EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) Sales Data and Animal Population Data Collection Protocol (version 4)

Superseded by a new version

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

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1. Introduction

1.1. Terms of reference

The European Commission has requested the European Medicines Agency to take the lead in collating data on the use of antimicrobial agents in animals in the European Union and to manage the database. The European Medicines Agency was asked to develop a harmonised approach for the collection and reporting of data based on national sales figures as well as data on usage in at least major groups of animal species and to ensure comparability with the sale/use of antimicrobial agents in human medicine. The intended use of the surveillance data, both at national and community level would be:

- To aid interpretation of patterns and trends regarding antimicrobial resistance (AMR);
- As input to risk profiling and risk assessment regarding AMR;
- For setting risk management priorities;
- For evaluation of the effectiveness of control measures being implemented;
- To identify emerging use of veterinary antimicrobial agents, e.g. of specific classes of antimicrobial agents such as those identified by World Health Organisation (WHO) as critically important for human medicine;
- To aid comparison of usage of veterinary antimicrobial agents between human and veterinary medicine, time periods and countries;
- As a basis for focused and targeted research and development.

This protocol addresses collection of sales data and data on animal population.

The revision of the Web Based Sales Data and Animal Population Data Collection Protocol includes updates concerning conversion factors and editorial amendments in regard to Table 2, Table 3 and Table 4.

1.2. Approach

To enable harmonised reporting of the data as well as comparison with data between time periods within and between different European countries standardisation and harmonisation of the data collected is of vital importance. This applies also for the animal demographic data that is used to normalise the sales data for reporting of the sales. In ESVAC, a population correction unit (PCU) is used as the denominator and this represents purely a technical unit of measurement. The data sources used and the methodology for the calculation of PCU are comprehensively described in Appendix 2 of the Agency's report 'Trends in the sales of veterinary antimicrobial agents in nine European countries: 2005-2009' (EMA/238630/2011)[1].

The data collection package consists of the following items:

- ESVAC sales and animal population data collection protocol (ESVAC Sales Protocol);
- ESVAC Sales Template;
- ESVAC population correction unit template (ESVAC PCU Template).

[1] Available from the Agency's website via: Home > Regulatory > Veterinary medicines > Overview > Antimicrobial resistance > European Surveillance of Veterinary Antimicrobial Consumption

In order to obtain reliable and harmonised data in the ESVAC database the ESVAC Sales Protocol, the ESVAC Sales Template and the PCU Template have to be adhered to.

1.3. Target groups of the protocol and templates

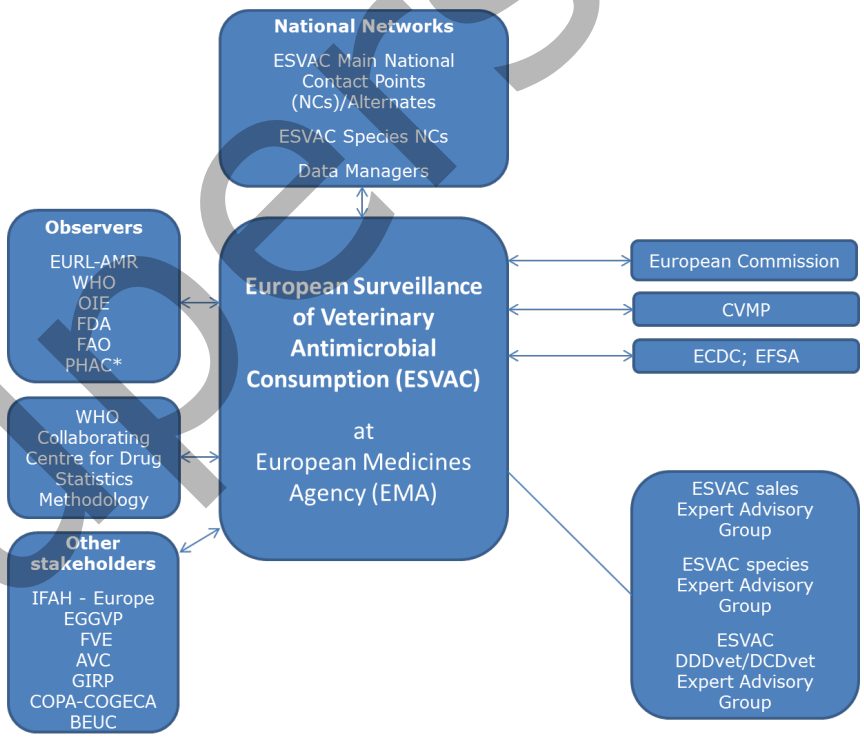
This version of the ESVAC Sales Protocol is primarily developed for web based submission of sales data and animal population data for countries participating in ESVAC but is thought to be applicable also for countries outside the EU/EEA area that want to collect such data.

