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Committee for Medicinal Products for Veterinary Use

Advice on implementing measures under Article 57(4) of Regulation (EU) 2019/6 on veterinary medicinal products – Report on the format of the data to be collected on antimicrobial medicinal products used in animals

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Introduction

On 1 July 2019 the European Commission requested the European Medicines Agency, hereafter referred to as the Agency, to provide scientific recommendations to set up the format for the data to be collected on antimicrobial medicinal products used in animals, taking into account the following:

- the requirements described in Article 57(3) of Regulation (EU) 2019/6;
- the work of the expert group on the collection of data on antimicrobial medicinal products used in animals, bearing in mind the minimum requirements as to the animal species and categories for which data need to be collected (Article 57(5) of Regulation (EU) 2019/6);
- the format defined in protocols or guidance documents for data collection used in the context of the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project;
- information to be included in veterinary prescriptions and in records kept by owners and keepers of food-producing animals (Article 105 and Article 108 of Regulation (EU) 2019/6);
- international guidelines on global antimicrobial data collection, in particular the guidance for completing the OIE template.

The Committee for Medicinal Products for Veterinary Use (CVMP) formed an expert group to prepare the scientific report. The group was composed of eight experts selected from the European network of experts, on the basis of recommendations from the national competent authorities and two Agency staff members with expertise on collection of data on antimicrobial consumption in animals.

The expert group submitted their report to the CVMP on 30 April 2020.

The CVMP adopted the scientific report on 18 June 2020.

Summary

Article 57 of the Regulation (EU) 2019/6 on veterinary medicinal products, hereafter referred to as the Regulation, published on 7 January 2019 (Official Journal of the European Union, 2019b) lays down the obligation, among others, for Member States to collect comparable data on the volume of sales and on the use of antimicrobial medicinal products in animals. Moreover, the Regulation states that the European Commission shall by means of implementing acts set up the format for the data to be collected on sales and use.

Within the scope of the European Commission's request, and in addition to the recommendations relating to the format of sales and use data to be submitted to the Agency, the advice provides recommendations concerning the format of information considered important for data validation, the format of the animal population data and the online data submission tools. This additional information is important for data validation and data analysis.

Data submission through a valid online application is important to enable that only standardised and harmonised data are uploaded, for validation purposes, and for automated data analysis.

The Regulation requests compulsory reporting of data on antimicrobial medicinal products used in animals. It states, that the Agency shall cooperate with Member States and with other Union agencies to analyse antimicrobial sales and use data and shall publish an annual report. In order to fulfil the requirements and to report comparable data on antimicrobial sales and on use by animal species, the animal population that could potentially be treated with antimicrobials should be considered – i.e. by applying an appropriate denominator to assess antimicrobial consumption.

The following points are therefore addressed in the report:

- format of the data on sales of antimicrobial veterinary medicinal products and on use of veterinary and human antimicrobial medicinal products by animal species;
- format of additional information to the sales and use data which is of importance for data validation;
- online data submission tools;
- format of the animal population data.

The recommended format applies to all antimicrobial medicinal products that should be included in the data submission – i.e. to all categories of antimicrobial agents, as recommended in the advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products – Report on specific requirements for the collection on antimicrobial medicinal products used in animals (EMA/CVMP, 2019), sold (veterinary medicinal products) or used in animals (veterinary and human medicinal products) per calendar year in the territory of a country for which data are reported.

This report outlines the considerations and recommended requirements regarding the format of the data on sales and use of antimicrobials to be submitted to the Agency. The annex of this report provides relevant additional information and considerations presenting background knowledge of antimicrobial data collection, e.g. the animal population data and the methodology for calculation of the denominators currently used and recommended for normalising the sales and the use data for the animal population that could potentially be treated with antimicrobials.

Overview of recommendations

Essential requirements have been determined to assist implementation of the obligations outlined in Article 57 of the Regulation, keeping in mind the purpose of the data collection as indicated in Recital 50. The main recommendations include technical specifications for the antimicrobial data collection, organisational aspects for submission to the Agency of antimicrobial sales data and use data per animal species, and they address the format for reporting of animal population data, which is needed to facilitate analysis of the data and the conduct of risk assessments.

1. In order to obtain comparable data, Member States should select data sources and types of data that **cover all sales and all use** in their territories, during the calendar year, for all antimicrobials as outlined in the relevant delegated act on requirements for the collection of data on antimicrobial medicinal products used in animals. The requirements for the format of the data apply to data submitted to the Agency on a mandatory or on a voluntary basis. To attain full coverage data, for all Member States where veterinary medicinal products can be sold in their territories based on special licence/marketing authorisation or through parallel trade (Article 102 of the Regulation) (hereafter referred to as special-licence medicinal products), these antimicrobial medicinal products should be included in the sales and use datasets for each reporting year. The source of sales data can be, but is not limited to, marketing authorisation holders, wholesalers, feed mills, pharmacies, importers of medicated feed and veterinary medicinal products or retailers; for the use data the source or type of data can be, but is not limited to, prescriptions (veterinarians), dispensed prescriptions (e.g. feed mills and pharmacies), purchased antimicrobials (farmers), health records (farmers) and administered amounts (veterinarians and farmers).
2. Member States should submit to the Agency the variables for the data on **sales and use** listed in sections 3.1.1 and 3.2.1, respectively. The format recommended for sales and use data applies to all antimicrobials to be included in the data collection – i.e. antibiotics, antifungals, antivirals,

antiprotozoals, antimycotics and antimycobacterials, and applies to special-license medicinal products, to antimicrobial human medicinal products[1] that may exceptionally be used in animals, and to both mandatory and voluntary data submissions, as recommended in the advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products – Report on specific requirements for the collection on antimicrobial medicinal products used in animals (EMA/CVMP, 2019).

3. Member States should provide relevant information that will allow for assessment of data validity and for interpretation of the data (sections 3.1.2 and 3.2.2) according to the reporting tool made available by the Agency. Responses to the questionnaire should be completed at the same time as when submitting **sales and use data**, respectively, to the Agency.
4. Member States should continue submitting the **sales data** electronically via the latest version of the Agency's online application already existing within the ESVAC project activity.
5. Member States should use an online application system that is to be developed for the submission of antimicrobial **use data** per animal species.
6. The format of the animal population data should be the number of heads for all terrestrial animals and produced biomass (tonnes) for farmed finfish.
7. For food-producing animal species, when available, animal population data extracted from Eurostat, TRACES or from national databases/statistics that are publicly accessible, should be used by the Agency for the calculation of the denominator for sales and use data analysis.
8. Member States should submit data on the animal population for food-producing animals that are not available in Eurostat or TRACES as requested in the latest version of the data reporting protocol, which will provide data submission guidelines for the Member States.
9. For horses, cats, dogs, minks and foxes, which are kept or bred, Member States should be able to submit data on animal population. As currently for most Member States the data on animal population for these species are incomplete, there is a need to set up systems for collection of data on the animal population; preferably this should be coordinated at the EU level, similar as done by Eurostat for other animal population statistics for Europe.
10. For analysis and reporting of the antimicrobial use data, the animal population data should be submitted in accordance with the progressive stepwise approach for the submission of data on use of antimicrobial medicinal products described in Article 57(5) of Regulation (EU) 2019/6.
11. Member States should submit the animal population data according to the online application made available by the Agency.

[1] Reporting of human medicinal products is of relevance to use data only.

Advice on the format of the data to be collected on antimicrobial medicinal products used in animals

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1. Terms of reference and scope

This report represents the advice of the Agency on implementing measures under Article 57(4) of Regulation (EU) 2019/6 on veterinary medicinal products (Official Journal of the European Union, 2019b).

The request for advice from the European Commission requires the Agency to provide scientific recommendations regarding the format for the data to be collected on antimicrobial medicinal products used in animals.

The advice is linked to the advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products - Report on specific requirements for the collection of data on antimicrobial medicinal products used in animals (EMA/CVMP, 2019), as provided by the Agency to the European Commission on 30 August 2019.

