USA Comments TAHSC September 2107 Report

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, and the
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.). The OIE encourages cooperation between all Member Countries conducting appropriately designed antimicrobial resistance surveillance and monitoring should be encouraged.

Rationale: The United States recommends the added text for clarity and pertinence.

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.

General aspects The development of antimicrobial resistance surveillance and monitoring programmes

1. General aspects
Surveillance of antimicrobial resistance and 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. Animal feed and the environment should also be considered according to national priorities, scientific knowledge and risk assessment needs.

Surveillance or 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 to provide data on potential public health exposures.

**Rationale** – The United States recommends the added text to help further define the purpose of such monitoring of food products (compared to monitoring of animal pathogens)

National antimicrobial resistance monitoring and surveillance programmes should be scientifically designed and may include the following components:

**Rationale** – the word “designed” is more appropriate in the context of this recommendation because it indicates a study design that is developed to meet certain objectives at a known confidence level.

1a) statistically based surveys;

2b) sampling and testing of food-producing animals on the farm, at live animal markets or at slaughter;

3c) an organised sentinel programme, for example targeted sampling of food-producing animals, herds, flocks, and vectors (e.g. birds, rodents);

4d) analysis of veterinary practice and diagnostic laboratory records;

5e) sampling and testing of products of animal origin intended for human consumption;

6f) sampling and testing of feed ingredients or feed.

**Article 6.7.4.**

**Sampling**

**Sampling strategies**

a) Sampling should be conducted on a statistical basis as outlined in the study design. The sampling strategy should ensure:

**Rationale** – the added text strengthens the point that a scientific study design is necessary to be able to meet objectives and understand the level of confidence in the data

- 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 method such as targeted, systematic random, non-random;

– type of sample (e.g. such as faecal, faeces, caeca, carcass, food product);

- Representativeness/appropriateness of the sample (e.g. does caeca sample represent farm, consumer exposure, etc.)

**Rationale** – while some samples may be convenient to collect, it may not be clear what such samples represent. Indeed, if policy decisions or risk assessments are to be based on such samples, it needs to be determined if samples collected are representative of the desired population.

– sample size.

22. **Sample size**

The sample size should be large enough to allow detection or determine prevalence of, or trends in, existing and emerging antimicrobial resistance phenotypes.

The sample should avoid bias and provide a representative sample of the animal population, process, product or other unit of interest whilst taking into account the expected prevalence of the bacteria in the sample type, the expected prevalence of the resistance phenotype and the desired level of precision and confidence.

The sample size calculation in Table 1 is based on independent samples. If there is any clustering at the establishment or animal level, the sample size should be adjusted accordingly.

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>

34. Sample sources (Table 2)

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.

- **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*.

- **Food-producing animals**
  
  Categories of food-producing animals considered for sampling should be relevant to the country’s production system. Resource allocation should be guided by production volume of the food-producing animal species and the prevalence of resistant bacteria.

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

- **Animal feed**
  
  Member Countries should consider including animal feed in surveillance and monitoring programmes based on available resources, species and national priorities as they may become contaminated with antimicrobial resistant bacteria, e.g. *Salmonella*.

**Rationale:** many studies have shown a lack of any relationship between serotypes of *Salmonella* found in animal feeds and those found in the animals consuming those feeds. Therefore, as this has been shown, it would be technically correct to delete the entire Point c). See further rationale and supporting technical documentation below. If deleting Point c) is not possible, the United States then recommends incorporating the noted changes. Additionally, since feeding systems and feedstuffs vary so much from country to country, testing feed may not be practical for many of the feedstuffs.

The United States has previously submitted this rationale that is fully supported by the scientific peer reviewed literature. As noted before, it is not
uniformly accepted that feed and feed ingredients present significant public health risk. Exposure doses of $10^3$ organisms given intranasally or orally are not sufficient to establish infections in pigs, and oral doses of $10^8$ cfu have been required to consistently produce experimental infections. Please refer to the extensive peer reviewed scientific publications cited in our previous comments.

45. **Type of sample to be collected (Table 2)**

While it is difficult to collect feed samples representative of the batch, they 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.

**Rationale:** many countries do not routinely conduct pathogen surveillance of feedstuffs. Furthermore, this chapter is focused solely on AMR, therefore, it is out of scope of this chapter to recommend surveillance for other pathogens in animal feeds.

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)</td>
<td>Age categories, production types, etc. Antimicrobial use over time</td>
</tr>
<tr>
<td></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></td>
<td>Carcass</td>
<td>Prevalence of resistant bacteria after carcass dressing, representative of the hygiene, of the process and the contamination during slaughter</td>
<td></td>
</tr>
<tr>
<td>Processing, packing</td>
<td>Food products</td>
<td>Prevalence of resistant bacteria after processing, representative of the hygiene, of the process and the 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>
Article 6.7.5. Bacteria subjected to surveillance and monitoring

6. Bacterial isolates

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

1a) Animal bacterial pathogens relevant to the countries’ priorities

a) 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) provide data guide for veterinarians to inform their prescribing treatment decisions;

v) provide information for epidemiological studies and trend analysis.
b) 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 of animal health concern. 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.

