contact with these animals take precautions to avoid infections.

#### *1.3.7 Separate milk from sick animals and animals under treatment and dispose of the milk appropriately*

Follow appropriate procedures to separate milk from sick animals and animals under treatment. This milk is not suitable for human consumption and if stored on farm should be clearly labelled as such. Clean milking equipment and utensils thoroughly to avoid carry-over contamination. Milk from cows treated with antimicrobial agents may contain inappropriate levels of residues and should be discarded and not used for human consumption (or fed to animals for human consumption) if it is within the WHP for the treatment.

#### *1.3.8 Keep written records of all treatments and identify treated animals appropriately*

It is important that staff, veterinarians and others involved with handling dairy animals on the farm know what treatments have been given to which animals. Put in place an appropriate system to readily identify treated animals, and record appropriate details in accordance with local regulations and to manage withholding periods for milk and meat.

#### *1.3.9 Manage animal diseases that can affect public health (zoonoses)*

Follow local regulations and OIE recommendations to control zoonoses. Aim to keep diseases of public health significance at a level in animal populations that is not hazardous to people. Avoid direct transmission to people through appropriate animal management and hygienic practices. Ensure the safe disposal of animal waste and carcasses. Prevent the contamination of milk with faeces and urine or other animal wastes. Do not use milk from sick animals for human consumption. Manage the risks posed by drinking raw milk from farms.

### **1.4 Use all antimicrobial agents as directed**

#### *1.4.1 Only use antimicrobial agents and veterinary medicines approved for supply and use under relevant legislation*

Only use antimicrobial agents that have been assessed and registered for use in dairy production by the competent authority. Refer to 1.4.3 for information on “off-label use”.

*1.4.2 Use antimicrobial agents according to directions, calculate dosages carefully and observe the appropriate withholding period as determined by the manufacturer and approved by the competent authority*

Using agricultural and veterinary antimicrobial agents for the purpose for which they were approved, and in accordance with label directions, gives a predictable outcome while managing the potential risks. Dairy farmers should manage the use of all antimicrobial agents to prevent the antimicrobial agents adversely affecting animal health and productivity, the health and safety of the user, the environment or the safety and quality of milk and meat products.

Be aware of antimicrobial agents that can leave residues in milk. These may include detergents, teat disinfectants, dairy sanitizers, anti-parasitics, antibiotics, herbicides, pesticides and fungicides.

Dairy farmers should:

- Use antimicrobial agents only for the purpose for which they are approved
- Read the label because it will contain all the information about the legal and safe use of the antimicrobial agents
- Follow the advice given on the label and in any antimicrobial agent data sheet or risk assessment
- Observe the specified withholding periods

*1.4.3 Only use veterinary medicines as prescribed by veterinarians*

Veterinary medicines pose risks to humans, animals and food safety and are subject to special controls on their supply and use.

Use only approved veterinary medicines, at the recommended dose according to the label directions, or as prescribed or advised by a veterinarian to ensure the most effective treatment. Do not under or over-dose. Relevant withholding periods must be observed.

All veterinary medicines and antimicrobial agents intended for treatment of food-producing animals should have a withholding period stated on the label. If label directions are not strictly followed, the stated withholding period will not be valid. If no withholding time is stated or no labelling instructions exist, the product should not be used.

The use of veterinary medicines contrary to the label recommendations is termed “off-label use” and poses additional risks. Off-label use of veterinary medicines must only occur under strict veterinary supervision and in compliance with national and regional regulations.

*1.4.4 Store antimicrobial agents and veterinary medicines securely and dispose of them responsibly*

Store antimicrobial agents and veterinary medicines at recommended temperatures and securely to ensure they are not used inappropriately or do not unintentionally contaminate milk and feed. Check and observe product expiry

dates. Antimicrobial agents and their containers should also be disposed of in a way that will not cause contamination to animals or the farm environment.

#### *1.4.5 Maintain records of what treatments were used, when administered, dose rates and withhold periods*

Relevant records should be kept to ensure the correct withholding periods can be observed.

### **1.5 Ensure milking routines do not injure the animals or introduce contaminants into milk**

#### *1.5.1 Identify individual animals that require special milking management*

Individual animals should be easily identifiable by all people who come in contact with them. The system used should be permanent, allowing individual animals to be identified from birth to death. Additional temporary identification systems should be in place on farms to manage animals that require special handling at milking, such as treated or diseased animals, or animals producing milk that is not suitable for human consumption.

#### *1.5.2 Segregate milk harvested from sick or treated animals for appropriate disposal*

Animals whose milk is unfit for human consumption should be milked last or with a separate bucket or system. Store or discard abnormal milk in a manner appropriate to the risk posed to people, animals and the environment.

### **1.6 Ensure animal feed and water are of suitable quantity and quality**

#### *1.6.1 Ensure the nutritional needs of animals are met*

To remain healthy, dairy animals should be provided with sufficient feed and water daily, according to their physiological needs. The quality and quantity of the feed, including appropriate fibre, should reflect the animal's age, body weight, stage of lactation, production level, growth, pregnancy, activity and climate.

Sufficient space and time needs to be given for each animal to get access to feed and water. Good feeding management will reduce competitive pressure and diminish aggressive behaviours between individual animals.

#### *1.6.2 Only use approved antimicrobial agents and veterinary medicines for treatment of animal feeds or components of animal feeds and observe withholding periods*

The prophylactic use of antimicrobial agents or veterinary medicines in dairy feed should be avoided if possible. If their use is necessary, only those approved for use in dairy operations should be used and the use should be under strict veterinary direction and supervision.

