WHO methodology for a global programme on surveillance of antimicrobial consumption

Version 1.0

World Health Organization

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Abbreviations

AMC	Antimicrobial consumption
ATC	Anatomical Therapeutic Chemical
CC	Collaborating Centre
DDD	Defined Daily Dose
DID	Defined Daily Doses/1000 inhabitants/day
EphMRA	European Pharmaceutical Market Research Association
GAP	Global Action Plan
INN	International Nonproprietary Name
OIE	World Organisation for Animal Health
OTC	Over-the-counter
PBIRG	Pharmaceutical Business Intelligence and Research Group
PDD	Prescribed Daily Dose
PIY	Packages/1000 inhabitants/year
WHA	World Health Assembly
WHO	World Health Organization

1. Background

At the Sixty-eighth World Health Assembly (WHA) held in May 2015, Member States adopted the Global Action Plan on antimicrobial resistance and the WHA urged Member States to implement the action plan recognizing this may need to be adapted to specific contexts and national priorities.

The Global Action Plan (GAP) has five objectives:

1. Improve awareness and understanding of antimicrobial resistance;
2. Strengthen surveillance and research;
3. Reduce the incidence of infection;
4. Optimize the use of antimicrobial medicines; and
5. Ensure sustainable investment in countering antimicrobial resistance.

Specifically related to objective 4, Member States are requested to provide "*stewardship programmes that monitor and promote optimization of antimicrobial use at national and local levels in accordance with international standards in order to ensure the correct choice of medicine at the right dose on the basis of evidence".* Thus, an important element of the GAP is monitoring the consumption of antimicrobials. All countries have some data related to the import, procurement, distribution or clinical use of antimicrobials in their communities that can be used as the basis of stewardship and monitoring programs.

Data on the consumption of antimicrobials have a number of uses, including:

- To relate exposure to antimicrobials to the development of antimicrobial resistance;
- To identify and provide early warning of problems relating to changes in exposure and utilization and to develop interventions to address problems identified;
- Monitoring the outcomes of interventions aimed at changing exposure;
- Assessing quality of prescribing against practice guidelines;
- Raising awareness in health professionals, consumers and policy makers about the issues of antimicrobial resistance and the contribution of inappropriate use of antimicrobials in humans.

Data on antibiotic use are collected and analysed in many high- and middle-income countries and the World Organisation for Animal Health (OIE) is developing a database on antibiotic use in animals. However, data are lacking on antibiotic use in human beings at the point of care and from lower-income countries. The WHO program on surveillance on antimicrobial consumption (AMC) is a global surveillance program for the collection and reporting of data on antimicrobial consumption in humans at country, regional and global level.

2. The WHO program on surveillance of antimicrobial consumption

2.1. Aim and objectives

2.1.1 Aim

The aim of the protocol presented here is to provide a common methodology for the measurement of the consumption of antimicrobial agents. This will allow monitoring of trends over time at the national level, facilitate some comparisons between countries and provide a common metric for reporting antimicrobial use at a global level.

2.1.2 Objectives

The primary objectives of the WHO program of surveillance of antimicrobial consumption are:

- to provide a common methodology to the countries for collecting and reporting national antimicrobial consumption data;
- to provide reliable and comparable national consumption data over time and between countries;
- to provide information on the level of use and types of antimicrobials for policy-makers and prescribers;
- to provide a methodology that can be integrated into a global WHO surveillance program.

The secondary objectives of the WHO program are:

- to provide, as part of a national package, a methodology that can be integrated in national program on surveillance of antimicrobial use and more generally in a national program on antimicrobial resistance;
- to provide comparable consumption data with animal and agricultural consumption data.

2.2. Activities at three levels

The WHO program on surveillance of antimicrobial consumption involves activities at three levels – national, regional and global levels.

2.2.1. National level

Member States participating in the WHO program on surveillance of antimicrobial consumption should set up a national team in charge of the surveillance of antimicrobial consumption in the country. The AMC national team is responsible for establishing and running the national surveillance program on antimicrobial consumption by collecting and

validating the consumption data, by reporting the consumption data at the regional and global level,and finally by publishing a report on the consumption of antimicrobials in the country. In order to have support from the national authorities, the AMC national team should be placed under the authority of the Ministry of Health.

To promote good integration of the surveillance of antimicrobial consumption with other national activities related to antimicrobial use and resistance, the AMC national team should have links with the national antimicrobial committee, and the program in charge of the surveillance of antimicrobial resistance. In addition, as part of the “One Health” approach, the AMC national team should have links with the programs in charge of the surveillance of antimicrobial use and resistance in the animal and agricultural sectors.

It is recommended that the AMC national team is a multi-disciplinary team with at least some members with pharmaceutical and data management skills. In some settings it may be appropriate to establish a Technical Working Group to coordinate the data collection. Where there are multiple data providers, including from the private sector, it may be necessary to put contracts in place in order to facilitate data release.