The data format, as defined in protocols or guidance documents for data collection, which were previously developed by the Agency in the context of the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project, have been reviewed to lay out fundamental components for reporting of antimicrobial data. These components are frequently defined as variables; hence this term is used throughout this advice. The following ESVAC and international antimicrobial data collection protocols and guidance have been considered in the context of this advice:

- European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) Sales Data and Animal Population Data Collection Protocol (version 3), including online-based data delivery (EMA/ESVAC, 2019b);
- Guidance on collection and provision of national data on antimicrobial use by animal species/categories (EMA/489035/2016) (EMA, 2018).
- International guidelines on global antimicrobial data collection, in particular, the guidance for completing the OIE template (OIE, 2019).

The scientific recommendations also consider Recital 50 of Regulation (EU) 2019/6 that sets out the purpose and intended use of antimicrobial data used in animals at the Union level.

The advice reflects on information included in veterinary prescriptions, in records kept by owners and keepers of food-producing animals and in prescriptions on medicated feed in line with the Regulation – i.e. this advice considers whether the information available from such sources is sufficient for Member States to obtain data on amounts used in animals (see Annex, Table A2) as referenced in:

- Article 105 of Regulation (EU) 2019/6 on veterinary prescriptions;
- Article 108 of Regulation (EU) 2019/6 on record-keeping by owners and keepers of food-producing animals;
- Article 16 of Regulation (EU) 2019/4 (Annex V) on prescriptions of medicated feed (Official Journal of the European Union, 2019a).

In the development of this advice, required data on animal populations as well as the format in which these data should be made available have been considered. The reason for requiring such information is that the reporting of the data on antimicrobial consumption has to take into account the animal population that may potentially be treated with antimicrobials. Therefore, this advice gives recommendations regarding the format of animal population data for reporting together with use and sales data, and also addresses which animal species should be included. The following documents and protocols linked to animal population data were considered:

- the advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products - Report on specific requirements for the collection of data on antimicrobial medicinal products used in animals (EMA/CVMP, 2019);
- European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) Sales Data and Animal Population Data Collection Protocol (version 3), including online-based data delivery (EMA/ESVAC, 2019b);
- Guidance on collection and provision of national data on antimicrobial use by animal species/categories (EMA/489035/2016) (EMA, 2018);
- OIE annual report on antimicrobial agents intended for use in animals: methods used (Góchez et al., 2019);
- Guidance from the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) (WHO, 2017).

The scientific recommendations regarding the format of antimicrobial sales and use data define the required variables to be reported that will allow calculation of the amount of active antimicrobial ingredients from veterinary medicinal products **sold** for use in animals and of active antimicrobial ingredients from medicinal products **used** in defined animal species or categories per country. Furthermore, the scientific recommendations take into account that the Agency's current online system for data submission and analysis of **sales** data should be **adapted for use** data collection per species by Member State (see Annex, Section 6).

The scientific recommendations propose variables that are mandatory for reporting to the Agency as they are essential to identify year of data collection, country, animal species (relevant to use data collection only), to calculate amounts (tonnes) of active antimicrobial agents sold or used - including route of administration, as well as variables important for quality check and data validation.

The expert group acknowledges that other variables, such as the number of treated animals, number of treatment days, indication for treatment or number of defined daily or course doses, are currently collected by different Member States for, amongst others, antibiotic stewardship purposes at farm level (AACTING, 2019). These variables were considered out of scope for this advice as the mandate requests to advise on the format for the sales and use data.

Pursuant to Article 55(2)(d) of Regulation (EU) 2019/6 the Union product database (UPD) shall contain the annual volume of sales for all veterinary medicinal products. Collection of sales by application of the UPD, which is currently under development, relates to data collection methodology and not to the format of data, and it is therefore out of the scope of this report. It is noted that in order to use UPD as a repository to retrieve detailed product information and also download relevant information for calculation of annual sales of antimicrobials per country the database would need to encompass elements per each antimicrobial product presentation as described in this report. It is important to note that Article 57 of Regulation (EU) 2019/6 outlines the responsibility of Member States to collect relevant and comparable data on the volume of sales and on the use of antimicrobial medicinal products used in animals, while reporting of sales data via the UPD application provisionally is responsibility of marketing authorisation holders. Attributed to the sales data reported within the ESVAC activity, for 2017 data only 9 participating countries have selected marketing authorisation holders as an exclusive sales data source. In order to obtain relevant and comparable data on the volume of antimicrobials sold reported to the UPD, harmonisation and standardisation requirements should be defined, and quality management systems established, and responsibilities assigned.

2. Data sources and data coverage

In the present advice, the definitions of antimicrobial sales and antimicrobial use are applied as provided in the advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products - Report on specific requirements for the collection of data on antimicrobial medicinal products used in animals (EMA/CVMP, 2019). In the definition of antimicrobial sales and use, reference is made to various relevant data sources, as follows:

Antimicrobial sales: Sales data for antimicrobial veterinary medicinal products obtained from marketing authorisation holders, wholesalers, retailers, pharmacies, feed mills.

Antimicrobial use: Amounts of antimicrobials prescribed, administered, delivered and/or purchased for defined animal species/categories.

Due to, amongst others, differences in the drug distribution systems and data sources for data on sales and use, respectively, various sources for data collection should be accepted, which may differ between Member States.

As noted in Recital 50 of the Regulation (EU) 2019/6 there is a need for sufficiently detailed and comparable data at Union level to determine trends and identify possible risk factors that could result in the development of measures to limit the risk from antimicrobial resistance, and to monitor the effect of measures already introduced.

Article 57 of the Regulation requires that Member States shall collect relevant and comparable data. Therefore, it is important to give Member States the opportunity to select type(s) of data, data source(s) and data collection methods that provide full data coverage for the antimicrobial medicinal products that are sold (i.e. sold to the end users in the territory of the country reporting) and used (i.e. prescribed or administered to the animals in the territory of the country reporting), respectively, in their territories, and that are to be included in the data collection.

3. Format of data to be reported for sales and use of antimicrobial medicinal products in animals

The online system provided by the Agency, currently as part of the ESVAC activity, and used by Member States for the submission of variables fulfils basic requirements and elements for gathering harmonised and standardised data on the volume of sales of antimicrobial medicinal products in animals. Applying automated rules, which ensure upload and reporting of harmonised data, the system only accepts those antimicrobials described in the ESVAC sales data protocol and uses standardised variables (formats) for automatic calculation of tonnes sold. Furthermore, the online system also immediately provides standardised reports that the submitting Member States can use for data validation. Similar basic requirements and elements for animal population data are also part of the Agency's online system that is an integrated part of the current ESVAC activity. Finally, through the ESVAC this online system was thoroughly validated before it was implemented in 2015, including specifications for functionality, operational and user requirements. Before 2015, data were submitted by use of a standardised spreadsheet template and were processed manually.

The concept of the format for sales and use data is very similar, therefore the lists of variables to be reported per each medicinal product allowing to calculate amounts of antimicrobial ingredient, as described in sections 3.1.1. and 3.2.1. are basically the same. It is recommended to continue using the current ESVAC online application for the submission of sales data. However, the system should be adapted for use data submission.

The online system should allow submission and analysis of both sales and use data to be managed in parallel. As the data models for submission of use data, including the data analysis and validation rules, are foreseen to differ between species, separate data collection templates and online modules for submission of use data should be developed for each species.

The formats recommended for sales and use data applies to all antimicrobials to be included in the data collection – i.e. antibiotics, antifungals, antivirals, antiprotozoals, antimycotics and antimycobacterials. The recommendations also apply to reporting of antimicrobial human medicinal products that may exceptionally be used in animals, that are of relevance to use data only (EMA/CVMP, 2019).

Of note is that each dataset should include all antimicrobial products sold for use in animals or used by animal species, per calendar year in the territory of a country for which data are reported, including special-licence medicinal products, provisional or limited authorisation (according to national provisions related to import of medicinal product), or parallel trade (Article 102 of Regulation (EU) 2019/6).