Use all antimicrobial agents and veterinary medicines in accordance with the manufacturers' recommendations. Check labels of all antimicrobial agents that are to be used around, on or in feeds or pastures for compatibility with food-producing animals, withholding requirements for milk and proper application rates and concentration of products.

Antimicrobial agents should be managed in a manner that avoids their accidental introduction into feed and water and, as a result, into milk.

## **1.7 Ensure animals are free from discomfort**

### *1.7.1 Design and construct buildings and handling facilities to be free of obstructions and hazards*

Consideration should be given to the free flow of animals when designing and building animal housing and/or milking sheds. Avoid dead ends, and steep and slippery pathways. Ensure dairy buildings are safely wired and properly earthed. Injury and disease is minimized when the animals are housed and handled in safe and comfortable facilities.

### *1.7.2 Provide adequate space allowances and clean bedding*

Avoid overcrowding of animals, even for short periods. Keep animal group sizes manageable and provide adequate feeding and watering space to reduce aggressive competitive behaviours.

Most dairy species have strong herding instincts. Group animals by similar weight and size if possible. Manage herd introductions to reduce fighting, particularly between mature and intact males.

Provide housed animals with adequate space for resting on comfortable bedding and protect from hard surfaces such as concrete. These areas should be kept clean (for example by replacing the bedding frequently). Grazing areas are usually suitable for resting, provided that they are rotated frequently and have adequate drainage.

### *1.7.3 Protect animals from adverse weather conditions and the consequences thereof*

As far as practicable, protect animals from adverse weather conditions and the consequences thereof. This includes stress factors such as weather extremes, forage shortages, unseasonal change and others causing cold or heat stress. Consider shade or alternative means of cooling such as misters and sprays. In cold conditions shelter, such as windbreaks and housing, and additional feed should be provided. Permanent shelters with lightning arresters may be warranted in some areas.

### *1.7.4 Provide housed animals with adequate ventilation*

All animal housing should be adequately ventilated allowing sufficient supply of fresh air to remove humidity, allow heat dissipation and prevent build-up of gases such as carbon dioxide, ammonia or slurry gases, and dust.

### *1.7.5 Provide suitable flooring and safe footing in housing and animal traffic areas*

Floors should be constructed to minimize slipping and bruising due to slippery or uneven floors. Excessively rough concrete or surfaces with sharp protrusions and stones can cause excessive wear or penetrations to the sole of the hoof, resulting in lameness. Unsuitable floors may inhibit mounting behaviours and lead to injuries. Protective floor coverings (for example, rubber matting or other non-slip surfaces) can be used on walkways to reduce hoof abrasions that lead to secondary hoof infections.

## **1.8 Ensure animals are free from pain, injury and disease**

### *1.8.1 Follow appropriate birthing and weaning practices*

New-born animals are susceptible to pathogens and should be fed adequate colostrum soon after birth. Calves with good passive immunity will be more resistant to disease and so are less likely to require antimicrobial treatments.

### *1.8.2 Protect against lameness*

Laneways, yards, milking stalls and housing should be constructed to minimize the incidence of lameness that requires antimicrobial treatment. Regular hoof care management practices should be implemented and the animals' diets adjusted to minimize lameness. Lameness should be investigated to determine underlying causes and treated appropriately. Allow animals to move at their own pace.

### *1.8.3 Milk lactating animals regularly*

Establish a regular milking routine appropriate to the stage of lactation that does not overly stress the animals. Regular milking practices lower the risks of mastitis and so minimize antimicrobial use for this condition.

### *1.8.4 Avoid poor milking practices as they may injure animals*

Poor milking practices can affect animal well-being, production and udder health. Milking equipment should be well maintained and regularly serviced.

## **1.9 Ensure farm tasks are carried out safely and competently**

### *1.9.1 Have appropriate procedures and equipment in place for undertaking dairy farming tasks*

It is important to ensure that tasks undertaken on the farm are done safely, correctly and consistently by all farm staff. It is the dairy farmer's responsibility to ensure that farm staff are appropriately trained, are aware of and understand the procedures specific to their enterprise. The dairy farmer also needs to clearly identify who is responsible for particular tasks.

To support a consistent approach, it is good practice to have a written procedure, usually called a Standard Operating Procedure (SOP), which details how to carry out a task in a controlled and repeatable manner. SOPs should cover all requirements to carry out the task, including details of process, equipment and materials, and any relevant risk and safety issues. It may be necessary to carry out a risk assessment on potentially hazardous tasks.

Clear procedures competently carried out minimize the risks to staff, animal health, animal welfare and milk quality and safety. This is especially relevant in the administration of antimicrobial agents to cattle.

#### *1.9.2 Induct and train or educate staff appropriately for their work*

Farm staff need to be properly trained to work productively and safely. This includes being formally introduced to the working environment and their specific role. New staff should be supervised by a competent person until they are familiar with their tasks and understand the farm's specific management systems and potential risks.

Training opportunities for existing staff can also improve productivity and increase work satisfaction. Training and educational opportunities can be used to monitor farm procedures and provide feedback for continual improvement. Specific training in the administration of veterinary medicines including antimicrobial agents is recommended.

#### *1.9.3 Ensure staff carry out their tasks competently*

Good managers have systems in place to ensure that tasks carried out by others on the farm are being undertaken competently and in a timely manner. Good communications, backed up by visual checks, appropriate record keeping or other methods of verification, are good practice. Records of all antimicrobial treatments must be kept on farms and can be scrutinized by the farm manager.

