USA Comments and observations noted in blue font

CHAPTER 6.7.

HARMONISATION OF NATIONAL ANTIMICROBIAL RESISTANCE SURVEILLANCE AND MONITORING PROGRAMMES

Article 6.7.1.

Objective

This chapter provides criteria for the:

1) development of national antimicrobial resistance surveillance and monitoring programmes,
2) harmonisation of existing national antimicrobial resistance surveillance and monitoring programmes,

in food producing animals and in products of animal origin intended for human consumption.

Article 6.7.2.

Purpose of surveillance and monitoring

Active (targeted) surveillance and monitoring are core parts of national antimicrobial resistance surveillance programmes. Passive surveillance and monitoring may offer additional information (refer to Chapter 1.4.). Cooperation between all Member Countries conducting antimicrobial resistance surveillance should be encouraged.

Surveillance and monitoring of antimicrobial resistance is necessary to:

1) assess and determine the trends and sources of antimicrobial resistance in bacteria;
2) detect the emergence of new antimicrobial resistance mechanisms;
3) provide the data necessary for conducting risk analyses as relevant to animal and human health;
4) provide a basis for policy recommendations for animal and human health;
5) provide information for evaluating antimicrobial prescribing practices and, for prudent use recommendations;
6) assess and determine effects of actions to combat antimicrobial resistance.

Article 6.7.3.

The development of antimicrobial resistance surveillance and monitoring programmes

1. General aspects

Surveillance of antimicrobial resistance at targeted intervals or ongoing monitoring of the prevalence of resistance in bacteria from animals, animal feed, food, environment and humans, constitutes a critical part of animal health and food safety strategies aimed at limiting the spread of antimicrobial resistance and optimising the choice of antimicrobial agents used in therapy.
Monitoring of bacteria from products of animal origin intended for human consumption collected at different steps of the food chain, including processing, packing and retailing, should also be considered. National antimicrobial resistance monitoring and surveillance programmes should be scientifically based and may include the following components:

a) statistically based surveys;

b) sampling and testing of food producing animals on the farm, at live animal markets or at slaughter;

c) an organised sentinel programme, for example targeted sampling of food producing animals, herds, flocks, and vectors (e.g. birds, rodents);

d) analysis of veterinary practice and diagnostic laboratory records;

e) sampling and testing of products of animal origin intended for human consumption.

2. Sampling strategies

a) Sampling should be conducted on a statistical basis. The sampling strategy should ensure:
   – the sample is representative of the population of interest;
   – the robustness of the sampling method.

b) The following criteria are to be considered:
   – sample source such as food producing animal, food, animal feed;
   – animal species;
   – category of animal within species such as age group, production type;
   – health status of the animals such as healthy, diseased;
   – sample selection such as targeted, systematic random, non-random;
   – type of sample (e.g. such as faecal, faeces, carcass, food product);
   – sample size.

3. Sample size

The sample size should be large enough to allow detection of existing and emerging antimicrobial resistance phenotypes.

Sample size estimates for prevalence of antimicrobial resistance in a large population are provided in Table 1 below.
Table 1. Sample size estimates for prevalence in a large population

<table>
<thead>
<tr>
<th>Expected prevalence</th>
<th>90% Level of confidence</th>
<th>95% Level of confidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Desired precision</td>
<td>Desired precision</td>
</tr>
<tr>
<td></td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td>10%</td>
<td>24</td>
<td>97</td>
</tr>
<tr>
<td>20%</td>
<td>43</td>
<td>173</td>
</tr>
<tr>
<td>30%</td>
<td>57</td>
<td>227</td>
</tr>
<tr>
<td>40%</td>
<td>65</td>
<td>260</td>
</tr>
<tr>
<td>50%</td>
<td>68</td>
<td>270</td>
</tr>
<tr>
<td>60%</td>
<td>65</td>
<td>260</td>
</tr>
<tr>
<td>70%</td>
<td>57</td>
<td>227</td>
</tr>
<tr>
<td>80%</td>
<td>43</td>
<td>173</td>
</tr>
<tr>
<td>90%</td>
<td>24</td>
<td>97</td>
</tr>
</tbody>
</table>

4. Sample sources

Member Countries should examine their livestock production systems on the basis of available information and assess which sources are likely to contribute most to a potential risk to animal and human health.

a) Animal feed

Member Countries should consider including animal feed in surveillance and monitoring programmes as they may become contaminated with antimicrobial resistant bacteria, e.g. Salmonella.

b) Food producing animals

Categories of food producing animals considered for sampling should be relevant to the country’s production system.

c) Food

Member Countries should consider including products of animal origin intended for human consumption in surveillance and monitoring programmes as foodborne transmission is considered to be an important route for the transfer of antimicrobial resistance.