The web delivery of data allows for the submission of data without using the ESVAC Sales Template; however, the requirements of the Data Collection Protocol should be fulfilled. If uploading data directly as comma-separated values (CSV) files without the use of the Excel template as the basis, please disregard the parts of this protocol that are not applicable.

1.4. Organization of the ESVAC project

The ESVAC project is organised into three main work streams: collection of sales data, collection of data on consumption by species and establishing and maintaining lists of defined daily doses animals (DDDvet) and defined course doses animals (DCDvet). Separate expert groups are established for these three work streams. The organisation of the ESVAC project is illustrated in Figure 1. The ESVAC main National Contact Point/Alternates and/or Data Managers are responsible for collecting, validating and submitting sales data and validating the PCU data uploaded by the ESVAC sales team. The ESVAC strategy 2016 – 2020 has been published on the ESVAC web page[2].

Figure 1. Organisation of the ESVAC project



[2] Available from the Agency's website via: Home > Regulatory > Veterinary medicines > Antimicrobial resistance > European Surveillance of Veterinary Antimicrobial Consumption

1.5. Web based delivery of data

The detailed user guide for web based delivery of sales data is described in the ESVAC web data collection – user guide. The user guidance describes the process of uploading the sales data via the web application, how to correct data sets with errors before submission and finally submission of the sales data via the web application. No information is provided in this protocol about the questionnaire as the questionnaire varies from year to year. This user guide also includes the collection of data on animal population by the ESVAC sales team and the validation of these data by the participating countries.

2. ESVAC sales data

2.1. Selection of data source

The infrastructure of the distribution of veterinary antimicrobial agents may vary considerably from country to country; such medicinal products are dispensed to the end-users by wholesalers, pharmaceutical industry, pharmacies, veterinarians or a combination of these. Wholesalers and pharmaceutical industries may also trade between each other and export veterinary antimicrobial agents to other Member States (MS). The first step in setting up surveillance of veterinary antimicrobial agents is therefore to identify and describe of the distribution system for veterinary antimicrobial agents. The data source selected should, if possible, provide data on sales to end-users within the country such as veterinarians, farmers and wholesalers.

2.2. Veterinary antimicrobial agents to be included in ESVAC sales data

To harmonise the veterinary antimicrobial agents to be included in the data sets, the Anatomical Therapeutic Chemical classification system for veterinary medicinal products (ATCvet) is applied (Table 1) (http://www.whocc.no/atcvet/atcvet_index/). This includes all pharmaceutical forms and medicated feed except dermatological preparations (ATCvet group QD) and preparations for sensory organs (ATCvet group QS). The contribution from these groups of antimicrobial agents, in tonnes of antimicrobial ingredient, to the total amounts is minimal, and therefore the effect of the deviation is negligible.

The veterinary antimicrobial agents (ATCvet groups) to be reported to the ESVAC database are shown in Table 1.

Table 1. Categories of veterinary antimicrobial agents to be included in ESVAC (http://www.whocc.no/atcvet/atcvet_index/)

Groups of antimicrobial agents	ATCvet codes
Antimicrobial agents for intestinal use	QA07AA; QA07AB
Antimicrobial agents for intrauterine use	QG01AA; QG01AE; QG01BA; QG01BE QG51AA; QG51AG
Antimicrobial agents for systemic use	QJ01
Antimicrobial agents for intramammary use	QJ51
Antimicrobial agents used as antiparasitic agents	QP51AG

2.3. Variables to be collected for each veterinary medicinal product (VMP) presentation

Table 2. Variables to be collected for each VMP presentation[3]

	Variable	Description of variable	Comments
	COUNTRY	**ISO Country Code**: 2 letter code (alpha-2 code), according to the International Standard for country codes (http://www.iso.org/iso/country_codes)	To identify country for which sales data are reported
	YEAR	Four-digit number	To identify the calendar year for collected and reported sales data
PRODUCT INFORMATION	**MA**	**Marketing Authorisation Identification** Number or number and letter combination or name of the marketing authorisation holder Additional information: For special licence products/marketing authorisation or through parallel trade identification of non-marketing authorisation medicinal product status should be included	To allow unique identification of the medicinal product and enable a link with other databases
	PRESENTATION ID	**Identification Number of Product Presentation** Medicinal product package code value (can be number or number and letter combination). The code is a unique identifier for each presentation of the medicinal product (name, package size, strength and formulation). As a key variable in many databases it should 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	• To allow identification of all antimicrobial medicinal product presentation marketed in a country • To enable validation and analysis of each presentation package size in which the veterinary medicinal product is sold • To enable the analysis of historical data • To identify duplicate reporting of sales
	NAME	**Medicinal Product Name (in national language)** Name of medicinal product as per product information (summary of product characteristics, package leaflet and labelling) E.g.: Harmony vet 50 mg tablets 2 x 30; Harmony vet long acting 10 mg/ml injection 10 ml	To identify and validate recorded details
	FORM	**Pharmaceutical Form** Form should be selected from the standardised defined list: Bolus (BOLUS), Injectable prep. (INJ), Intramammary prep. (INTRAMAM), Intramammary dry cow treatment prep. (INTRAMAM-DC), Oral solution and oral powder for water administration (ORAL SOLU), Oral paste (ORAL PASTE), Oral powder (ORAL POWD), Premix (PREMIX), Capsule and Tablet etc. (TABL), Intrauterine preparation (INTRAUT)	To allow analysis of data by administration route/ pharmaceutical form
	LONG ACTING	**Long-acting injectable preparations** It refers to injectable preparations that provide	Optional