#### *1.9.4 Choose competent sources for training, advice and interventions*

Choose competent and qualified people to develop and deliver staff training. Only seek and act on advice from sources and individuals that are appropriately skilled or qualified. Veterinarians are appropriately qualified to provide advice on the use of antimicrobial agents. In many regions, the delivery of veterinary services is restricted by law to appropriately registered veterinarians to protect animal health and welfare and food safety.

**1.10 Ensure that dairy farming practices do not have the potential to increase the frequency of antimicrobial resistance in animals and the environment**

*1.10.1 Contain dairy run-off on the farm*

Ensure that all dairy effluent is contained on the farm and does not enter waterways or other areas that may impact on the environment

*1.10.2 Use veterinary medicines appropriately to avoid contamination of the local environment*

Care should be taken to ensure that antimicrobial agents are not inadvertently administered to wild life, unnecessarily expanding the pool of treated animals.

## Fact sheet 2: Veterinarians

Veterinarians have special skills and professional responsibilities to contribute to the animal health of dairy herds and the safety of milk and meat by keeping them free of contamination by veterinary medicines. Veterinarians should take notice of the OIE List of Antimicrobial Agents of Veterinary Importance [8], including information on recommended use.

### 2.1 Assess the requirements for antimicrobial treatment

At the point of supply, veterinarians must be satisfied that the antimicrobial agent selected is the most appropriate treatment for the disease on the farm. The prescribing veterinarian needs to consider the animal's prospects for recovery, its welfare and future productivity, as well as the capability of the farm manager to implement the treatment regime and manage any resultant residues and other risks of antimicrobial agent use.

#### 2.1.1 *Be knowledgeable in the health status of the animals being treated*

Veterinarians are responsible for ensuring that antimicrobial agents are only administered to animals that require treatment. Having prior knowledge of the herd's management and disease history can help veterinarians determine the most appropriate treatment regime for individual farm circumstances. Veterinarians should foster a strong relationship with the farmers that they service and keep detailed clinical records to build up a history of the health status of each dairy herd.

The health status of the herd can also be determined through careful questioning and/or additional diagnostic testing in circumstances where there is no existing relationship between the farmer and the prescribing veterinarian. For new farmer clients, and wherever possible, veterinarians should request herd health status details from the farmer's previous veterinarian or the appropriate government agency.

#### 2.1.2 *Diagnose the condition requiring antimicrobial treatment by considering the animal's history, signs, results of a clinical examination and/or by carrying out further diagnostic tests*

Veterinarians must use their clinical experience and skills, considering the herd's history and the animal's signs in determining a diagnosis that justifies antimicrobial treatment. Experienced farmers can often provide assistance in determining a diagnosis for common conditions.

A clinical examination of the affected animal or a representative sample of the herd is necessary to investigate new disease conditions and should be conducted periodically for on-going disease conditions to ensure that the treatments prescribed and the management of the animals is still appropriate. Additional diagnostic tests may be required to determine the specific pathogen causing the disease and guide antibiotic selection.

### *2.1.3 Consider preventive and other measures that may eliminate or reduce the need to use antimicrobial agents*

Changes to the animals' management or environment could reduce or eliminate the need for antimicrobial agents by improving the animal's immunity and/or reducing the number of pathogens in the animal's immediate environment. Early treatment and measures to limit the spread of disease will reduce the requirement for the use of antimicrobial agents.

Good nutrition and husbandry will help to keep animals healthy and improve their resistance to disease. Likewise, careful handling and correctly functioning equipment such as milking machines can reduce injury to the cows and so the chance of pathogens causing disease. Veterinarians should assess these aspects of the animal's care as they establish a diagnosis, and give appropriate instructions to correct deficiencies. Antimicrobial agents should not be supplied to compensate for poor housing, management or nutrition, except for short term animal welfare considerations.

## **2.2 Select an appropriate antimicrobial product for the circumstances**

The veterinarian is in a privileged position in controlling the supply of antimicrobial agents to farmers. This privilege comes with the responsibility to ensure that the antimicrobial agents dispensed and/or administered are the most suitable treatment for the disease and individual farm circumstances. Effective treatment minimizes the spread of infection and reduces the amount of antimicrobial agents used.

### *2.2.1 Select antimicrobial products that have good efficacy for the disease being treated while minimizing risks to the animal, product and user*

Veterinarians should use their clinical experience and/or the results of diagnostic tests and previous treatments in the herd to guide the selection of an appropriate antimicrobial agent. Consideration should be given to the activity of the drug towards the specific pathogen(s) involved, the route of administration and the known pharmacokinetics and tissue distribution of the drug to ensure that it will be active at the site of infection. The product selected should be registered for use on dairy cattle by the competent authority.

The selection must also be guided by the abilities of the farm staff and/or infrastructure available. The treatment regime must be manageable for the farmer, minimizing the risks to animal welfare, occupational health and safety and the risks from antimicrobial residues in milk and meat.

*2.2.2 Use reliable, accurate and validated diagnostic tests to inform antimicrobial selection, especially for complicated or non-responsive disease*

Where appropriate, veterinarians should undertake further tests to characterize the microorganisms involved in the disease. Consider opportunities to investigate and collect samples both ante and post mortem for serious diseases. Gross pathological findings can be enriched by microbiological and/or serological examination. Culture and sensitivity tests can identify the pathogens and their potential resistance to antimicrobial agents.