2.2.2. Regional level

WHO Regional offices should set up an antimicrobial consumption team (AMC regional team). The AMC regional team is responsible for supporting countries to implement a national surveillance program on antimicrobial consumption and coordinating the WHO surveillance program at regional level. As part of their tasks, the AMC regional team should collate national antimicrobial consumption data from the countries, validate and analyse these data, communicate with the countries on the data validation and finally publish a regional report on antimicrobial consumption.

2.2.3. Global level

At global level, WHO should set up a global team for antimicrobial consumption (AMC global team). This team is responsible for supporting regional offices and countries for the surveillance of antimicrobial consumption and for coordinating the global surveillance program on antimicrobial consumption. The AMC global team will collate data from the regional offices and make these data available to the public in agreement with national authorities.

Antimicrobial consumption is only one element of a national program on antimicrobial use. Activities such as the development of clinical guidelines and protocols, the availability and affordability of antimicrobial agents, restrictions on use of agents for particular clinical conditions or to nominated prescribers and other activities related to the responsible use of antimicrobials are beyond the scope of this document.

2.3. Setting up a national surveillance program on antimicrobial consumption

There are a number of steps in setting up a national program on surveillance of antimicrobial consumption:

1. Establish the AMC national team with at least some members with skills on pharmaceuticals and data management. A person of the AMC national team should be nominated as WHO focal point for AMC and responsible for communication with WHO.
2. Define the objectives of the surveillance program
3. Based on the defined objectives and available resources:
4. Identify the sources of data to be used in the surveillance program.
5. Communicate and organise meetings with the data providers to inform them on purpose of the surveillance program and on the requested data. If needed organise workshop with the data providers.
6. Start collecting the requested data from the data providers
7. Validate the data in cooperation with the data providers
8. Analyse the data
9. Report information on antimicrobial consumption to inform the national strategy and publish the data at national level
10. Report the data to WHO
11. Provide feedback of the data collection and validation process to the data providers

3. Methodology

3.1. Definitions

For the purpose of the protocol presented:

- ***Consumption data*** refer to estimates derived from aggregated data sources such as import or wholesaler data, or aggregated health insurance data where there is no information available on the patients who are receiving the medicines or why the antimicrobials are being used. These data sources provide a *proxy* estimate of use of antimicrobials.

  Consumption data may be presented as total consumption for a country or may be disaggregated by setting (community or hospital; public or private sectors).

- ***Antimicrobial use data*** refer to estimates derived from patient-level data. These data may allow disaggregation of data based on patient characteristics (gender, age), or indication for which the medicine is being used. Depending on the source of information, it may be possible to determine the patients' symptoms, physician diagnoses and medications ordered. This will facilitate assessment of clinical practice against agreed protocols and treatment guidelines.

Measuring consumption data is an important starting point for countries with limited experience in data collection. With experience and as more sophisticated data sources become available (e.g. e-prescribing records), it is expected that there will be more emphasis on measuring antimicrobial use.

3.2. Measurement issues

There is a need for a common system of classification and standard metrics to facilitate comparisons of antimicrobial consumption between health facilities, between countries and between regions. The most commonly used classification system is the Anatomical Therapeutic Chemical (ATC) classification system. The most commonly used measurement metric is the number of Defined Daily Doses (DDDs). These are discussed in more detail in the following section and in Annex 1.

3.3. ATC Classification system

The Anatomical Therapeutic Chemical (ATC) classification system is the most commonly used method for aggregation of medicines data and allows flexibility in reporting by medicine or groups of medicines. In this system, the active substances are divided into different groups according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties.

Medicines are classified in groups at five different levels.

Level 1:	indicates the anatomical main group and consists of one letter. There are 14 main groups. The group most relevant to work on antimicrobials is group **J** *Anti-infectives for systemic use*. However, there are some examples of antimicrobials classified in other main groups, e.g. antibiotics used as intestinal anti-infectives are in ATC main group A *Alimentary tract and metabolism,* while some oral and rectal anti-protozoal agents are in ATC main group P *Anti-parasitic products, insectides and repellants.*
Level 2:	pharmacological/therapeutic subgroups, e.g. J**01** is *Antibacterials for systemic use*, J**02** *Antimycotics* and J**04** *Antimycobacterials*.
Level 3:	chemical/pharmacological subgroups, e.g. J01**C** is *Beta-lactam antibacterials, penicillins*
Level 4:	pharmacological subgroup, e.g. J01C**A** is *Penicillins with extended spectrum*
Level 5:	chemical substance, e.g. J01CA**01** is *ampicillin* and J01CA**04** is *amoxicillin.*

More information on the ATC system is provided in Annex 1 and the full list of assigned ATC codes is available at http://www.whocc.no/atc_ddd_index/.