[3] Of note is that this protocol and 2019 sales data reporting template do not display requirements as outlined in Article 57 of Regulation (EU) 2019/6.

Variable	Description of variable	Comments
	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	
PACKSIZE	**Content Quantity in Package: Pack size** 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)	• To allow for calculation of the amount of antimicrobial ingredient in each product presentation • For validation at country level prior to submission via web application • Validation by BI (Business Intelligence) after submission of data
PACKSIZEU	**Content Unit of Measurement** E.g.: ML, L, G, KG, PIECE (e.g. tablets, capsules, bolus and intramammary preparations) The pack size unit should be harmonised with the strength unit, e.g. if pack size is 1 KG, the strength unit should be per KG	• To enable calculation of amount of antimicrobial ingredient in each product presentation • For validation at country level prior to submission via web application • By BI after submission of data
ATCVET	**ATCvet- 5th level: Anatomic Therapeutic Chemical (Classification) Veterinary** Value to be selected as per the latest version of the ATCvet index	To ensure a standardised language for analysis and reporting of data per antimicrobial classes as well as anatomical and therapeutic groups If an ATCvet code has not been assigned for an ingredient, the ESVAC sales team has to be contacted
SPECIES	**Animal Species** All the animal species for which the VMP is approved (e.g. cattle (CA), pig (PIG), poultry (POU), turkey (TU), ducks (DU), geese (GE), sheep (SH), goat (GO), horse (HO), food-producing rabbits (RA), finfish (FI), dog (DOG), cat (CAT), minks (MI), foxes (FO), other food-producing animals (ZZ), not given (NO), other non-food-producing animals (YY))	Optional Species details are currently used to support data preparation for the JIACRA[4] reports until use data will be provided, we suggest to detail the type of species, when the category others is applicable, e.g. ZZ (quail, partridges, pheasants) and YY (pet rabbits, ornamental birds, racing pigeons)

[4] Joint inter-agency antimicrobial consumption and resistance analysis (JIACRA) reports present work done by European Medicines Agency, European Food Safety Authority and the European Centre for Disease Prevention and Control to analyse the potential relationship between the consumption of antimicrobials by humans and animals and the occurrence of antimicrobial resistance.

	Variable	Description of variable	Comments
	NO PACKS	**Number of Packages Sold** Numerical value to disclose number of packages of product presentation sold within the reporting period (year) in the reporting country	• To calculate weight of antimicrobial ingredient sold for each product presentation • For validation at country level prior to submission via web application • Validation by BI after submission of data; • For validation by ESVAC after data submission
	INGR_ID	**Ingredient Code Value** Automatically attributed by the macro or ESVAC web application tool	Serve as a unique identifier for each ingredient for each product Needed for data management purposes
	INGR	**Antimicrobial Ingredient Name** Name to be selected from the defined 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 separately	Only last version of names published in the ATCvet index will be accepted by the system If an ingredient name is not published in the ATCvet index, the ESVAC sales team has to be contacted
INGREDIENT	**SALT**	**Salt of Antimicrobial Ingredient when strength expressed in IU** Name to be selected from the defined list of names of salt of antimicrobial ingredient. Currently only applicable for colistin sulfate and colistin methane sulfonate	• Only in cases where the strength of an antimicrobial ingredient is given in IU (IU/G, IU/ML or IU/PIECE) and when different salts exist, to allow for conversion to weight of (active) antimicrobial ingredient • For validation at country level prior to submission via web application • Validation by BI after submission of data
	DERIVATIVE[5]	**Name of Derivative or Compound of Antimicrobial Ingredient** Name to be selected from the defined list of derivatives/compounds (Table 3). E.g.: For procaine benzylpenicillin this name should be given and not benzylpenicillin	• To allow for calculating the weight of the (active) antimicrobial ingredient • For validation at country level prior to submission via web application • By BI after submission of data