*2.2.3 Only use combinations of antimicrobial agents that are synergistic and approved by competent authorities for use together*

Combinations of antimicrobials may be used for their additive effect to increase therapeutic efficacy or to broaden the spectrum of activity. Only use combinations that are supported scientifically. In most circumstances, veterinarians should limit the use of combination therapies to those registered by the competent government authority.

*2.2.4 Prescribing or using antimicrobial agents off-label must only be undertaken if permitted under national legislation and if the risks can be adequately managed*

Veterinarians must provide users of antimicrobial agents with instructions for use that ensures the treatment is effective and will not cause undue harm. Varying the instructions for use from those evaluated during the registration process (and stipulated on the manufacturer's label) increases the risks of unexpected outcomes. In countries where it is legal to do so, veterinarians may prescribe antimicrobial agents to be used "off-label" but, in these circumstances, have additional responsibilities to ensure that the treatment is effective and the risks to the animals, people and the dairy supply chain are managed.

Veterinarians can manage the risks by closely monitoring the dairy animal(s) during treatment, keeping appropriate records and giving clear instructions to those managing the treated animal(s) with regards to withholding periods for meat and milk. Unexpected outcomes should be investigated.

*2.2.5 Prescribing or using unregistered antimicrobial agents must only be undertaken if permitted under national legislation and if the risks can be adequately managed*

Treating food-producing animals with antimicrobial agents that have not been evaluated for veterinary use is high risk and is restricted or prohibited in many countries. Where it is legal to do so, the use of unregistered antimicrobial agents in dairy cattle should be minimized and restricted to individual high value animals under the direct supervision of the prescribing veterinarian. This is particularly relevant for the use of antimicrobial agents that are registered for humans in food-producing animals.

As the pharmacokinetics of unregistered preparations is unlikely to be known or predictable, the milk and meat from treated animals may need to be tested to ensure its suitability prior to being used for human consumption. Treated animals must be permanently identified and treatment records kept. The veterinarian is also responsible for monitoring and investigating issues that may arise from the use of the unregistered antimicrobial agents.

## **2.3 Give clear advice on the appropriate use of the antimicrobial agent**

Veterinarians have specialized knowledge and skills in the most appropriate ways to treat diseased animals. It is the prescribing veterinarian's responsibility to ensure that their treatment instructions are clearly communicated to the person responsible for administering the treatment.

### *2.3.1 Consider advice from the manufacturer and on the product label when prescribing and/or administering antimicrobial agents*

Wherever possible, veterinarians should follow the directions of use stated on the product label or those provided by the product manufacturer when administering or prescribing antimicrobial agents for cattle on dairy farms. The product will have been evaluated as efficacious and safe by the competent authority when used according to these directions, resulting in predictable outcomes of the treatment.

### *2.3.2 Give clear instructions to persons that are responsible for administering antimicrobial agents about dose rates, method of administration and withholding period*

In circumstances where the antimicrobial agents are not being administered by the prescribing veterinarian, it is the veterinarian's responsibility to ensure that clear instructions accompany the preparation so that it is used as intended. Written instructions from the veterinarian are required by law in many countries. In situations where literacy is poor, the veterinarian must ensure that the person responsible for the animal's treatment understands fully the instructions for administering the full treatment.

### *2.3.3 Label all medicines supplied according to national legislation*

Antimicrobial agents should be labelled by the prescribing veterinarian in accordance with the law. Typically, as a minimum the veterinarian's label on antimicrobial agents should include the following:

- The statement "For animal treatment only"
- Veterinarian's name and contact details
- Date of supply
- Name of the person in control of the animal(s) or supplied with the product
- Identity or description of the animals to be treated
- Product name or active ingredient and strength
- Route of administration

- Dose rate required
- Relevant withholding periods for milk and meat

This label should not be placed where it obscures the manufacturer's label.

#### *2.3.4 Record details of treatments administered and antimicrobial agents supplied in line with national legislation*

In most countries, veterinarians are required by law to keep records of the antimicrobial agents they administer and supply to farmers. These records are useful should problems emerge and are important for regulating the supply and use of antimicrobial agents in the community. The records that veterinarians should keep include:

- Quantities of antimicrobial agents prescribed
- Types and quantities of treatments supplied to individual farms
- List of withholding times
- Records of animal responses to treatment, including adverse responses

### **2.4 Review treatments**

Veterinarians are in the best position to review the effectiveness of the treatments they prescribe. Animals prescribed longer term or prophylactic antimicrobial use should be reviewed periodically and the effectiveness and need for ongoing treatment evaluated.

#### *2.4.1 Periodically review the health status of livestock being treated and the appropriateness of antimicrobial agent therapies*

Veterinarians need to ensure that the animals being treated are monitored for signs of disease. Treatment regimes should be re-evaluated if the treatment appears to be ineffective or periodically (for example, every 6 months) should longer term antimicrobial use be indicated. A periodic review improves the veterinarian's knowledge of the herd's disease status and provides the opportunity for the veterinarian and farmer to review and discuss alternative management and treatment options. There may be a need for additional testing to help with decisions on other treatment options.

#### *2.4.2 Report unexpected outcomes of antimicrobial use to the competent authority*

Most countries keep a register of adverse experiences relating to the use of agricultural and veterinary antimicrobial agents. Veterinarians should investigate and report instances where the antimicrobial treatments they prescribe do not result in the outcomes they expect. Statistics collated by a central agency can identify emerging problems with a particular antimicrobial agent, including quality issues with a particular batch or the development of microbial resistance.