Requirements for prescriptions and records to be kept according to Regulation (EU) 2019/4 and Regulation (EU) 2019/6 have been also considered (see Annex, Section 1) to assess whether essential variables that shall be reported to the Agency are available. While gathering details relating to dosage regimen, duration of treatment or therapeutic indications would provide additional aspects for analysis of antimicrobial medicinal products used in animals, the required variables are not harmonised and standardised. Furthermore, neither Regulation (EU) 2019/6 nor other relevant texts define rules and harmonised approaches for collecting these types of variables across the European Union, therefore such additional information would enable only limited further analysis. The variables for the data on sales and use listed in sections 3.1.1 and 3.2.1, respectively, are needed to calculate the amount of active antimicrobial ingredients in antimicrobial medicinal products used in animals, and support reporting of comparable data across years and across Member States.

3.1. Format of sales data

The reporting of data on the volume of sales of antimicrobial medicinal products used in animals to the Agency should include the following components (variables) per each product presentation. These variables should be reported also for antimicrobial sales data that can be submitted on voluntary basis.

3.1.1. Variables to be submitted

1. ISO Country code

   Description: 2 letter code (alpha-2 code), according to the International Standard for country codes (ISO, 2013).

   Purpose: To identify country for which sales data are reported.

2. Year

   Description: Four-digit number.

   Purpose: To identify the calendar year for which sales data were collected and submitted.

3. Marketing authorisation identification

   Description: Free-text field to include number, or number and letter combination, or name of the marketing authorisation holder.

Purpose: To allow unique identification of the medicinal product and enable a link with other databases.

Additional information: For special-licence medicinal products or products sold on exceptions from national marketing authorisations or through parallel trade (Article 102 of Regulation (EU) 2019/6) identification of respective marketing authorisations should be included.

4. Identification number of product presentation

   Description: Free-text field to show medicinal product package code value (can be number and letter combination). The code is a unique identifier for each presentation of the medicinal product (name, strength, formulation and pack size). The unique identifier of product presentation is a key element in many databases, it must be stable over time, so that medicinal products that are no longer marketed or registered can be identified to enable the analysis of historical data.

   Purpose: To allow identification if all products marketed in a country are reported. To enable validation and analysis of each presentation package sizes in which the veterinary medicinal product is sold. To enable the analysis of historical data. To enable identification of duplicate reporting of sales.

5. Medicinal product name

   Description: Free-text field to include name of medicinal product as per product information, e.g. summary of product characteristics or labelling.

   Purpose: To identify and validate recorded details.

6. Pharmaceutical form

   Description: Form to be selected from the harmonised pre-defined list: Bolus (BOLUS), Injectable preparation (INJ), Intramammary injector (INTRAMAM), Intramammary injector drying-off (INTRAMAM-DO), Oral solution (ORAL SOLU), Oral paste (ORAL PASTE), Oral powder (ORAL POWD), Premix (PREMIX), Capsules and Tablets (or other similar oral pharmaceutical forms) (TABL), Intrauterine product (INTRAUT), Topical products[2] (TOPICAL) (include dermatological products, ophthalmologicals, otologicals, nasal products), Other forms[3] (OTHER).

   Purpose: To allow analysis of data by administration route/pharmaceutical form.

7. Pack size (numerical value)

   Description: Numerical value only to disclose the pack size (e.g. 100 for 100 tablets or 100 intramammary injectors; 10 for 10 ml injection; 2 for a package of 2 kg premix; 300 for a box of 10 blisters of 30 tablets; 12 for a box of 12 injectors.).

   Purpose: To enable calculation of the amount of antimicrobial ingredient in each package presentation.

8. Pack size unit

   Description: Content unit of measurement to select corresponding value from the defined list (e.g. ml, l, g, kg, piece (for example, for tablets, capsules, boluses and intramammary injectors). The pack size unit should be compatible with the strength unit.

   Purpose: To enable calculation of amount of antimicrobial ingredient in each product presentation.

[2] In the future the topical products might be required to be detailed by the organ systems.
[3] Other forms to be selected when no alternative forms from the provided list are suitable, e.g. antimicrobial medicinal products for the treatment of honeybees.

9. ATCvet Anatomical Therapeutic Chemical (Classification) veterinary

   Description: Value to be selected as per the latest version of the ATCvet index. The WHO Collaborating Centre for Drug Statistics Methodology maintained ATCvet system for the classification of substances intended for therapeutic use in veterinary medicine is used for classification of medicinal products.

   Purpose: To ensure a standardised language for analysis and reporting of data per antimicrobial classes as well as anatomical and therapeutic groups.

10. Authorised for companion animals only

    Description: A field to label medicinal products authorised for use in companion animals only.

    Purpose: To enable identification of sales for those medicinal products authorised for use in companion animals only.

11. Number of packages sold

    Description: Numerical value only, to disclose number of packages of product presentation sold within the reporting period (year) in the reporting country.

    Purpose: To calculate volume of antimicrobial ingredient sold.

12. Antimicrobial ingredient name

    Description: Name to be selected from the predefined list of antimicrobial ingredient names as presented according to the latest version of the ATCvet index. In case of fixed combination products, all the antimicrobial ingredients' names must be provided.

    Purpose: To report antimicrobial sales in a standardised manner per antimicrobial classes and ingredients.

13. Salt of antimicrobial ingredient when strength expressed in international unit (IU)

    Description: Name to be selected from the latest version of predefined list of names of salt of antimicrobial ingredient.

    Purpose: In cases when the strength of an antimicrobial ingredient is given in IU (IU/ML or IU/PIECE) and when different salts exist, to allow for conversion to weight of active principle of an antimicrobial ingredient. Currently the ESVAC sales dataset includes one substance (colistin) with two salts giving the strength as IU: colistin sulfate and colistin methanesulfonate.

14. Name of derivative or compound of antimicrobial ingredient

    Description: Name of derivative or compound to be selected from the defined list provided in the latest version of the sales data reporting protocol.

    Purpose: To allow for calculation of weight of the active principle of an antimicrobial ingredient.

15. Strength

    Description: Numerical value of strength or quantity of the antimicrobial ingredient in mg/g/IU per relevant unit ml/mg/l/g/kg/piece as declared in the product information (e.g. 10 for 10 MG/ML). In case of fixed combinations, the strength for all the antimicrobial ingredients per presentation must be provided.

Purpose: To enable calculation of the amount of the antimicrobial ingredient(s) in each product presentation and to validate ingredient content.

Additional information: The strength(s) of the antimicrobial ingredient(s) should be reported as given in the summary of product characteristics or in the label of the veterinary medicinal products.

16. Unit of measurement for strength

    Description: Unit of measurement of strength to be chosen from a defined list (e.g. mg/ml, g/l, IU/g, IU/ml, IU/piece, g/kg, mg/piece) and should be compatible with the pack size unit. In case of fixed combinations, the unit of measurement for all the antimicrobial ingredients per presentation must be provided.

    Purpose: To enable calculation of the amount of the antimicrobial ingredient(s) in each product presentation.

3.1.2. Information required in addition to sales data variables

In order to support understanding the collected data it is important to have access to some key information such as types of data and data sources. Therefore, a set of questions have been defined to gather important details in addition to sales data variables.

It is recommended to make it mandatory for the Member States to record the below listed information using the reporting tool made available by the Agency.

1. Data source

    Description: Data source to be chosen from a defined list: Marketing Authorisation Holders, Wholesalers, Feed mills, Pharmacies, Importers of medicated feed, Retailers, Other (to provide brief clarification). More than one type of data source can be selected in order to capture all sales of antimicrobial medicinal products used in animals per calendar year in the territory of a country for which data are reported.

    Purpose: To identify source of data.

2. Number of data sources providing sales data

    Description: Numerical value to be provided to clarify total number of data sources/data providers registered for contributing to the sales data collection in a given Member State and number of data sources/providers from which data have been collected.

    Purpose: Provides information on, and draws attention to, data completeness.

3. National data provider

    Description: Free-text field to identify the institution or organisation responsible for data validation at national level and submission of data to the Agency.

    Purpose: Provides details on who should be contacted in case of further questions in reference to the data provided by the Member State. For transparency reasons this information should be included in the annual reports.