[5] Previously referred to as prodrug

	Variable	Description of variable	Comments
	STRENGTH	**Quantity of the Antimicrobial Ingredient** 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 strengths for all the antimicrobial ingredients per presentation must be provided separately	• To enable calculation of the amount of antimicrobial ingredient in each product presentation and to validate the calculated ingredient content • For validation at country level prior to submission via web application • Validation by BI after submission of data
	STRENGTHU	**Unit of Measurement for Strength** Unit of measurement of strength to be chosen from a defined list (e.g.: IU/G, IU/ML, IU/PIECE, G/KG, G/L, G/PIECE, MG/ML, MG/G, 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 separately	• To enable calculation of the amount of antimicrobial ingredient in each product presentation • For validation at country level prior to submission via web application • Validation by BI after submission of data
	CONV FACT IU	**Conversion Factor when Strength is given in IU** When strength unit is e.g. IU/ML or IU/PIECE, a conversion factor from the defined list (Table 4) is assigned automatically by the macro or ESVAC web application tool for the harmonised calculation of weight of an antimicrobial ingredient	To allow for calculation of the weight of (active) antimicrobial ingredient per product package If an antimicrobial ingredient with strength given in IU is not listed, ESVAC sales team should be contacted
	CONV FACT DERIV	**Conversion Factor of certain Derivatives or Compounds** Only when strength of the presentation is given for the listed derivatives/compounds and not for the (active) antimicrobial ingredient (e.g. procaine benzylpenicillin that is a derivative/compound for benzylpenicillin), a conversion factor from a defined list (Table 3) is automatically assigned by the macro or ESVAC web application tool, for the harmonised calculation of weight of an antimicrobial ingredient	• To enable for the calculation of the weight of the (active) antimicrobial ingredient per product package • Validation by BI after submission of data If a derivative/compound is not listed, ESVAC sales team should be contacted
	CONTENT	**Content of Antimicrobial Ingredient in Package** 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 value is calculated automatically by the macro or ESVAC web application tool	• To enable calculation of volume of sales • Validation by BI after submission of data
	CONTENTU	**Unit of Antimicrobial Ingredient in Package** The unit of antimicrobial ingredient per product package is given in grams for all antimicrobial agents This field is filled automatically by the macro or ESVAC web application tool	This allows the MS to evaluate the output of calculation of volume of sales prior to the submission via web application

	Variable	Description of variable	Comments
	TONS SOLD	**Tons Sold of Antimicrobial Ingredient** Based on unified details provided represents volume of antimicrobial ingredient in tonnes per product presentation This value is calculated automatically by the macro or ESVAC web application tool	Provides volume of antimicrobial ingredient in tonnes sold or used For validation by ESVAC after data submission

2.3.1. Conversion factors of certain derivatives or compounds

In order to obtain harmonised data, the conversion factors for certain derivatives or compounds of antimicrobials shown in Table 3 are applied to calculate amount of (active) antimicrobial ingredient.

Table 3. Name of derivates/compounds for which conversion factors are applied

Derivative or Compound[6]	Conversion factor
Benethamine benzylpenicillin[7]	0.61
Benzathine benzylpenicillin	0.74
Cefapirin benzathine[8]	0.78
Cefalexin benzathine[9]	0.74
Cloxacillin benzathine[10]	0.78
Oxacillin benzathine[11]	0.77
Penethamate hydriodide[12]	0.60
Procaine benzylpenicillin[13]	0.57

2.3.2. Conversion factors when strength is given in IU

When strength is given in international units (e.g. IU/ML) the amount sold has to be calculated to present data in weight of (active) antimicrobial ingredient. In order to obtain harmonised data, the conversion factors shown in Table 4 are applied by ESVAC to calculate amount of antimicrobial ingredient sold. Note that if the strength of an ingredient is reported in IU, the conversion factor from IU to mg as shown in Table 4 is applied to calculate amount of (active) antimicrobial ingredient sold.

Table 4. Conversion factors for calculation from IU to mg of (active) antimicrobial ingredient

Ingredient	IU/MG	Conversion factor (MG/IU)
Apramycin	556	0.0018
Bacitracin	74	0.01351
Benzylpenicillin[14]	1667	0.00060
Chlortetracycline	900	0.00111
Colistin sulfate	20500	0.00005

[6] Previously referred to as prodrugs
[7] Conversion factor for benethamine benzylpenicillin is updated from 0.65 to 0.61
[8] Conversion factor for cefapirin benzathine is updated from 0.41 to 0.78
[9] Conversion factor for cefalexin benzathine is updated from 0.36 to 0.74
[10] Conversion factor for cloxacillin benzathine is updated from 0.43 to 0.78
[11] Conversion factor for oxacillin benzathine is updated from 0.69 to 0.77
[12] Conversion factor for penethamate hydriodide is updated from 0.63 to 0.60
[13] Conversion factor for procaine benzylpenicillin is updated from 0.61 to 0.57
[14] Applies to all derivatives/compounds of benzylpenicillin