## Fact sheet 3: Food processing companies

Food processing companies sourcing milk and meat from dairy farms need to provide farmers with clear specifications about the quality of the raw products they will accept. Food safety issues such as antibiotic residues must be included in these specifications. Companies can also play a role in providing advice to farmers on recommended practices to comply with their requirements. These issues may form all or part of a company's Supplier Quality Assurance System.

Post farm gate, food processing companies should monitor the quality of incoming supplies and provide rapid feedback if non-compliances are detected. Moreover, food companies should have measures in place to detect milk that does not match their specifications as early as possible and to exclude it from further processing. hazard analysis and critical control point (HACCP)-based food safety programs contribute to minimizing transfer of microorganisms and antimicrobial resistance in food.

### **3.1 Provide clear specifications for raw materials and the quality management systems to help farmers meet them**

#### *3.1.1 Implement a documented food safety/QA system for all suppliers*

Food companies should provide a suitable quality assurance (QA) framework and adequate training for farmers to implement it. The program should be designed and implemented within the context of the HACCP system as described by CODEX in the General Principles of Food Hygiene [21]. Where there are limitations to the full application of HACCP principles on the farm, good dairy farming practices should be followed, as described in the FAO/IDF Guide to Good Dairy Farming Practice (2011) [1]. The requirements for the prudent use of antimicrobials or veterinary substances should be aligned with national legislation and company requirements.

#### *3.1.2 Provide clear specifications for purchasing raw materials from suppliers and an incentive system to foster compliance*

Dairy farmers should understand the company's specifications for the supply of milk or meat and the incentives or penalties provided to meet these requirements. Both should be documented in the farm's food safety/QA system documentation and/or in the commercial contract for supply. Any changes to the requirements should be rapidly communicated to suppliers along with information to assist the farmer to conform to the new requirements.

Appropriate rewards and penalties should be in place to encourage dairy farmers to comply with company requirements, and these should be applied fairly to all suppliers.

### *3.1.3 Audit/assess the effectiveness of on-farm food safety/QA systems regularly*

Companies should arrange audits or assessments of the dairy farm's food safety/QA system on a regular basis. The company should monitor the results of the audits and follow up on any non-conformances in a timely manner. The frequency of auditing may be determined by the past performance of the supplier, by regulatory requirements or by the customers of the processing company.

If screen testing of incoming supplies (see 3.2.1) detects a positive result, the company should arrange for a follow-up investigation on the farm and temporary withdrawal of milk collection until the farm milk is checked for compliance with antimicrobial residue criteria. The follow-up investigation may include a detailed audit of the farm's food safety/QA system.

### *3.1.4 Work with farmers to improve performance*

Purchasing companies should actively work with suppliers to improve farm risk management procedures with regard to antimicrobial use. Formal recommendations should be incorporated into the farm's food safety/QA documentation and followed up at subsequent visits. The farm's prescribing veterinarian should be consulted and involved if issues with antimicrobial use are identified on the farm.

Training for dairy farmers on the safe and prudent use of antimicrobial agents is highly recommended.

## **3.2 Detection and exclusion of contaminated supplies**

The early detection of milk and meat that does not comply with the residue criteria ensures that it can be readily excluded from further processing. Food processing companies can provide support for farmers in detecting contaminated produce before it leaves the farm, and should have systems in place to screen raw materials arriving at the processing facility in line with their factory's food safety/QA system.

### *3.2.1 Provide guidance for on-farm milk testing*

Using the antimicrobial product strictly according to label and veterinary direction and following the withholding period is the best way to comply with the antimicrobial residue requirements for milk. "Cow-side" tests may be advised by veterinarians or milk companies in some circumstances to verify that milk from individual cows complies with the residue criteria. Milk should not be delivered if a screening test result is positive, unless suitable confirmation reveals that the result is not significant.

### *3.2.2 Provide screening of farm supplies*

Food processing companies should screen the raw milk supplied by farmers for the presence of antimicrobial agent residues. The aim of screening is to detect non-conforming supplies. The screening may be conducted by testing all suppliers, a statistically significant sample and/or on the basis of past performance. Testing protocols can allow contaminated produce from individual farms to be identified prior to further processing but, in many situations, test results on individual farm supplies do not become available in time. Generally, milk processing companies rely on the examination of tanker milk or bulk milk samples that are delivered to the processing facility with the milk (see 3.2.3). Meat processors also generally screen animals during further processing.

The extent of follow-up investigations and testing to be conducted on samples with presumptive positive results from the screening test is dependent on the stated requirements by the food company and local regulations. The follow-up may range from a simple confirmation of the screening result to the application of group-specific tests and/or a full identification of the responsible substance.

Non-conforming suppliers must be notified promptly. Companies should follow up this notification with further actions, which may include checking on the farm's next supply before collection; an on-farm investigation or visit to examine antimicrobial use and help the farmer to use antimicrobial agents prudently; contacting the farm's veterinarian or antimicrobial supplier; and implementing penalties.

The companies should understand the limitations of the screening test in regard to detection of antibiotics, the test sensitivity and potential causes of false positive and negative results.

### *3.2.3 Screen incoming supplies at processing facilities*

Screening of incoming supplies by food companies is aimed at detecting raw product that is unfit for further processing.

With milk this is generally undertaken on each "batch" (tanker load) as it enters the processing facility. Rapid tests are most suitable for screening in this situation. A risk assessment should determine the choice of which antimicrobial agents to be screened.

Meat processing facilities can screen animals that are deemed to be high risk of containing antimicrobial agents. Urine microbial inhibition tests (MIT) are suitable for this purpose. Individual carcasses failing the screening test can be held for further confirmatory testing and/or excluded from further processing.