**Rationale:** samples entering diagnostic laboratories represent clinically ill animals that are unlikely to enter the food chain. As such, they should not be considered representative of a public health exposure.

c) 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:

- 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 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, such as vaccines and Good Agricultural Practices.

The table below, derived using the above criteria, lists suggested animal bacterial pathogens for inclusion in a surveillance or 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 pathogens</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></td>
<td><em>Streptococcus suis</em></td>
</tr>
<tr>
<td></td>
<td></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></td>
<td><em>Escherichia coli</em></td>
</tr>
</tbody>
</table>

2b) Zoonotic bacteria

2a) *Salmonella*

*Salmonella* should be sampled from animal feed, food-producing animals, and animal-derived food products. When resources are adequate and animal feed samples are considered a national priority.
Salmonella from animal feed may be sampled and animal feed. For the purpose of consistency and harmonisation, feed samples should preferably be taken at the feed mill and animal samples should be preferably be taken at the slaughterhouse/abattoir from healthy animals and feed samples should preferably be taken at the feed mill.

**Rationale** – depending on the objective of the national surveillance system, on-farm sampling may be desirable over sampling at the slaughterhouse since it is well known that serotype and prevalence may vary widely from the farm to the slaughterhouse. Additionally, depending on the objective for any feed sampling, the desired sample source may differ. This language is prescriptive and does not allow for the design of epidemiological studies to meet national priorities.

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 in surveillance and monitoring programmes. The inclusion of other relevant serovars will depend on the epidemiological situation in each country.

All Salmonella isolates should be characterised by serotyped and, where appropriate, phage-typed according to standard genotypic methods used in the nationally designated laboratories. For those countries that have the capabilities, Salmonella could be genotyped using genetic fingerprinting methods.

**bii** Campylobacter

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

**ciii** Other bacteria that are pathogenic for humans, emerging bacterial pathogens

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

**Rationale** – if the national priority is to monitor the prevalence of resistant campylobacter on animal products (meat and poultry) to be able to assess the effectiveness of slaughter hygiene and public health exposure, then it may not be necessary to sample animals.

**3e** 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 or preferably meat and poultry, preferably at the slaughterhouse/abattoir for the purpose of surveillance of antimicrobial resistance in commensal organisms, consistency and harmonisation and be monitored for antimicrobial resistance.
**Rationale** – while healthy animals entering an abattoir are a potentially convenient sampling source, they are not the only sample source. Furthermore, such animals provide a less representative profile of potential public health exposure to these organisms than would meat and poultry. Finally, since this chapter is focused on AMR, the goal of collecting these samples should be for the monitoring of AMR in commensal organisms – not for determining the prevalence of these organisms.

**Article 6.7.6.**

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.

**Article 6.7.7.**

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 surveillance and monitoring purposes. However, recognising that the number of tested *antimicrobial agents* may have to be limited according to financial resources.

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.

**Article 6.7.8.**

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

1a) 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.

2b) 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.

3e) Consideration should be given to the technical requirements of computer systems when an exchange of data between different systems (compatibility or comparability of automatic recording of laboratory data and transfer of these data between and within resistance surveillance and monitoring programmes) is envisaged. Results should be collected in a suitable national database. They should be and recorded quantitatively:

   a) as distributions of MICs in micrograms per millilitre;

   b) or inhibition zone diameters in millimetres.

4d) The information to be recorded should include, where possible, the following aspects:

   a) sampling programme;

   b) sampling date;

   c) animal species and production type;
The reporting of laboratory data should include the following information:

- **Identity of laboratory,**
- **Isolation date,**
- **Reporting date,**
- **Bacterial species,**
and, where relevant, other typing characteristics, such as:

- **Serotype or serovar,**
- **Phage type,**
- **Antimicrobial susceptibility result or resistance phenotype,**
- **Genotype.**

The proportion of isolates regarded as resistant should be reported. The number of isolates regarded as resistant should be reported as a proportion of the number of isolates tested, including the defined interpretive criteria used.

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.

The bacterial isolation methods, antimicrobial susceptibility testing methods, standards and guidelines used should be recorded.

For surveillance and monitoring purposes, use of the clinical breakpoint as well as microbiological breakpoint cut off (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 should be reported. 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.

**Rationale** – the epidemiological “cutoff” is a relatively new tool that may be used to identify shifts in resistance patterns. However, the clinical breakpoint provides data that is useful by clinicians using such data to guide treatment decisions. Reporting both will allow this information to be used by a wider group of stakeholders.

Ideally, data should be collected at the individual isolate level. **This will allow allowing antimicrobial resistance patterns to be recorded over time to be recorded, along with relevant data, when available, on usage of antimicrobial agents and management practices.**
10. Reference laboratory and annual reports

1a) Member Countries should designate a national reference centre that assumes the responsibility to:

   a) coordinate the activities related to the antimicrobial resistance surveillance and monitoring programmes;

   b) coordinate and collect information from participating surveillance laboratories within the country;

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

2b) The national reference centre should have access to the:

   a) raw data;

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

   c) inter-laboratory proficiency testing results;

   d) information on the structure of the surveillance or monitoring system;

   e) information on the chosen laboratory methods.