4. Sales between wholesalers and/or marketing authorisation holders excluded

    Description: A choice of yes/no to be selected to indicate if necessary actions have been taken to avoid double reporting of sales.

Purpose: Draws attention to possible caveats in data reported.

Additional information: If applicable, sales between retailers should also be excluded to avoid double reporting, and of note is that sales between retailers are typically negligible.

5. Percentage of sales accounted for by veterinary medicinal products sold on special licence or parallel trade

   Description: Numerical value of percentage to be provided of overall sales accounted for by veterinary medicinal products sold on exceptions from the national marketing authorisations or parallel trade per calendar year in the territory of a country for which data are reported.

   Purpose: To specify the proportion of sales in the reported dataset, which are based on exceptional/special marketing authorisations, provisional or limited authorisation (according to national provisions related to import of medicinal product), or parallel trade (Article 102 of Regulation (EU) 2019/6).

   Of note is that each dataset should include all antimicrobial products sold for veterinary use, including those noted above, per calendar year in the territory of a country for which data are reported.

The above variables provide reliable details associated with assessment and interpretation of data quality and of comparability. The reporting tool made available by the Agency, which should capture these additional details regarding sales data may be subject to change, to the extent necessary to clarify the process of data collection at national level, meaning that any changes to the questionnaire will require only information what is already in possession of Member States.

3.2. Format of use data

The reporting of data on the volume of use of antimicrobial medicinal products used per animal species to the Agency should include the following components (variables) per each product presentation, as listed in the sections below.

These variables should be reported also for antimicrobial use data that can be submitted on a voluntary basis, as outlined in the advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products - Report on specific requirements for the collection of data on antimicrobial medicinal products used in animals (EMA/CVMP, 2019).

3.2.1. Variables to be submitted

The reporting of use data should follow a progressive stepwise approach with regards to animal species to be included in the dataset, as per Article 57(5) of Regulation (EU) 2019/6. To support use data analysis by animal species, one additional variable should be provided for the use data when compared to sales data, and that is the animal species.

1. Animal species

   Description: Animal species for which data are reported has to be selected from a predefined list: Bovine, Bovine below 1 year when production of meat is above 10 000 tonnes slaughtered per year, Pigs, Chicken, Turkeys, Ducks, Geese, Sheep, Goats, Horses, Rabbits, Finfish, Any other food-producing animals, Cats, Dogs, Minks, Foxes, Other non food-producing animals.

   Purpose: To identify which animal species the use data covers.

Of note, use data should be collected for all animal production stages and types (see Table 3 of the advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products - Report on specific requirements for the collection of data on antimicrobial medicinal products used in animals (EMA/CVMP, 2019)) but reported by animal species.

2. ISO Country code

   Description: 2 letter code (alpha-2 code), according to the International Standard for country codes (ISO, 2013).

   Purpose: To identify the place of collected use data.

3. Year

   Description: Four-digit number.

   Purpose: To identify the calendar year for collected and submitted use data.

4. Marketing authorisation identification

   Description: Free-text field to include number or number and letter combination or name of marketing authorisation holders.

   Purpose: To allow identification of the medicinal products and to enable a link with other databases.

   Additional information: For special-licence medicinal products or products available on the market based on exceptions from national marketing authorisations or through parallel trade (Article 102 of Regulation (EU) 2019/6) identification of respective marketing authorisations should be included.

5. Identification number of product presentation

   Description: Free-text field to cover medicinal product package code value (can be number and letter combination). Digit code is a unique identifier for each product presentation - i.e. package size, strength and formulation. As a key element in databases, it must be stable over time, so that medicinal products that are no longer marketed or registered can be identified to enable the analysis of historical data, moreover, it assists checking of volume of use data per presentation against sales data for the same presentation.

   Purpose: To enable the analysis of historical data. To enable identification of duplicate reporting of use data.

6. Medicinal product name

   Description: Free-text field to include name of medicinal product as per product information, e.g. summary of product characteristics or labelling.

   Purpose: To identify and validate recorded details.

7. Pharmaceutical form

   Description: Form to be selected from the defined list: Bolus (BOLUS), Injectable preparation (INJ), Intramammary injector (INTRAMAM), Intramammary injector drying-off (INTRAMAM-DO), Oral solution (ORAL SOLU), Oral paste (ORAL PASTE), Oral powder (ORAL POWD), Premix (PREMIX), Capsules and Tablets(or other similar oral pharmaceutical forms) (TABL), Intrauterine

product (INTRAUT), Topical products4 (TOPICAL) (include dermatological products, ophthalmologicals, otologicals, nasal products), Other forms5 (OTHER).

Purpose: To allow analysis of data by administration route/ pharmaceutical form.

8. Identification of long-acting injectable preparations

   Description: 2-letter (LA) code.

   Purpose: To allow for identification of the DDDvet and DCDvet for analysis of long-acting injectable preparations when DDDvet and DCDvet for the active ingredient differ from conventional injectables.

9. Pack size (numerical value)

   Description: Numerical value only to disclose the pack size (e.g. 100 for 100 tablets or 100 intramammary prep.; 10 for 10 ml injection; 2 for a package of 2 kg premix; 300 for a box of 10 blisters of 30 tablets; 12 for a box of 12 injectors.).

   Purpose: To enable calculation of the amount of antimicrobial ingredient in each package presentation.

10. Pack size unit

    Description: Content unit of measurement to select corresponding value from the defined list (e.g. ml, l, g, kg, piece (for example, for tablets, capsules, boluses and intramammary prep.). The pack size unit should be compatible with the strength unit.

    Purpose: To enable calculation of amount of antimicrobial ingredient in each product presentation.

11. ATC or ATCvet: Anatomical Therapeutic Chemical classification code for human and veterinary medicinal products

    Description: Value to be selected as per the latest version of the ATC or ATCvet index. WHO CC ATC or ATCvet code per product presentation are also provided in the summary of product characteristics.

    Purpose: To ensure a standardised language for analysis and reporting of data per antimicrobial classes.

12. Number of packages used

    Description: Numerical value only to disclose number of packages of product presentation used within the reporting period (year) per country and per species category.

    Additional information: In case any data at national level are collected in other units than packages used for each antimicrobial product by the animal species in question, the number of packages used can be calculated from amounts used in weight (e.g. kg, tonnes) used before submitting to the Agency.

    Purpose: To calculate weight of antimicrobial ingredient used.

[4] In the future the topical products might be required to be detailed by the organ systems.
[5] Other forms to be selected when no alternative forms from the provided list are suitable, e.g. antimicrobial medicinal products for the treatment of honeybees, and those human medicinal products that are used off-label e.g. impregnated material for implantation, inhalation solutions or powders.

13. Antimicrobial ingredient name

    Description: Value to be selected from the predefined list of antimicrobial ingredient names as per latest ATC or ATCvet index. In case of fixed combination products, all the antimicrobial ingredients' names must be provided.

    Purpose: To report antimicrobial used in a standardised manner per antimicrobial classes and ingredients.

14. Salt of antimicrobial ingredient when strength expressed in IU

    Description: Value to be selected from the predefined list of names of salt of antimicrobial ingredient. Use dataset includes 2 salts: colistin sulfate and colistin methanesulfonate.

    Purpose: In cases when the strength of an ingredient is given in IU (IU/ML or IU/PIECE) and when different salts exist, to allow for conversion to weight of active principle of an antimicrobial ingredient. Currently the ESVAC sales dataset includes one substance (colistin) with two salts giving the strength as IU: colistin sulfate and colistin methanesulfonate.

15. Name of derivative or compound of antimicrobial ingredient

    Description: Name of derivative or compound to be selected from the defined list provided in the latest version of the use data reporting protocol.

    Purpose: To allow for calculation of weight of active principle of an antimicrobial ingredient.

16. Strength

    Description: Numerical value of strength or quantity of the antimicrobial ingredient in mg/g/IU per ml/mg/l/g/kg/piece as declared in the summary of product characteristics or label of the veterinary medicinal product or medicinal product for human use. In case of fixed combinations, the strength for all the antimicrobial ingredients per presentation must be provided.

    Purpose: To enable calculation of amount of antimicrobial ingredient(s) in each product presentation and to validate ingredient content.