Companies should set aside milk and meat supplies if a positive result to the screening test is found. Further investigations should then be conducted to confirm the non-compliance and determine the options for use of the product. If the specific raw material cannot be processed, measures taken to dispose of the milk or meat should consider ways to reduce the risk to the environment

and to prevent cross-contamination of other raw materials and products.

Food processing companies must have systems in place to enable raw materials (milk and meat) to be traced from the source farm, right through the processing chain through to the final product and its distribution to wholesalers and retailers.

#### *3.2.4 Testing of product*

Food processing companies should have systems in place that provide assurance that end products are fit for human consumption and, hence, comply with all food safety requirements. Product should be tested against the maximum residue limits (MRLs) for end products established by Codex Alimentarius and/or specific levels set by some regions or countries.

The choice of the test method is dependent on the criteria set. Where an absence of microbial growth has to be shown, a suitable microbiological test will do. Where compliance against MRLs has to be checked, substance-specific quantitative methods should be applied.

Some regions or countries may require competent authorities to be notified of positive results, the recall and removal of product and the outcomes of follow-up investigations.

### **3.3 HACCP management of microbiological hazards**

Implementation of HACCP-based food safety programs by food processors ensures control and minimizes the presence of microorganisms in food. This contributes to reducing food-borne transfer of antimicrobial resistance.

#### *3.3.1 Control measures for microbiological hazards*

Food processing companies should assess microbiological hazards and implement effective control measures, which may include temperature controls; use of sanitizers and disinfectants; and heat treatments.

## Test Methods for the Detection of Antimicrobial Residues

For the detection of antimicrobial residues, a wide range of test methods is available. Food companies should be aware of the suitability and limitations of different test principles, should use test methods of known sensitivity and selectivity for testing of supplies and should take measures to ensure that test results are reliable. The following measures may be required:

- On-going training for technicians
- Known positive and negative standards to confirm the claimed detection ability of the tests
- Participation of technicians in proficiency testing programs

Available test methods can be grouped as below. Each group is listed with their advantages and limitations:

### 1. Microbiological inhibition tests

The principle is based on growth inhibition of certain test bacteria that are seeded in a specific test medium.

#### Advantages

- + Exhibit a broad detection pattern for a wide range of antimicrobials, thereby also detecting growth inhibition by combinations of substances and/or through synergistic effects
- + Simple facilities generally suffice for a successful execution, either on-farm, at the dairy plant or in a laboratory. Required expertise is limited, although the proper reading interpretation of tests results does require some experience
- + Suitable for large scale testing in laboratories, easy to automate and can be performed relatively cheaply
- + Can to some extent be used as group-specific tests by introducing antagonists like  $\beta$ -lactamases (for the group of  $\beta$ -lactam antibiotics) and para-aminobenzoic acid (for sulfonamides) in parallel tests

#### Limitations

- Detectability of individual substances is widely different. Most relevant substances are detected with enough sensitivity, but some others may go undetected
- Methods allow limited identification of growth inhibitors at the group level (see above), but are not able to identify and quantify individual substance

- Suitable for screening, but subsequent confirmatory testing is needed in case a group identification is required or compliance against MRLs must be checked
- Not fast; tests may take at least 2.5 hours
- Not specific for antimicrobial agents and may be susceptible to interfering substances in raw milk such as naturally occurring inhibitors (for example, lysozyme and lactoferrin), free fatty acids and cleaning and disinfection agents.

## 2. Fast receptor tests

The principle is based on the binding of antimicrobials to one or more group-specific receptors that then react with a substrate to provide a quantitative reaction. Commercial tests are mostly offered as so-called strip tests for one or two groups of antimicrobial agents, for example,  $\beta$ -lactams or  $\beta$ -lactams+tetracyclines.

### Advantages

- + Group-specific and exhibit a broad detection pattern for antimicrobials belonging to the targeted group(s) of substances
- + Simple facilities generally suffice for successful execution, either on-farm, at the dairy plant or in a laboratory. Required expertise is limited, although the proper reading and interpretation of tests results does require some experience
- + Suitable for field use
- + Results are quickly available, in 2–15 minutes
- + Relatively inexpensive

### Limitations

- Only detects substances from targeted groups, other substances may go undetected
- Not able to identify and quantify individual substances
- Suitable for screening, but subsequent confirmatory testing is needed to check for compliance against MRLs
- False negatives due to sensitivity issues may be a concern

More recently, analytical concepts with specific receptors for individual substances have been introduced in so called micro-array formats. These allow semi-quantitative detection of targeted individual antimicrobials or veterinary substances and can be applied in confirmatory testing in cases of a positive screening result.

### 3. Qualitative and quantitative instrumental methods

The principle is generally based on chromatographic separation of individual substances and their subsequent identification and quantification using systems such as high-performance liquid chromatography (HPLC) or liquid chromatography in combination with mass spectrometry (LC/MS-MS) or HPLC in combination with time-of-flight mass spectrometry U(H)PLC-ToF

#### Advantages

- + Specific, the modern multi-component methods exhibit a broad detection pattern for antimicrobials. If required, additional tests can be targeted on non-covered individual substances
- + Sensitive; detection limits are usually far below existing MRLs
- + Suitable for checking definitive compliance against MRLs

#### Limitations

- Only targeted substances are detected
- Requires specific equipment and expertise
- Laborious and time-consuming in execution, not suitable for large numbers of samples
- Relatively expensive

## Fact sheet 4: Pharmaceutical companies

Pharmaceutical companies manufacture and market antimicrobial agents and so play an important part in manufacturing high quality products and controlling the supply of these products to the market place. They also hold data that are needed to evaluate properly the efficacy and safety of the product during registration. These companies also have an after-market responsibility to investigate potential issues with their products and report the outcomes to the appropriate regulatory agency.