Ingredient	IU/MG	Conversion factor (MG/IU)
Colistin methane sulfonate	12700	0.00008
Dihydrostreptomycin	820	0.00122
Erythromycin	920	0.00109
Gentamicin	620	0.00161
Kanamycin	796	0.00126
Neomycin	755	0.00133
Framycetin	670	0.00149
Oxytetracycline	870	0.00115
Paromomycin	675	0.00148
Polymyxin B	8403	0.00012
Spiramycin	3200	0.00031
Streptomycin	785	0.00127
Tetracycline	982	0.00102
Tobramycin	875	0.00114
Tylosin	1000	0.00100

3. Call for data

Prior to the annual call for data the ESVAC team updates the lists of ATCvet codes and names as per the ATCvet index for each country specific ESVAC sales register (ESVAC Sales Template). A list of new ATCvet codes and ingredient names as per ATCvet index will be provided together with the call.

The ESVAC Data Collection Form contains lists to facilitate that the data are standardised and harmonised prior to the submission.

3.1. Data submission

Data must be submitted using the ESVAC web application. For supporting accuracy check of sales data, the NCs/DMs are requested to send to the ESVAC secretariat also the Microsoft Excel template to the ESVAC project team - i.e. the complete sales file used to create 3 CSV files for uploading on the ESVAC web application.

4. Filling in the ESVAC Sales Template

4.1. General considerations

The sales data should always be recorded in the country specific ESVAC register (template) provided together with the call for data. For new countries the general ESVAC template should be applied.

In case of fixed combination products, the columns for the INGREDIENT variables have to be filled in for each ingredient in separate columns in the same row.

Enzyme inhibitors such as clavulanic acid, which does not pose any antimicrobial activity by itself and are not included in the latest ATCvet index, are not accepted by the ESVAC web system. As it is important to quantify use of e.g. amoxicillin+ clavulanic acid the ATCvet code for the combinations should be given (e.g. QJ01CR02 for amoxicillin+ clavulanic acid).

Other ingredients, which are not classified as antibiotics, e.g. anti-inflammatory ingredients, fall out of scope of the present protocol and should not be included in the sales template.

Antimicrobial products with any other pharmaceutical forms not listed in Table 2, e.g. dermatological products, nasal products, ophthalmological formulations and otological formulations, also fall out of scope of this protocol and should not be submitted via ESVAC web application.

Although the species column is optional to be completed and intended to provide better understanding of the data, the species details are used to support data preparation for the JIACRA reports until antimicrobial use data per animal species will be provided, but it is encouraged to complete the details as per latest version of the approved product information.

4.2. Comments on the various fields' components

Presentation identifier (ID) (Medicinal Product Package Code Value)

When this information is not available, it is necessary to assign individual value for each package.

The use of a standard and stable Presentation ID, e.g. International Article Number (EAN) (originally European Article Number), might facilitate the traceability of products as well as interaction with other databases (e.g. the EU Veterinary Medicinal Product Database). Furthermore, it enables identification of duplicates.

In case Presentation IDs are not available, these IDs can be derived from other variables. It is recommended to combine the marketing authorisation number (MA), name with the FORM, the PACKSIZE and PACKSIZEU variables. This combination of MA+NAME+FORM+PACKSIZE+PACKSIZEU should be unique per medicinal product package.

Finally, in case marketing authorisation numbers are not available, it is recommended to use the line number as Presentation ID. All missing Presentation IDs must be entered without sorting in between to avoid assigning the same ID to two different products.

ATCVET [ATCvet code- 5th LEVEL]

If an ingredient ATCvet code has not been assigned for the VMP/ingredient/combination VMP in question please contact the ESVAC sales team that will ask the WHO Collaborating Centre for Drug Statistics Methodology Norwegian Institute of Public Health (WHO Centre) to provide a code for such products and the dataset will be updated by ESVAC sales team when the codes have been assigned.

The ESVAC web system would not allow the upload of a product unless a valid ATCvet code has been assigned (see the user's guide for further information).

INGR _ID [Ingredient Code Value]

If using the macro of the excel template, the INGR_IDs is assigned automatically by the macro.

If the template is not used or the macro is not used, it is recommended to assign the INGR_ID by concatenating the Presentation ID with the sequence of the ingredient in the medicinal product package separating by a '#', e.g. for a medicinal product package with a presentation ID of "AZE10" containing two ingredients the first ingredient will be coded "AZE10#1" and the second one "AZE10#2".

INGR [Antimicrobial Ingredient Name (ATCvet name)]

If a name is not published in the ATCvet index, it is necessary to inform the ESVAC project team as soon as possible. When receiving your email the ESVAC project team will ask the WHO Centre to provide the ATCvet code and ingredient name for such ingredients and the ESVAC project team will

provide you temporary solution or the correct name when the ATCvet codes and ingredient names have been assigned by the WHO Centre.