5. Type of sample to be collected

Feed samples should be collected in amounts sufficient for isolation of resistant bacteria of concern (at least 25 g) and should be linked to pathogen surveillance programmes.

Faecal samples should be collected in amounts sufficient for isolation of the resistant bacteria of concern (at least 5 g from bovine and porcine and whole caeca from poultry).

Sampling of carcasses at the slaughterhouse/abattoir provides information on slaughter practices, slaughter hygiene and the level of microbiological contamination and cross-contamination of meat. Further sampling of the product at retail sales level may provide additional information on the overall microbiological contamination from slaughter to the consumer.

Existing food processing microbiological monitoring, risk-based management and other food safety programmes may provide useful samples for surveillance and monitoring of resistance in the food chain after slaughter.

Table 2 provides examples of sampling sources, sample types and monitoring outcomes.
Table 2. Examples of sampling sources, sample types and monitoring output

<table>
<thead>
<tr>
<th>Source</th>
<th>Type</th>
<th>Output</th>
<th>Additional information required or additional stratification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herd or flock of origin</td>
<td>Faeces or bulk milk</td>
<td>Prevalence of resistant bacteria originating from animal populations (of different production types) Relationship between resistance and antimicrobial use</td>
<td>Age categories, production types, etc. Antimicrobial use over time</td>
</tr>
<tr>
<td>Abattoir</td>
<td>Faeces</td>
<td>Prevalence of resistant bacteria originating from animals at slaughter</td>
<td></td>
</tr>
<tr>
<td>Abattoir</td>
<td>Caeca or intestines</td>
<td>As above</td>
<td></td>
</tr>
<tr>
<td>Abattoir</td>
<td>Carcass</td>
<td>Hygiene, contamination during slaughter</td>
<td></td>
</tr>
<tr>
<td>Processing, Abattoir</td>
<td>Food products</td>
<td>Hygiene, contamination during processing and handling</td>
<td></td>
</tr>
<tr>
<td>Point of sale (Retail)</td>
<td>Food products</td>
<td>Prevalence of resistant bacteria originating from food, exposure data for consumers</td>
<td></td>
</tr>
<tr>
<td>Various origins</td>
<td>Animal feed</td>
<td>Prevalence of resistant bacteria originating from animal feed, exposure data for animals</td>
<td></td>
</tr>
</tbody>
</table>

Please note for consideration: the sample size calculation is based on independent samples. If these is any ‘clustering’ for farm or animal, these recommended sample sizes would not be sufficient.

6. Bacterial isolates

The following categories of bacteria could be included in surveillance and monitoring programmes monitored:

a) Animal bacterial pathogens relevant to the countries’ priorities

i) Surveillance and monitoring of antimicrobial resistance in animal bacterial pathogens is important, both to:
   i) detect emerging resistance that may pose a concern for animal and human health;
   ii) detect changes in susceptibility patterns;
   iii) provide information for risk analysis;
   iv) guide veterinarians in their prescribing treatment decisions.

ii) Information on the occurrence of antimicrobial resistance in animal bacterial pathogens is in general either derived from routine clinical material sent to veterinary diagnostic laboratories or from an active monitoring programme. These samples, often derived from severe or recurrent clinical cases including therapy failure, may provide biased information. Although antimicrobial resistance information provided by diagnostic laboratories is primarily for treatment purposes, it is also useful for identification of novel resistance patterns and can possibly assist in identifying emerging resistance. However, in order to estimate accurately the prevalence of antimicrobial resistance in the bacterial pathogen, in a larger population of animals, an active sampling programme should be implemented.

iii) To promote a harmonised global approach to the selection of animal bacterial pathogens for inclusion in national surveillance and monitoring programmes, bacteria should be selected using the following criteria:

   i) impact on animal health and welfare;
implication of antimicrobial resistance in the bacterial pathogen on therapeutic options in veterinary practice;
- impact on food security and on production (economic importance of associated diseases);
- bacterial diseases responsible for the majority of veterinary antimicrobial usage (stratified by usage of different classes or their importance);
- existence of validated susceptibility testing methodologies for the bacterial pathogen;
- Existence of quality assurance programmes or other pathogen reduction options that are non-antimicrobial (vaccines, alternatives to antimicrobials and hazard analysis critical control points based production practices).