    Additional information: The strength of the antimicrobial ingredient(s) should be reported as given in the summary of product characteristics or label of the veterinary medicinal products or medicinal product for human use.

17. Unit of measurement for strength

    Description: Unit of measurement of strength to be chosen from a defined list (e.g. IU/g, IU/ml, IU/piece, g/kg, g/l, mg/ml, mg/piece) and compatible with the pack size unit. In case of fixed combinations, the unit of measurement for strength for all the antimicrobial ingredients per presentation must be provided.

    Purpose: To enable calculation of the amount of antimicrobial ingredient(s) in each product presentation and to validate ingredient content.

3.2.2. Information required in addition to use data variables

In order to support interpretation of the data it is important to have access to some key information, such as types of data and data sources. Therefore, a set of questions should be defined to gather important details in addition to use data variables.

It is recommended to make it mandatory for the Member States to record the below listed information using the reporting tool made available by the Agency.

1. Type of data

   Description: Type of data to be chosen from a predefined list included in the questionnaire: Prescriptions for medicinal products and medicated feed (veterinarians), Dispensed prescriptions (delivered by feed mills, veterinarians and pharmacies), Purchase data (delivery notes), Health records (farmers), Treatment log books (veterinarians), Medication administration records (veterinarians and farmers), Others (brief description of source(s) to be provided). More than one type of data source can be selected in order to capture all use of antimicrobial medicinal products used in animals per calendar year in the territory of a country for which data are reported.

   Purpose: Provides information for interpretation and better understanding about the submitted data.

2. Data source(s)

   Description: Data source(s) to be chosen from the last version of a defined list included in the questionnaire: Pharmacies, Feed mills, Veterinarians, Farmers, Others (brief description of source(s) to be provided).

   Purpose: To identify data source.

3. National data provider

   Description: Free-text field to identify the responsible institution or organisation for data validation at national level and for submission of data to the Agency.

   Purpose: Provides details on who should be contacted in case of further questions in reference to the data provided at country level. For transparency reasons this information should be included in the annual reports.

The above variables provide reliable details associated with assessment and interpretation of data quality and comparability. The reporting tool made available by the Agency, which should capture these additional details of use data might be subject to change, only to the extent to clarify process of data collection at national level, meaning that any changes to the questionnaire will require only information which is already in possession of Member States.

4. Format of the animal population data

In order to report comparable data on sales and on use by animal species of antimicrobials, respectively, the animal population that could potentially be treated with antimicrobials should be considered – i.e. by applying an appropriate denominator. For the analysis and reporting of antimicrobial use data, the animal population data should be made available according to the progressive stepwise approach as outlined in Article 57(5) of Regulation (EU) 2019/6. The years from which onward the use data have to be submitted by the Member States for certain animal species, and the corresponding animal population data that have to be available to the Agency for analysis and reporting, are shown in Table 1.

Of note is that the Agency acknowledges that it is not its role to define protocols for the collection of animal population data in individual Member States or at the EU level, this is under the competence of national statistics offices and Eurostat. It is also known that National competent authorities collecting sales and use data usually do not collect animal population data.

The advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products – Report on specific requirements for the collection on antimicrobial medicinal products used in animals (EMA/CVMP, 2019) recommends the population correction unit (PCU) as an appropriate denominator for both sales and use data. The recommendation was, however, conditional as it was suggested that the denominator be revised in the future with regard to animal categories to be included as well as the animal weight used to calculate the PCU (see Annex, Section 4.). The animal categories for the food-producing animals included in the calculation of current ESVAC sales data denominator, as shown in Table A2 (see Annex, Section 5.1.).

Table 1. Animal species, including fish, for which antimicrobial use data are to be provided, data sources for the animal population data and for which years the animal population data has to be available to the Agency (see Table 3 of the advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products – Report on specific requirements for the collection on antimicrobial medicinal products used in animals (EMA/CVMP, 2019)

From 2023 onwards	From 2026 onwards	From 2029 onwards	Data sources
Cattle Aggregated for all categories, including bovine under 1 year of age, specifying use for bovine < 1 year[(a)]	**Cattle** Aggregated for all categories, including bovine under 1 year of age, specifying use for bovine < 1 year[(a)]	**Cattle** Aggregated for all categories, including bovine under 1 year of age, specifying use for bovine < 1 year[(a)]	Eurostat, and where applicable, importation and exportation of animals from the TRACES database
Pigs	**Pigs**	**Pigs**	Eurostat, and where applicable, importation and exportation of animals from the TRACES database
Poultry • ***Chicken (Gallus gallus)*** • **Turkey[(a)]** For each species aggregated for all production categories/stages: breeders, chicken, layers	**Poultry** • ***Chicken (Gallus gallus)*** • **Turkey[(a)]** • **Duck** • **Geese** For each species aggregated for all production categories/stages: breeders, chicken, layers	**Poultry** • ***Chicken (Gallus gallus)*** • **Turkey[(a)]** • **Duck** • **Geese** For each species aggregated for all production categories/stages: breeders, chicken, layers	Eurostat or national data for species or categories where production level is <10 000 tonnes slaughtered per year (e.g. geese, fattening turkeys), and where applicable, importation and exportation of animals from the TRACES database
	Sheep	**Sheep**	Eurostat and where applicable, importation and exportation of animals from the TRACES database
	Goats	**Goats**	Eurostat and where applicable, importation and exportation of

From 2023 onwards	From 2026 onwards	From 2029 onwards	Data sources
			animals from the TRACES database
	Finfish	**Finfish**	Eurostat[(b)]/National data
	Horses – both food-producing and non food-producing	**Horses** – both food-producing and non food-producing	National data[(c)]
	Rabbits (food-producing)	**Rabbits** (food-producing)	National data
	Any **other food-producing animals**	Any **other food-producing animals**	National data
		Dogs	National data[(d)]
		Cats	National data[(d)]
		Fur animals • **Minks** • **Foxes**	National data[(d)]

(a) For Member States where production of meat is more than 10 000 tonnes slaughtered per year, in line with Commission Implementing Decision 2013/652/EU.
(b) Specifying the species reported; may vary per Member State.
(c) For some countries based on estimates obtained through sample surveys performed at regular intervals.
(d) Of note is that data might not be available for all countries.

4.1. Format of the data

For terrestrial animals, the recommended format of the animal population data is the number of heads per corresponding year, independent of the data source and animal categories to be included. For farmed fish, the data format is tonnes live weight per corresponding year; examples can be seen in the Annex, Table A2.

4.2. Sources for the animal population data - methodology

The key criteria for the selection of the source(s) for the animal population data and methodology for calculation of denominator recommended are as follows:

1. Animal population data to be applied for calculation of the denominator should be publicly available and harmonised across all MSs;
2. Harmonised data on the animal population by category to be gathered from the Eurostat database and from TRACES, or from national statistics when any of the required data are not available from the first two databases;
3. Published methodology for calculation of the denominator by the Agency should be applied;
4. To the extent possible, the animal population data and calculation of denominator used for international reporting should be considered (e.g. OIE methodology).

Data on animal population for food-producing animals and by animal category, when relevant, available from Eurostat and TRACES fulfil the above criteria. It is therefore recommended to use Eurostat and TRACES as source for the collection of the animal population data. Of note is that data for horses, cats, dogs, minks and foxes are not available in the Eurostat database, therefore there is a need to set up systems for collection of standardised and harmonised data for these species so data are in place by the time reporting for antimicrobial use data for these species becomes mandatory.

4.3. Animal species and categories to be covered

It is recommended to continue the current approach used for the ESVAC collection of animal population data to enable the analysis and reporting of antimicrobial sales data for food-producing animals (see Annex, Section 5. and Table A2 in the same section). This means that the reference data on the animal population for food-producing species, used in the calculation of the denominator, are collected by the Agency from the Eurostat and TRACES database and where Member States subsequently review the reference data.

If reference data are not available in Eurostat or TRACES, the necessary data on animal population, as defined in the most recent version of data collection protocol, should be submitted by the Member States.