### 4.1 Provide the necessary information to allow the scientific assessment of antimicrobial products

The purpose of registration is to regulate the quality and supply of antimicrobial agents to assure their correct use. In considering whether a product is suitable to be registered, the registering authority as a minimum must be satisfied that the use of the product will not result in unacceptable risks to animals, people and the environment.

#### *4.1.1 Generate and provide the required information/data to allow antimicrobial products to be assessed by the competent authority*

Data are required for the registering authority to be able to undertake an evidence-based risk assessment. The data required as evidence may vary between jurisdictions, but in every case the risks to food safety from antimicrobial residues and to the wider community from antimicrobial resistance should be considered.

Pharmaceutical companies must guarantee the quality of this data by ensuring it is generated in accordance with good manufacturing, laboratory and clinical practices.

#### *4.1.2 Provide the competent authorities with data on the type and amount of antimicrobial agents being manufactured and/or marketed*

On request, pharmaceutical companies should be able to provide the competent authorities with data on the quantity of the various antimicrobial agents being marketed. This information is important for managing antimicrobial resistance within animal and human populations.

### 4.2 Only supply approved antimicrobial agents through regulated channels

#### *4.2.1 Ensure antimicrobial agents are appropriately registered and approved by the competent authority before being marketed and supplied*

The supply of unregistered antimicrobial agents to farmers is illegal in most countries because the risks to the animals, users, environment and the wider

community have not been scientifically evaluated. Pharmaceutical companies must not supply antimicrobial agent products until the product had been assessed by the competent authority and approval for its supply and use has been granted. Limited scale use (with authority from the regulator) should be acceptable to enable the data to be generated for evaluation.

#### *4.2.2 Use GMP in the manufacture of antimicrobial agents*

The manufacture of antimicrobial products must be consistent with good manufacturing practice. The quality of raw materials should be tested and be consistent with internationally recognized pharmaceutical standards, such as the British Pharmacopoeia, EU Pharmacopoeia or US Pharmacopoeia. The manufacturing process must be documented with quality control systems in place to ensure compliance with the manufacturer's approved methodology. Proper certification and packaging for market in accordance with the requirements of registration ensures that the antimicrobial products meet the quality expectations of the end users.

#### *4.2.3 Supply antimicrobial agents through authorized and regulated channels*

Most countries have tight regulatory controls on the manufacture, distribution and sale of antimicrobial agents. These controls are in place to ensure that the antimicrobial agents are used judiciously and so have long-term benefits for animal health and welfare and animal productivity. Uncontrolled supply of antimicrobial agents can lead to inappropriate use and overuse, increasing the risks to the community from a lack of efficacy and/or antimicrobial resistance.

#### *4.2.4 Information on the use of antimicrobial agents should not have an advertorial character*

Marketing antimicrobial agents directly to farmers increases the potential for the products to be used inappropriately. These risks can be minimized by ensuring that farmers consult with a veterinarian to establish a diagnosis and the recommended treatment regime prior to being supplied with a product.

### **4.3 Monitor after-market product performance**

#### *4.3.1 Have systems in place to monitor for and receive feedback from product users*

Pharmaceutical companies should have systems in place to receive and collate feedback from the end users of their products. This serves as an early warning system should issues arise with one of their products and is a potent source of market research for future product developments.

#### *4.3.2 Actively investigate problems reported with antimicrobial agent use*

Should problems arise, pharmaceutical companies need to work with regulators and local agencies to address them. Prompt investigation and action can stop the issue from becoming major.

#### *4.3.3 Implement a pharmaco-vigilance program and, on request, a specific surveillance program for bacterial susceptibility and resistance*

The efficacy of various antimicrobial agents on specific pathogens is likely to vary over time. As such, it is prudent to actively monitor farm microorganisms for resistance to the commonly used antimicrobial agents. Monitoring and surveillance can be undertaken at veterinary laboratories from samples sent in for routine testing. Specific programs may be appropriate if farms are reporting a decline in efficacy of a particular antimicrobial product over time.

## Fact sheet 5: Competent authorities

Competent authorities underpin the prudent use of antimicrobial agents on dairy farms by approving products for supply and use, monitoring information provided by pharmaceutical companies, regulating the supply by authorized distributors such as veterinarians and periodically reviewing the suitability of antimicrobial agents used in dairy food production.

### 5.1 Assess the suitability of antimicrobial agents for use on dairy animals prior to registration

The purpose of registration is to allow the manufacture, supply and use of veterinary medicines to treat sick animals but also to assure their correct use and prevent their overuse or misuse. Amongst other things, the registering authority must be satisfied that the use of the product will not result in unacceptable risks to animals, people and the environment.