**Rationale:** the United States suggests these added examples highlighted for completeness.

The table below, derived using the above criteria, lists suggested animal bacterial pathogens for inclusion in a monitoring programme of food-producing animals. This list is not exhaustive and should be adapted according to the situation in the country.

**Table 3. Examples of target animal species and animal bacterial pathogens that may be included in resistance surveillance and monitoring programmes**

<table>
<thead>
<tr>
<th>Target animals</th>
<th>Respiratory pathogens</th>
<th>Enteric pathogens</th>
<th>Udder pathogens</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle</td>
<td><em>Pasteurella multocida</em></td>
<td><em>Escherichia coli</em></td>
<td><em>Staphylococcus aureus</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Mannheimia haemolytica</em></td>
<td><em>Salmonella spp.</em></td>
<td><em>Streptococcus spp.</em></td>
<td></td>
</tr>
<tr>
<td>Pigs</td>
<td><em>Actinobacillus pleuropneumoniae</em></td>
<td><em>Escherichia coli</em></td>
<td><em>Streptococcus suis</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Pasteurella multocida</em></td>
<td><em>Salmonella spp.</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poultry</td>
<td></td>
<td><em>Salmonella spp.</em></td>
<td><em>Escherichia coli</em></td>
<td></td>
</tr>
</tbody>
</table>

**Clarity requested:** does this refer to *E. coli* as a pathogen (i.e., causing colibacillosis in calves), or *E. coli* as a commensal in adult cattle? The column indicated that these are pathogens.

b) Zoonotic bacteria

i) *Salmonella*

*Salmonella* should be sampled from animal feed, food producing animals and animal derived food products. For the purpose of consistency and harmonisation, samples should be preferably taken at the slaughterhouse/abattoir.

Surveillance and monitoring programmes may also include bacterial isolates originating from other sources obtained from designated national laboratories originating from other sources. Isolation and identification of bacteria and bacterial strains should follow nationally or internationally standardised procedures.

Serovars of public health importance such as S. Typhimurium and S. Enteritidis should be included. The inclusion of other relevant serovars will depend on the epidemiological situation in each country.
All *Salmonella* isolates should be serotyped and, where appropriate, phage-typed according to standard methods used at the nationally designated laboratories. For those countries that have the capabilities, *Salmonella* could be genotyped using genetic finger-printing methods.

**ii) Campylobacter**

*Campylobacter jejuni* and *C. coli* should be isolated from food producing animals and associated food products (primarily from poultry). Isolation and identification of these bacteria should follow nationally or internationally standardised procedures. *Campylobacter* isolates should be identified to the species level.

**iii) Other emerging bacterial pathogens**

Other emerging bacterial pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA), *Listeria monocytogenes* or others which are pathogenic to humans, may be included in resistance surveillance and monitoring programmes.

c) Commensal bacteria

*E. coli* and *enterococci* (*Enterococcus faecium* and *E. faecalis*) may be sampled from animal feed, food producing animals and products of animal origin intended for human consumption.

These bacteria are commonly used in surveillance and monitoring programmes as indicators, providing information on the potential reservoir of antimicrobial resistance genes, which may be transferred to pathogenic bacteria. It is considered that these bacteria should be isolated from healthy animals, preferably at the slaughterhouse/abattoir, for the purpose of consistency and harmonisation and be monitored for antimicrobial resistance.

7. **Storage of bacterial strains**

If possible, isolates should be preserved at least until reporting is completed. Preferably, appropriate isolates should be permanently stored. Bacterial strain collections, established by storage of all isolates from certain years, will provide the possibility of conducting retrospective studies.