CONV FACT IU (Conversion Factor IU) and CONV FACT DERIV (Conversion Factor of certain Derivatives or Compounds)

These will be recorded automatically by use of a macro designed for the ESVAC Sales Template.

If a Conversion Factor IU or Conversion Factor of certain Derivatives or Compounds for the antimicrobial ingredient or derivative/compound in question is not included in the ESVAC Data Collection Form, the ESVAC Sales Team (ESVAC@eu.europa.eu) has to be contacted and will provide the (standardised) value.

5. ESVAC data quality check

The ESVAC sales and animal data quality requirements are confirmed by representatives of the ESVAC participating countries and by the ESVAC secretariat at the data entry and data checking phase. Responsibility to ensure that sales data submitted to EMA fulfil business information demand largely lies on the ESVAC NCs (National Contact Points) and/or DMs (Data Managers). Suitable quality control procedures are defined by each country taking into account their individual data collection process. It is strongly advised to establish a procedure for checking the data quality, including data coverage, prior to data collection and reporting; this includes steps to be taken before, during and after data collection, in order to obtain high quality of data available in the ESVAC database.

Although ESVAC NCs/DMs validate their data prior to submission via ESVAC web-based application, the ESVAC project team in addition gathers essential details via the annual questionnaire. In line with the EMA proposed framework intended to serve as quality indication for data completeness and logical consistency of every approved dataset, the ESVAC secretariat follows up with the responsible NCs/DMs on any potential outlier identified.

A brief overview of the outlier-detection measures taken by the ESVAC secretariat to assist in the identification of possible errors in data submitted to the ESVAC database are included in Annex 1 of this protocol.

For the EU Member States, the ESVAC reference animal data are downloaded from the Eurostat and TRACES databases and provided to the NCs and/or DMs for their approval; EEA countries have to fill in these data themselves. Typically, ESVAC representatives approach suitable institutions in their country to confirm statistics and where it's necessary replace reference values with the data provided from their national statistical offices.

5.1. Checking the completeness of the sales data

A verification that the sales data submitted to the ESVAC web system are as complete as possible is expected from every ESVAC NC and/or DM; therefore, it is highly recommended to follow processes listed below.

Table 5. Processes for ensuring the completeness of the sales data

Item	Steps	Comments
Stage 1. Establishing a procedure for checking the data quality, including data coverage, prior to the data collection	1.1. Identify ALL the actual data providers through the national register of VMP suppliers – e.g. wholesalers, MAHs, pharmacies, feed mills etc.	• The National Medicines Authority is usually responsible for keeping registers of authorised VMPs and VMP suppliers; exceptionally no such information may be available of feed mills. • Identify if there are any other data sources of sales data that can be used for comparison or for cross-checking of data
	1.2. In case sales data are obtained from prescriptions (e.g. from pharmacies, veterinarians), identify all antimicrobial agents for which data are to be collected	
	1.3. Specify the veterinary antimicrobial agents to be included in the data call/selection[15] – i.e. the ATCvet codes to be covered (see Table 1.)	
Stage 2. Sending a call for data or download data from the system		
Stage 3. Data collection – after a deadline has passed for data to be delivered by the national data providers	3.1. Check that all data providers have delivered the data	• In case not all data providers have delivered the data, submit a reminder; ask for a written confirmation in case of no sales of specific VMP • Alternatively, after entering data into the ESVAC template compare the output with the filled-in national data • As an additional verification step, data can be cross-checked with other sales sources, if available
	3.2. Identify/review that all VMPs presentations are included in the dataset for the corresponding year	
Stage 4. When responses received from all identified data providers	4.1. After entering data in ESVAC template, compare NO PACKS, e.g. number of packages, and TONS SOLD, e.g. calculated tonnes sold, by ID number with data in template for previous year(s) to identify potential outliers (if applicable)	
	4.2. For the assumed outliers contact corresponding data provider(s) and ask for verification	

[15] It is a responsibility of the National Authority to ensure the collection of other antimicrobial agents, if required for national reporting.

Item	Steps	Comments
	4.3. Run a validation by using the macro included in the template to identify any inconsistencies in the data and correct any identified mistakes	
	4.4. Additionally, cross-check ATCvet entries and corresponding ingredients per presentation	
Stage 5. Submitting sales data after the initial validation via the ESVAC web system for corresponding year	5.1. Run validation reports from the ESVAC BI application to identify any outliers (see Annex 1)	• For potential outliers compare latest submitted dataset with dataset approved for previous year by classes of antimicrobials and by pharmaceutical forms
	5.2. After receiving validation report, clarify the major differences in sales, if possible	
Stage 6. After sales data are finalised and corrected, sending approval to the ESVAC team to confirm that corresponding dataset can be used for further analysis and for preparation of the next report	6.1. Upload the final sales dataset into the ESVAC web application, if necessary, and send a final excel file to the ESVAC secretariat	
	6.2. Review suggestions sent by the ESVAC secretariat, when applicable, and send your approval to use the finalised dataset for further analysis	