#### 5.1.1 Conduct risk assessment prior to registration

The risk assessment should consider the potential for development of antimicrobial resistance in the animal that will impair the efficacy of any other antimicrobial agents for human or animal use. Examples of the information that may be required for the assessment include:

- Antimicrobial-resistance mechanisms and genetics
- Occurrence and rate of transfer of antimicrobial-resistance genes
- Potential for antimicrobial-resistant microorganisms to occur in animals
- Amount and frequency of exposure of susceptible humans to antimicrobial-resistant microorganisms
- Perceived and known clinical importance of antimicrobial agents to humans
- Benefits of the antimicrobial agent's use in animal health

#### 5.1.2 Establish maximum residue limits in food products

The maximum residue limit (MRL) is recognized as the maximum permitted level of antimicrobial agents in foods following recommended and legal guidelines for use. MRLs are usually set by Codex. The following factors may be considered when establishing a MRL:

- MRLs established by Codex and major trading partners
- Acceptable dietary exposure to low levels of antimicrobial agents in food
- How accurately the antimicrobial agents or toxicologically significant metabolites can be measured
- How rapidly the antimicrobial agents is processed by animal tissue
- Frequency of use of the antimicrobial agents, taking into account the potential for bio-accumulation
- Time period between treatment and consumption as food
- The effect of processing

### 5.1.3 Establish withholding periods for milk and meat after treatment

The withholding period for each antibiotic will consider the following:

- MRL for the antibiotic
- Formulation of the treatment
- Target animal
- Dosage of likely treatment
- Duration of treatment
- Route of administration
- Metabolism or excretion of the antibiotic

### 5.1.4 Approve product label information

Pharmaceutical companies are required to provide clear information on the product label, including details of the active constituent, dose rates, route of administration, restrictions on use, recommended withholding times, expiry date and storage conditions. The details on the product label need to be assessed and approved by the competent authority. The competent authority must be satisfied that the label information is consistent with the efficacious and safe use of the antimicrobial product.

Competent authorities will monitor the information printed on labels and datasheets on an ongoing basis.

### 5.1.5 Review product registration in the light of adverse reports of the antimicrobial's use

The competent authority will monitor reports from around the world about specific issues relating to antimicrobial usage such as:

- Reduction in the efficacy of treatments
- Results of adverse treatments
- Information on antimicrobial resistance from human and animal health areas

The monitoring is conducted on an ongoing basis to ensure that appropriate decisions are made about the ongoing registration of antimicrobial agents.

## 5.2 Implement controls over the supply of antimicrobial agents

Regulators must maintain controls over the supply of antimicrobial agents – from the point of manufacture or importation, through the distribution chain to the point of sale to the farmer. The aim is to ensure that only good quality product that has been assessed and approved for use by the competent authority is available for farmers. Farmers should only be able to access supplies of antimicrobial agents from veterinarians or other suitable persons authorized to prescribe antimicrobial agents in accordance with national legislation and under the supervision of a veterinarian, who can assess the appropriateness of supplying the antimicrobial agents to farmers.

### *5.2.1 Restrict the supply of antimicrobial agents to licensed distributors*

Regulators should regulate the companies distributing and handling antimicrobial agents between the manufacturer and the point of supply to the farmer, usually a veterinarian. Distributors must keep records that allow regulators to audit the movement of product along the supply chain and account for the quantity of product supplied. The licensee should be subject to periodic review and audit.

### *5.2.2 Register and regulate veterinarians as appropriate*

Veterinarians should be appropriately educated, trained and subsequently licensed by a competent authority before being given the right to supply antimicrobial agents to farmers. They must be required to keep records of all antimicrobial agents dispensed to farmers. A procedure to remove prescribing rights should be in place to ensure that veterinarians act ethically in the supply of antimicrobial agents and comply with all legislative requirements.

Veterinarians should be required to report adverse results of treatments to the pharmaceutical suppliers and competent authorities.

Regulators should require licensed veterinarians to keep their skills and knowledge current. Participation in professional development programs and ongoing personal development will increase the understanding of effective therapies and antimicrobial resistance by practicing veterinarians.

## **5.3 Implement controls on the use of antimicrobial agents on dairy farms**

Competent authorities should have controls over the use of antimicrobial agents on farms so that inappropriate use can be stopped. The authorities need to work proactively with veterinarians, milk and meat processors, agents, dairy advisers and farmers to monitor current use patterns and address potential issues before they cause harm.

### *5.3.1 Check the labelling and distribution of antimicrobial agents on dairy farms*

Competent authorities should periodically review the labels and prescribing information provided with the antimicrobial agents used on dairy farms for compliance with product registration requirements and relevant legislation.

### *5.3.2 Verify on-farm quality assurance programs and farm practices with regard to the use of antimicrobial agents*

Competent authorities should verify and assess on-farm food safety and quality assurance programs, especially focusing on the storage and use of antimicrobial agents. Farm records of the identity of the animal treated and the antimicrobial agents used should be available.

The competent authority should ensure that auditors are competent and monitor their performance.

#### *5.3.3 Conduct surveys of milk and dairy products or monitor for the presence of antimicrobial residues*

Competent authorities should monitor farm milk and meat supplies for antibiotic residues or evaluate available data from appropriate monitoring systems operated by others in the supply chain. These surveys will provide further evidence of the effective management of the farm practices in the use of antibiotics for treatment of animals.

### **5.4 Monitor for adverse outcomes of antimicrobial use, including antimicrobial resistance**

Patterns of antimicrobial resistance should be monitored and disseminated to appropriate national and international authorities.

#### *5.4.1 Monitor for changes in antimicrobial agent susceptibility of selected microorganisms from food, animals and clinical samples*

Competent authorities must cooperate on a national and international basis to monitor changes in the susceptibility of selected microorganisms from food, animal and human clinical samples. Information should be reviewed on a regular basis for potential issues. The information should be distributed to registration agencies, pharmaceutical companies, veterinarians and medical professions to ensure that all possible measures are being taken to minimize the potential for antibiotic resistance in animals and humans.



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International Dairy Federation (I.N.P.A.)  
Boulevard Auguste Reyers 70/B, 1030 Brussels - Belgium

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