For calculation of the current denominator for reporting of the sales data in the ESVAC, the animal species and categories of food-producing animals are described in Table A2 of the Annex (see Annex, Section 5.1.). Specification of animal species and categories allows collection of standardise animal population data from Eurostat and TRACES, and when necessary, to acquire substitute statistics from the national statistics offices. The experience from the ESVAC activity regarding data not available in Eurostat and TRACES, is that these data are available in national public databases – i.e. cattle, pigs, broilers, turkey, goats, sheep, farmed fish, rabbits (food-producing) and horses. As mentioned above, the advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products – Report on specific requirements for the collection on antimicrobial medicinal products used in animals (EMA/CVMP, 2019) recommends conducting a scientific assessment on different denominators and indicators for analysing use data (see also Annex, Section 5.2.). The outcome of such assessment might propose adding other animal categories or to use other type of data, e.g. living animals. The criterion for changing or adding new animal categories or changing the type of data for the above-mentioned animal species should be that the data proposed are available in Eurostat and TRACES or in national public databases.

In the advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products – Report on specific requirements for the collection on antimicrobial medicinal products used in animals (EMA/CVMP, 2019) it reads: *"When data on food-producing animal population are not available in e.g. Eurostat or at national level, because the production is very low, such species need not be reported separately and may be reported under "any other food-producing animal species"*. This is likely to apply to geese that are typically minor species in terms of production volume, and which are consequently not reported to Eurostat. The implication of the recommendation in the advice on implementing measures under Article 57(3), as noted above, is that the Member States would not have to set up systems for collecting those data.

Moreover, for some Member States population data for horses are based on estimates obtained through sample surveys performed at regular intervals, or the data from the public national database do not cover all horses in the country. It is recommended that the Member States establish systems for collecting animal population data for horses in order to be able to submit such data to the Agency by 2026 as per Article 57(5)(b). Preferably, development of necessary systems for collecting data on

the horse population should be coordinated at the EU level, similar as it is done by Eurostat for other animal population statistics.

For any other food-producing animal species (see Table 1.), it is likely that no statistics are collected on animal population either by Eurostat and TRACES databases or at the national level due to the low production. It is recommended that data on use of antimicrobial medicinal products for any other food-producing animal species submitted to the Agency are presented in tonnes of active substance by antimicrobial class for any other food-producing animal species; in consequence data on the animal population would not need to be collected.

For the non food-producing species, referred to in Table 1. dogs, cats, minks and foxes, it is generally recognised that full coverage data on the population statistics are rarely available in most Member States. For these species, it is recommended that the Member States set up systems for collecting animal population data in order to be able to submit such data to the Agency by 2029 as per Article 57(5)(c). Preferably, development of necessary systems for collecting data on the dog, cat, mink and fox population should be coordinated at the EU level, similar as it is done by Eurostat for other animal population statistics.

Annex

1. Requirements for prescriptions and records to be kept in line with Regulation (EU) 2019/4 and 2019/6

Considering the Article 105 of the Regulation (EU) 2019/6, the Commission may, by means of implementing acts, set a model format for the required data in veterinary prescriptions. Considering the Article 108 of the Regulation (EU) 2019/6, the Member States may lay down additional requirements for record-keeping by owners and keepers of food-producing animals.

Table A1: Summary of requirements for prescriptions and records to be kept based on Regulation (EU) 2019/4 and 2019/6

Subject matter	Veterinary prescriptions (Regulation (EU) 2019/6 Article 105)	Record-keeping by owners and keepers of food-producing animals (Regulation (EU) 2019/6 Article 108)	Prescription of medicated feed (Regulation (EU) 2019/4 Article 16, Annex V)
Identification of the animal(s)	(a) Identification of the animals or groups of animals to be treated	(f) identification of the animal or group of animals treated	Annex V (4) Identification (including category, species and age) and number of animals or, where appropriate, the weight of the animals
Identification of the animal owner or keeper	(b) Full name and contact details of the animal owner or keeper		Annex V (3) Full name and contact details of the animal keeper, and identification number of the establishment, if existing.
Date	(c) Issue date	(a) Date of the first administration of the medicinal product to the animals	Annex V (2) Issue date
Identification of the veterinarian	(d) Full name and contact details of the veterinarian including, if available, the professional number	(g) Name and contact details of the prescribing veterinarian, if applicable	Annex V (1) Full name and contact details of the veterinarian including, if available, the professional number
	(e) Signature or an equivalent electronic form of identification of the veterinarian		Annex V (2) Signature or an equivalent electronic form of identification of the veterinarian
Medicinal Product (MP)	(f) Name of the prescribed medicinal	(b) Name of the medicinal product	Annex V (6) Designation (name and

Subject matter	Veterinary prescriptions (Regulation (EU) 2019/6 Article 105)	Record-keeping by owners and keepers of food-producing animals (Regulation (EU) 2019/6 Article 108)	Prescription of medicated feed (Regulation (EU) 2019/4 Article 16, Annex V)
	product, including its active substances		marketing authorisation number) of the veterinary medicinal product or products, including the name of the active substance or substances.
	(g) Pharmaceutical form and strength		
Use of the VMP	(h) Quantity prescribed, or the number of packs, including pack size	(c) Quantity of the medicinal product administered;	Annex V (8) Inclusion rate of the veterinary medicinal product or products and active substance or substances (quantity per weight unit of medicated feed).
	(i) dosage regimen	(i) duration of treatment.	Annex V (10) Instructions for use for the animal keeper, including the duration of the treatment
Withdrawal period	(j) for food-producing animal species, withdrawal period even if such period is zero	(h) Withdrawal period even if such period is zero	Annex V (12) For food-producing animals, withdrawal period, even if such period is zero.
Prudent use of antimicrobials	(k) Any warnings necessary to ensure the proper use including, where relevant, to ensure prudent use of antimicrobials		Annex V (13) Any warnings necessary to ensure the proper use including, where relevant, to ensure prudent use of antimicrobials
Identification of the supplier		(d) Name or company name and permanent address or registered place of business of the supplier;	Annex V (15) The following mentions to be completed by the supplier of the medicated feed or the on-farm mixer, as appropriate:

Subject matter	Veterinary prescriptions (Regulation (EU) 2019/6 Article 105)	Record-keeping by owners and keepers of food-producing animals (Regulation (EU) 2019/6 Article 108)	Prescription of medicated feed (Regulation (EU) 2019/4 Article 16, Annex V)
Validation of the delivery		(e) Evidence of acquisition of the medicinal products they use;	Annex V (16) Signature of supplier to the animal keeper or of on-farm mixer
Identification of the prescription			Annex V (2) Unique number of prescription, expiry date of prescription
Indication			Annex V (5) Diagnosed disease to be treated (or disease to be prevented for vaccines and antiparasitics without antimicrobial effects)
Other information	The Commission may, by means of implementing acts, set a model format for these requirements. That model format shall also be made available in electronic version.	If the information to be recorded in accordance with paragraph 2 of this Article is already available on the copy of a veterinary prescription, in a record kept on the farm or for equine animals recorded in the single lifetime identification document referred to in Article 8(4), it does not need to be recorded separately	
Particular use	(l) if a medicinal product is prescribed in accordance with Articles 112, 113 and 114, a statement to that effect		Annex V (7) If the veterinary medicinal product is prescribed under Article 107(4), Article 112, Article 113 or Article 114, of Regulation (EU) 2019/6, a statement to that effect.
	(m) if a medicinal product is prescribed in		Annex V (14) For food-producing animals and

Subject matter	Veterinary prescriptions (Regulation (EU) 2019/6 Article 105)	Record-keeping by owners and keepers of food-producing animals (Regulation (EU) 2019/6 Article 108)	Prescription of medicated feed (Regulation (EU) 2019/4 Article 16, Annex V)
	accordance with Article 107(3) and (4), a statement to that effect		fur animals, the mention 'This prescription shall not be re-used'.

2. Supplementary variables - sales and use data - for calculation and data validation

In the current ESVAC sales data collection template (EMA/ESVAC, 2019b) additional variables as listed below are included. The purpose of adding these variables in the data collection template at national level is to facilitate the calculation of tonnes of antimicrobial ingredient per product presentation for subsequent validation of the data – e.g. by comparing the outputs with data from previous years - before submission to the Agency. Furthermore, outputs from the calculation of tonnes sold is an important element for cross-checking the use data submitted to the Agency.