6. ESVAC PCU data

6.1. Animal categories included in PCU

Eurostat, the Statistical Office of the European Union, covers data on numbers and biomass of food-producing animals slaughtered, as well as data on livestock food-producing animals per EU MS. Therefore, Eurostat[16] is selected as the source for data on this animal category. In cases where data are not available in Eurostat (e.g. for rabbits), national statistics is applied. For horses (food-producing species according to the EU legislation), national statistics provided by the ESVAC national representatives are used. As data on population of dogs and cats are not available in all participating countries, these species are not included in the PCU, in order to have comparable data. Therefore, antimicrobial VMPs approved for use in companion animals only, i.e. tablets, are excluded from the datasets prior to the normalisation of the sales by the PCU.

Animals exported for fattening or for slaughter in another Member State are likely to be treated with antimicrobial agents in the country of origin, and therefore it is important to correct this for the major species (cattle, pigs, poultry and sheep). However, the Eurostat data on numbers of animals exported or imported for fattening or slaughter are not valid, as these are reported only when above a certain limit, which implies that the Eurostat data represent an underestimate of these for most species and

[16] http://epp.eurostat.ec.europa.eu/portal/page/portal/statistics/themes

countries. Such data are therefore obtained from TRACES (DG SANCO, European Commission), as these are based on health certificates, which are obligatory for all animals crossing any border.

Typically, at the start of September of each year the ESVAC sales team provides the reference data for the animal categories shown in Table 6 available in Eurostat and TRACES for the categories available from these databases. These are the only animal categories that are accepted by the ESVAC web application. For categories for which data are not available in Eurostat or TRACES, countries may submit missing values in addition for the PCU calculations.

EEA countries are requested to upload all animal population data per specified categories as no values are available through Eurostat and TRACES.

Table 6. Animal categories included in the calculation of the population correction unit (PCU) and data types to be reported

Animal category
Slaughtered cows
Slaughtered heifers
Slaughtered bullocks and bulls
Slaughtered calves and young cattle
Slaughtered bovine - Import
Slaughtered bovine - Export
Fattening bovine - Import
Fattening bovine - Export
Living dairy cows
Slaughtered pigs
Slaughtered pigs - Import
Slaughtered pigs - Export
Fattening pigs - Import
Fattening pigs - Export
Living sows
Slaughtered broilers
Slaughtered turkeys
Slaughtered poultry - Import
Slaughtered poultry - Export
Slaughtered sheep and goats
Slaughtered sheep - Import
Slaughtered sheep - Export
Fattening sheep - Import
Fattening sheep - Export
Living sheep
Slaughtered goat - Import
Slaughtered goat - Export
Fattening goat - Import
Fattening goat - Export
Living horses
Slaughtered rabbits
Biomass of farmed fish produced

6.2. Calculation of PCU

Essentially, the PCU for each animal category is calculated by multiplying numbers of livestock animals (dairy cows, sheep, sows and horses) and slaughtered animals (cattle, pigs, lambs, poultry and turkeys) by the theoretical weight at the time most likely for treatment. In case of animals exported or imported for fattening or slaughter (cattle, pigs and poultry), the PCU is calculated by multiplying the number of animals with a standardised weight (Table 7).

For farmed fish, Eurostat data is given only as live-weight slaughtered, as information on weight at treatment has not been identified; therefore, in case of farmed fish, the PCU is taken as a biomass live-weight slaughtered in each country. The PCU of the animals exported for fattening or for slaughter in another Member State is added to the PCU of livestock and to the PCU of slaughtered animals in the country of origin, because young animals are typically treated more frequently than at other age classes. The PCU for animals imported for fattening or for slaughter in another Member State is subtracted from the total PCU of livestock and slaughtered animals, since it is included in the data of slaughtered animals (Eurostat data) and in order to avoid double counting (both in exporting and importing country).

Table 7. Weights used to calculate the population correction unit

Animal category	Weight in kg
Slaughtered or livestock (Eurostat)	
Slaughtered cow	425
Slaughtered heifer	200
Slaughtered bullocks and bulls	425
Slaughtered calves and young cattle	140
Living dairy cow	425
Slaughtered pig	65
Living sow	240
Slaughtered broiler	1
Slaughtered turkey	6.5
Slaughtered sheep and goats	20
Living sheep	75
Living horse	400
Slaughtered rabbit	1.4
Imported/exported for fattening or slaughter (TRACES data)	
Slaughtered bovine	425
Fattening bovine	140
Slaughtered pig	65
Fattening pig	25
Slaughtered poultry	1
Slaughtered sheep	20
Fattening sheep	20
Slaughtered goat	20
Fattening goat	20

PCU calculation by species, age class and production type

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.