8. **Antimicrobial susceptibility testing**

Clinically important antimicrobial agents or classes used in human and veterinary medicine should be included in antimicrobial resistance surveillance programmes. Member Countries should refer to the OIE list of antimicrobials of veterinary importance for monitoring purposes. However, recognizing that the number of tested antimicrobial agents may have to be limited according to financial resources.

**Rationale:** Improved syntax.

Appropriately validated antimicrobial susceptibility testing methods should be used in accordance with Guideline Chapter 3.1. of the *Terrestrial Manual*, concerning laboratory methodologies for bacterial antimicrobial susceptibility testing. Antimicrobial susceptibility data should be reported not only qualitatively (susceptible or resistant), but also quantitatively (minimum inhibitory concentrations [MICs] or inhibition zone diameters), rather than qualitatively.

9. **Recording, storage and interpretation of data**

a) Because of the volume and complexity of the information to be stored and the need to keep these data available for an undetermined period of time, careful consideration should be given to database design.

b) The storage of raw (primary, non-interpreted) data is essential to allow the evaluation in response to various kinds of questions, including those arising in the future.

c) Consideration should be given to the technical requirements of computer systems when an exchange of data between different systems (comparability or compatibility of automatic recording of laboratory data and transfer of these data between and within resistance monitoring programmes) is envisaged. Results should be collected in a suitable national database. They should be recorded quantitatively:
i) as distributions of MICs in micrograms per millilitre;

ii) or inhibition zone diameters in millimetres.

d) The information to be recorded should include, where possible, the following aspects:

i) sampling programme;

ii) sampling date;

iii) animal species and production type;

iv) type of sample;

v) purpose of sampling;

vi) type of antimicrobial susceptibility testing method used;

vii) geographical origin (geographical information system data where available) of herd, flock or animal;

viii) animal factors (e.g. such as age, condition, health status, identification, sex);

ix) exposure of animals to antimicrobial agents;

x) bacterial recovery rate.

e) The reporting of laboratory data should include the following information:

i) identity of laboratory,

ii) isolation date,

iii) reporting date,

iv) bacterial species,

and, where relevant, other typing characteristics, such as:

v) serotype or serovar,

vi) phage type,

vii) antimicrobial susceptibility result or resistance phenotype,

viii) genotype.

f) The proportion of isolates regarded as resistant should be reported, including the defined interpretive criteria used.

NOTE/observation for consideration: regarding Point f) above, is this the proportion of isolates in a particular sampling scheme within a program? Within a sample?

g) In the clinical setting, breakpoints are used to categorise bacterial strains as susceptible, intermediate or resistant. These clinical breakpoints may be elaborated on a national basis and may vary between Member Countries.

NOTE/comment: is Point g) above intended to make exception to the standardization sought under Item 8 in this Article? Appropriately validated antimicrobial susceptibility testing methods should be used in accordance to Chapter 3.1 of the Terrestrial Manual. Antimicrobial susceptibility data should be reported not only
qualitatively (susceptible/resistant), but also quantitatively (minimum inhibitory concentrations [MIC]).

h) The antimicrobial susceptibility testing standards and guidelines used should be recorded.

i) For surveillance purposes, use of the microbiological breakpoint (also referred to as epidemiological cut-off point), which is based on the distribution of MICs or inhibition zone diameters of the specific bacterial species tested, is preferred. When using microbiological breakpoints, only the bacterial population with acquired resistance that clearly deviates from the distribution of the normal susceptible population will be designated as resistant.

j) Ideally, data should be collected at the individual isolate level, allowing antimicrobial resistance patterns over time to be recorded, along with relevant use data and management practices.

Rationale: added language for clarity and completeness.

10. Reference laboratory and annual reports

a) Member Countries should designate a national reference centre that assumes the responsibility to:

i) coordinate the activities related to the antimicrobial resistance surveillance and monitoring programmes;
ii) coordinate and collect information from participating surveillance laboratories within the country;

iii) produce an annual report on the antimicrobial resistance situation in the country.

b) The national reference centre should have access to the:

i) raw data;

ii) complete results of quality assurance and inter-laboratory calibration activities;

iii) inter-laboratory proficiency testing results;

iv) information on the structure of the monitoring system;

v) information on the chosen laboratory methods.

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— Text deleted.