Also, to ensure harmonised calculation of volume of sales (in tonnes), harmonised variables i.e. conversion factors for strength given in IU and for derivatives of antimicrobial ingredients, as applied in the Agency's data analysis system, are applied as listed below. Of note is that all supplementary variables are automatically filled fields by the Agency's systems when data are uploaded via online application.

The supplementary variables recommended to be included in the data collection template for sales and use data, respectively, are:

1. Conversion factor when strength is given in IU

   Description/purpose: When strength unit is e.g. IU/ML or IU/PIECE, the Agency's system assigns automatically a conversion factor from the pre-defined list for the harmonised calculation weight of antimicrobial ingredient sold/used. This is a calculation that also can be performed by the MS for the validation of data before submission.

   Purpose: To enable calculation of weight of the antimicrobial ingredient per product package.

2. Conversion factor of derivative

   Description/purpose: When strength is given for the derivative of antimicrobial ingredient and not for the active principle, the Agency's system assigns a conversion factor automatically from a predefined list (for the harmonised calculation of weight of antimicrobial ingredient sold). This calculation can also be performed by the Member States for the validation of data before submission.

   Purpose: To enable calculation of the weight of the antimicrobial ingredient per product package.

3. Content of active ingredient in package

   Description/purpose: As a clarifying step for calculation of volume of antimicrobial ingredient, this variable provides weight of antimicrobial ingredient per one unit of product package. This will assist

the Member State to calculate ingredient content per product presentation that can be used for validation of the data at product presentation level before submission.

Purpose: To enable calculation of volume of sales and use.

4. Unit of active ingredient in package

   Description/purpose: The unit of antimicrobial ingredient per product package is given in grams for all antimicrobial agents. This allows the Member States to evaluate the output of calculation of volume of sales and use.

5. Tonnes sold or used of antimicrobial ingredient

   Description/purpose: Based on unified details provided represents amount of antimicrobial ingredient per product presentation. This will assist the Member States to calculate tonnes antimicrobial ingredients per product presentation that can be used for validation of the data at product presentation level before submission.

   Purpose: Provides volume of antimicrobial ingredient sold or used.

3. Animal population data

In order to support analysis, which amongst others includes presentation of comparable data across years and Member States and at global level, the reporting of the data have to take into account the animal population that could potentially be treated with antimicrobials treatment.

The mandate from the European Commission did not directly request an advice on the format of the animal population data, but it was considered appropriate to address this in line with the mandate, including the following considerations:

1. The work of the expert group on the collection of data on antimicrobial medicinal products used in animals;
2. The format defined in ESVAC protocols and/or guidance documents for data collection;
3. The data format, including variables and units of measurement, used in the international guidelines, wherever possible and appropriate.
4. Recommendations in the advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products – Report on specific requirements for the collection on antimicrobial medicinal products used in animals (EMA/CVMP, 2019):

"*It is recommended to continue to use PCU as the denominator for reporting of sales data. Of note is that some Member States, through their ESVAC national contact points, have requested a revision of the PCU methodology, including the animal categories as well as the weights used to calculate this technical unit. Discussions on this topic are on-going, and the outcome may result in an updated denominator for normalising the animal population at risk of being treated.*"

"*Currently, the ESVAC project does not collect data on use of antimicrobials by animal species, but in the Guidance on collection and provision of national data on antimicrobial use by animal species or categories published by the Agency on 6 February 2018 (EMA, 2018) it is suggested to use animal species PCU as the denominator referred to as the 'species PCU'.*

It is acknowledged that there may be concerns or questions regarding the use of the species PCU as a denominator to report use data, also in relation to the objectives of the analysis, e.g., trend analysis within Member States, comparison of use of antimicrobials between Member States. It is therefore

recommended to conduct a scientific assessment on different denominators and indicators for analysing use data."

5. Furthermore the "Guidance on collection and provision of national data on antimicrobial use by animal species/categories" (EMA, 2018) recommends the species PCU.
6. Finally, the OIE applies a similar methodology and animal population data for calculation of the denominator (Góchez et al., 2019).

4. Denominators - methodology

4.1. ESVAC sales and species denominator: animal species population correction unit

Animal species PCU is a technical unit and includes livestock animals and slaughtered animals (and import and export of animals within the EU/EEA) multiplied by the theoretical weight at the most likely time for treatment (EMA/ESVAC, 2019a).

The PCU is calculated for each species, weight class or production type, as follows

PCU domestic

- Number of animals slaughtered × estimated weight at treatment
- Number of livestock × estimated weight at treatment

PCU export

- Number of animals transported to another country for fattening or slaughter × estimated weight at treatment

PCU import

- Number of animals imported from another country for fattening or slaughter × estimated weight at treatment

The total PCU by country is calculated as follows: PCU = total $PCU_{Domestic}$ + total PCU_{Export} – total PCU_{Import}

1 PCU = 1 kg of animal biomass.

4.2. OIE: animal population for global denominator. Calculation of biomass

OIE applies a similar approach as maintained for the PCU, where number of animals slaughtered and number of livestock (census data) are included in the calculation of the denominator. Animal biomass is calculated as the total weight of the live domestic animals present during a year in a specific area, used as a proxy to represent those likely exposed to the quantities of antimicrobial agents reported (Góchez et al., 2019).

Basically, the OIE methodology takes into consideration: census population data, number of animals slaughtered and a sub-regional mean live weight.

Examples of animal population data used and calculation of the OIE denominator:

Bovine biomass was calculated by multiplying the representative weight determined for each sub-region by the census population of bovines for each country within the sub-region, according to the following formula:

$$\begin{aligned} &census\ population \times [(sub\ regional\ mean\ live\ weight \\ &\times LSU_{calves} \times P.pop_{calves}) + (sub\ regional\ mean\ live\ weight \\ &\times LSU_{young\ 1-2yrs} \times P.pop_{young\ 1-2yrs}) \\ &+ (sub\ regional\ mean\ live\ weight \times LSU_{adults} \times P.pop_{adults})] \end{aligned}$$

Whereby,

$P.pop_{calves}$, $P.pop_{young\ 1-2years}$, $P.pop_{adults}$ represents, respectively, the proportion (P.pop) of calves, young (between 1 and 2 years of age) and adults in the total living cattle population, as calculated from Eurostat animal population data.

LSU_{calves}, $LSU_{young\ 1-2years}$, LSU_{adults} represents, respectively, the livestock unit ratios (LSU) for calves, young and adults as defined by Eurostat (15).

And, *sub regional mean live weight* represents the calculated mean live weight for adult cattle at the sub regional level.

Swine biomass was calculated according to the following formula:

$$\begin{aligned} &(live\ weight \times number\ slaughtered) + (census\ population \\ &\times sow\ weight \times 0.09) \end{aligned}$$

Whereby,

live weight × *number slaughtered* represents the expected biomass of fattening pigs slaughtered in a country in 1 year,

And *census population* × *sow weight* × 0.09 represents the expected biomass of pigs retained for breeding purposes, calculated with the following considerations:

- The number of boars for breeding purposes is negligible compared to the number of sows;
- Sow weight: the standard weight of a sow in Europe is 240 kg (9). This weight was adapted by region using livestock unit ratios (Americas = 240 kg, Asia and the Pacific = 240 kg, Africa = 192 kg);
- 0.09 is the expected percentage of sows in a given swine population, as calculated from Eurostat animal population data.

Poultry biomass was calculated according to the following formula:

$$\begin{aligned} &(live\ weight\ chicken \times number\ of\ chicken\ slaughtered) \\ &+ (live\ weight\ turkey \times number\ of\ turkey\ slaughtered) \\ &+ (live\ weight\ ducks \times number\ of\ ducks\ slaughtered) \\ &+ (live\ weight\ geese \times number\ of\ geese\ slaughtered) \end{aligned}$$

5. Format of animal population data for the denominator

In order to report comparable data on sales and use of antimicrobials, the animal population that could potentially be treated with antimicrobials has to be taken into account – i.e. by applying an appropriate denominator. The advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products – Report on specific requirements for the collection on antimicrobial medicinal products used in animals (EMA/CVMP, 2019) recommends the population correction unit (PCU) as a denominator for both sales and use data. The recommendations were however conditional as it was suggested to be subjected to revision.