7. Indicator for reporting of the sales data

The main indicator to be applied expressing the sales of veterinary antimicrobials is mg of antimicrobial ingredient normalised by the population correction unit (mg/PCU):

$$\frac{\text{Amount sold in metric tonnes} \times 10^9}{\text{PCU in kg}}$$

The data are presented according to the ATCvet hierarchical system, and for combination preparations - each antimicrobial ingredient is allocated to the relevant ATCvet code for single ingredients (e.g. spectinomycin is included in 'Other antibacterials').

8. Confidentiality and security of submitted sales data

Prior to the publication of the submitted data, NCs and/or DMs are requested to inform the ESVAC secretariat on any data which for reasons of commercial confidentiality (or any other grounds) cannot be disclosed either on the ESVAC annual report and/or on the ESVAC Interactive Database.

Data published by the Agency, either on the public web page or as part of scientific or other publication, do not contain, or in any other way disclose, any commercially confidential information on specific veterinary products. Principles for ensuring the confidentiality of data supplied to the ESVAC project (EMA/327935/2010) are published on the EMA web page.

EMA has dedicated controls that adhere to the three main requirements related to the security of information: availability, confidentiality and integrity.

- Data is stored in a secure location on EMA premises and backed-up regularly. The EMA IT infrastructure provides high availability of services.
- Data is made publicly available by the ESVAC secretariat at the agreed date of publication (typically the same day when the ESVAC annual report is published). Until this time, only users can see their own datasets (to which they have full access). As no personal data are held in the ESVAC databases, no specific controls are required.
- Networks are segregated so that stored data is filtered with only relevant data being exposed, in a consolidated format, to the public via the BI platform. Data is not otherwise classified.

ANNEX 1

1. Additional information for review of ESVAC data quality

The ESVAC web-based application runs data accuracy check ensuring that information provided is in compliance with the requirements, as noted in sections 2.2 of this protocol, and as per predefined lists, as available in the sales data template, e.g., confirmed ATCvet codes and ingredient names. In case of any inconsistencies identified, the system does not allow to proceed with the submitted dataset, instead a list with errors identified is provided for follow-up actions.

1.1. Validation of sales data

To facilitate quality and validity checks of the submitted data, validation reports are provided via the Oracle Business Intelligence Enterprise Edition (BI) tool, known as ESVAC BI application.

A set of ESVAC BI validation templates are available to each ESVAC representative to run analysis for any uploaded datasets of their own country. Validation reports include:

1.1 Substance Sales Report;

1.2 Register Report;

1.3 Product Sales Report;

1.4 PCU Category Report;

1.5 PCU Report;

1.6 Sales Data Compare Report.

Validation reports support comparison of sales and animal population data with previously uploaded values. The comparison between two datasets is provided by antimicrobial classes and/or pharmaceutical forms, and also by presentations.

1.2. Accuracy check of sales data (supplementary information to section 5)

For supporting accuracy check of sales data, the NCs/DMs are requested to send to the ESVAC secretariat also the Microsoft Excel template (previously named INPUT file) to the ESVAC project team - i.e. the complete sales file used to create 3 CSV files for uploading on the ESVAC web application. To identify any possible errors, e.g. missing ingredients, inaccurate strength value, imprecise ATCvet codes, data recorded per each product in the excel file are compared with the details from the publicly available product information by the ESVAC team. All identified potential discrepancies are reported to the NCs/DMs for their attention and confirmation.

Manual checking, run by the ESVAC team, for standardization and harmonization concern the following fields of the excel template:

1. COUNTRY – to confirm if all lines are completed;
2. YEAR – to confirm if all lines include reference to corresponding year;
3. PRESENTATION ID – to confirm if ID is provided in all lines and if there are any possible duplicates;
4. FORM – to filter by form and gradually cross-check with product names and ATCvet codes;

5. LONG ACTING – to confirm if all injectable preparations with indication to long acting duration (e.g. LA or L.A) or any previously identified VMPs and/or ingredients are marked as long acting;
6. ATCvet – to confirm codes with a special attention to intramammary, intrauterine preparations and penicillins; to confirm if all ingredients are reported in the line with ATCvet index indicating combination products;
7. SPECIES – to confirm if species information is provided in the template; to search for corresponding product information to add missing details for NCs and/or DMs consideration;
8. INGR – to cross-check if all ingredients are provided as per corresponding product information;
9. SALT – to filter any lines where strength is given in IU and to confirm details as per available product information; to confirm that salts are only provided for colistin;
10. STRENGTH – to confirm if strength is in line with the name of VMP or as per available product information, when applicable; and to identify any peculiar strength values reported;
11. STRENGTHU – filtering by PACK SIZEU, to ensure that strength unit is given in a harmonised manner (e.g. if pack size unit is provided in ML, then strength unit should be given as IU/ML or MG/ML); all strength units should be checked by line for all ingredients.