5.1. Sales data denominator

In the advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products – Report on specific requirements for the collection of data on antimicrobial medicinal products used in animals (EMA/CVMP, 2019) it reads:

"It is recommended to continue to use PCU as the denominator for reporting of sales data. Of note is that some Member States, through their ESVAC national contact points, have requested a revision of the PCU methodology, including the animal categories as well as the weights used to calculate this technical unit. Discussions on this topic are on-going, and the outcome may result in an updated denominator for normalising the animal population at risk of being treated."

Therefore, Table A2 describes the animal categories that are currently included in the calculation of the denominator and the format of the sales data. The final categories to be included in the animal population data should be provided in the data collection protocol.

Table A2. Animal population data for calculation of sales data denominator for the current ESVAC denominator and their format for data that are not available in Eurostat or TRACES database

Animal category	Animal population data
Cattle	
Slaughtered cows	Head (number of animals)
Slaughtered heifers	Head (number of animals)
Slaughtered bullocks and bulls	Head (number of animals)
Slaughtered calves and young cattle	Head (number of animals)
Slaughtered bovine – Import	Head (number of animals)
Slaughtered bovine – Export	Head (number of animals)
Fattening bovine – Import	Head (number of animals)
Fattening bovine – Export	Head (number of animals)
Living dairy cows	Head (number of animals)
Pigs	
Slaughtered pigs	Head (number of animals)
Slaughtered pigs – Import	Head (number of animals)
Slaughtered pigs – Export	Head (number of animals)
Fattening pigs – Import	Head (number of animals)
Fattening pigs – Export	Head (number of animals)
Living sows	Head (number of animals)
Poultry	
Slaughtered broilers	Head (number of animals)

Animal category	Animal population data
Slaughtered turkeys	Head (number of animals)
Slaughtered poultry – Import	Head (number of animals)
Slaughtered poultry – Export	Head (number of animals)
Caprinae	
Slaughtered sheep and goats	Head (number of animals)
Slaughtered sheep – Import	Head (number of animals)
Slaughtered sheep – Export	Head (number of animals)
Fattening sheep – Import	Head (number of animals)
Fattening sheep – Export	Head (number of animals)
Living sheep	Head (number of animals)
Slaughtered goats – Import	Head (number of animals)
Slaughtered goats – Export	Head (number of animals)
Fattening goats – Import	Head (number of animals)
Fattening goats – Export	Head (number of animals)
Equidae	
Horses (both food-producing and non food-producing)	Head (number of animals)
Rabbits	
Slaughtered rabbits	Head (number of animals)
Finfish	Biomass (tonnes) finfish live weight of farmed fish produced

5.2. Use data denominator

In the advice on implementing measures under Article 57(3) of Regulation (EU) 2019/6 on veterinary medicinal products - Report on specific requirements for the collection of data on antimicrobial medicinal products used in animals (EMA/CVMP, 2019) it reads:

"Currently, the ESVAC project does not collect data on use of antimicrobials by animal species, but in the Guidance on collection and provision of national data on antimicrobial use by animal species or categories published by the Agency on 6 February 2018 (EMA, 2018) it is suggested to use animal species PCU as the denominator referred to as the 'species PCU'.

It is acknowledged that there may be concerns or questions regarding the use of the species PCU as a denominator to report use data, also in relation to the objectives of the analysis, e.g., trend analysis within Member States, comparison of use of antimicrobials between Member States. It is therefore recommended to conduct a scientific assessment on different denominators and indicators for analysing use data."

At this point, any recommendation on the animal categories to be included for the animal population data for the calculation use data denominator cannot be provided as no scientific assessment on different denominators has been conducted. However, the format of the data on animal population will be the number of heads apart from for farmed fish where amounts (tonnes) live weight produced should be used.

6. Online-based data submission and analysis systems

The online-based data submission and analysis systems are an essential aspect of data reporting and validation, and further analysis.

6.1. Online-based application for data submission

As maintained with the latest application supporting ESVAC data submission, advantages of online-based data submission include:

- immediate feedback on submitted data entry check is provided directly to the representative who is uploading data;
- automated data entry check is linked to rules to identify any inconsistencies with standardised requirements per each data field (variable);
- automated data entry checks identify any possible duplicates linked to unique identification value;
- automated data check-ups support and ensure harmonised and standardised data submission.

6.2. Data analysis application

Online-based data analysis tools, such as the ESVAC BI application, allow successfully submitted data to be accessed and analysed at any time. Data analysis reports, e.g. data validation reports can be used by Member States to assess the validity of data submitted.

Acronyms, terms and definitions

Acronym or term	Full name	Definitions (when appropriate)
ATC	Anatomical Therapeutic Chemical classification	The Anatomical Therapeutic Chemical (ATC) classification system for medicines
ATCvet	Anatomical Therapeutic Chemical veterinary classification	The ATC classification system adapted to veterinary medicine. ATC and ATCvet are maintained, by the WHO Collaborating Centre for Drug Statistics Methodology, the Norwegian Institute of Public Health
CVMP	Committee for Medicinal Products for Veterinary Use	The Committee for Medicinal Products for Veterinary Use (CVMP) is the Agency's committee responsible for veterinary medicines
DDDvet	Defined daily dose for animals	
DCDvet	Defined course dose for animals	

Acronym or term	Full name	Definitions (when appropriate)
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption	The European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project collects information on how antimicrobial medicines are used in animals across the European Union (EU). It is coordinated and maintained by the European Medicines Agency (EMA) following a request from the European Commission.
Numerator		In the context of this document: Amounts of antimicrobials sold or used
Denominator		In the context of this document: The animal population that could potentially be treated with antimicrobials
Indicator		In the context of this document: Measurement to evaluate exposure to antimicrobials
Eurostat		Eurostat is the statistical office of the European Union
HMP	Human Medicinal Product	The current and new veterinary medicines legislation, under specific circumstances, allows the use of HMPs in animals
MAH	Marketing Authorisation Holder	A Marketing Authorisation Holder (MAH) is a company, firm or non-profit organisation that has been granted a marketing authorisation. The marketing authorisation allows the holder to market a specific medicinal product for human or veterinary use, in one or more EU member states
LA	Long-acting injectable preparations	Long-acting injectable medications containing antimicrobial agents that provide sustained concentrations at the site of infection. Long-acting/extended release formulations, as noted in the product information, provide therapeutic levels after a single administration for a longer period of time.
OIE	World Organisation for Animal Health	The World Organisation for Animal Health, founded in 1924, is an

Acronym or term	Full name	Definitions (when appropriate)
		intergovernmental organization coordinating, supporting and promoting animal disease control, also setting of international standards.
PCU	Population Correction Unit	Denominator developed for the reporting of data on sales of veterinary antibiotics in the ongoing ESVAC project.
Product information		Documents providing officially approved information for healthcare professionals on a medicine. The product information includes the summary of product characteristics, package leaflet and labelling.
SPC	Summary of Product Characteristics	Summary of Product Characteristics (SmPC or SPC) is a legal document approved as part of the marketing authorisation of each medicine. It is the basis of information for health professionals on how to use the medicinal product.
TRACES	Trade Control and Expert System	TRACES is the European Commission's multilingual online management tool for all sanitary requirements on intra-EU trade and importation of animals, semen and embryo, food, feed and plants
VMP	Veterinary Medicinal Product	Veterinary medicinal products (VMPs), are substances or combinations of substances authorised to treat, prevent or diagnose disease in animals. The current requirements and procedures for granting a marketing authorisation for veterinary medicinal products are laid down primarily in Directive 2001/82/EC and in Regulation (EC) No 726/2004
WHO	World Health Organisation	The World Health Organization is a specialised agency of the United Nations that is concerned with international public health

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