3.3.1. Unit of measurement Defined Daily Dose (DDD)

The most commonly used measurement statistic is the number of Defined Daily Doses (DDDs). The Defined Daily Dose (DDD) is the assumed average maintenance dose per day for a medicine used for its main indication in adults. A DDD is only assigned for drugs that already have an ATC code. The DDD, however, is only a **technical unit of use** and does not necessarily reflect the recommended or average prescribed dose.

The DDDs for the anti-infectives are as a main rule based on the use in infections of moderate severity. However, some anti-infectives are only used in severe infections and their DDDs are assigned accordingly.

There are no separate DDDs for children which makes the DDD estimates for paediatric formulations more difficult to interpret.

The numbers of DDDs is calculated as follows:

$$\textbf{Number of DDDs} = \frac{Total\ grams\ used}{DDD\ value\ in\ grams}$$

Where the total grams of the medicine used is determined by summing the amounts of active ingredient across the various formulations (different strengths of tablets or capsules, syrup formulations, injections etc.) and pack sizes.

The numbers of DDDs provides a measure of extent of use, however for comparative purposes these data are usually adjusted for population size or population group, depending on the medicines of interest and the level of data disaggregation that is possible.

For most antimicrobials, the DDDs/1000 inhabitants/day (DID) will be calculated for the total population including all age and gender groups.

It may also be possible to stratify the national estimates by age group, gender, sectors (community and hospital, public and private). Where there is stratification there needs to be careful consideration of the appropriate estimate for the denominator, e.g. DDDs/1000 children under 5 years/day or DDDs/1000 women/day.

3.4. Antimicrobials included in monitoring

The WHO surveillance program focuses only on antimicrobials for systemic use. Topical antimicrobials are excluded.

WHO has defined a core set of antimicrobials that all countries should include in their surveillance program:

Antibacterials	**J01**
Antibiotics for alimentary tract	**A07AA**
Nitroimidazole derivatives for protozoal diseases	**P01AB**

In addition, the WHO surveillance program includes an optional list of antimicrobials that countries may include in their surveillance program according to local needs and resources:

Antifungals	**J02**
Antimycotics	**D01BA**
Antivirals	**J05**
Antimycobacterials for treatment of tuberculosis	**J04A**
Antimalarials	**P01B**

Finally, countries may include extra antimicrobial agents that are not in the core oroptional lists in their national surveillance program. In this case, countries should collect and report the results of these additional analyses separately at national level.

Countries should liaise with their Regional AMC team regarding reporting of any additional analyses at regional level. For example, there may be interest in reporting consumption of tuberculosis medicines in regions where there are several countries with large populations of patients requiring treatment.

A list of medicines and ATC codes is provided in Annex 2 and also as a worksheet in the Excel Template for reporting (worksheet tab ATC).

3.5. Healthcare sectors to be monitored

Different types of healthcare sectors may be considered in monitoring of antimicrobial consumption including:

- community and hospital sectors
- public and private sectors.

In many countries that are starting data collection, it will not be possible to disaggregate data by sector and only total consumption data will be able to be reported.

3.5.1. The community sector

The community sector corresponds to primary care and may also include out-patient hospital care; it is sometimes referred to as ambulatory care. Primary care corresponds to care provided by general practitioners, family doctors, nurses, physician assistants, pharmacists or clinical officers.

Residential care (e.g. nursing homes, day care centres) is also typically considered to belong to the community sector.

As an example, in many countries, antimicrobials reported in the community sector are usually prescribed by general practitioners and dispensed or supplied to the patients in pharmacies or licensed drug stores.

3.5.2. The hospital sector

The hospital sector corresponds to care provided to in-patients (admitted patients) in healthcare facilities. These can include general and district hospitals as well as secondary and tertiary care hospitals and other specialist health clinics.

As an example, in many countries, antimicrobials reported in the hospital sector are usually prescribed by hospital doctors and administered to the patients directly by the healthcare professionals in those facilities.

3.5.3. Public and private sectors

Countries may also be able to collect antimicrobial consumption separately for public and private sectors. This can provide important information about differences in prescribing practices in the two sectors. However, national committees should report both sectors combined to the WHO global reporting system.

4. Data collection for antimicrobial consumption

Antimicrobial consumption is defined as quantities of antimicrobials used in a specific setting (total, community, hospital) during a specific period of time (e.g. days, months, and year). For global reporting, national estimates of consumption are reported for the calendar year (January to December). The ATC/DDD methodology is used to standardise the data collection and reporting of antimicrobial consumption.

4.1. Elements of data collection

There are three elements to the data collection, namely antimicrobial consumption data, denominator data and descriptive or contextual information that is relevant for interpreting the consumption estimates calculated (see Figure 1).

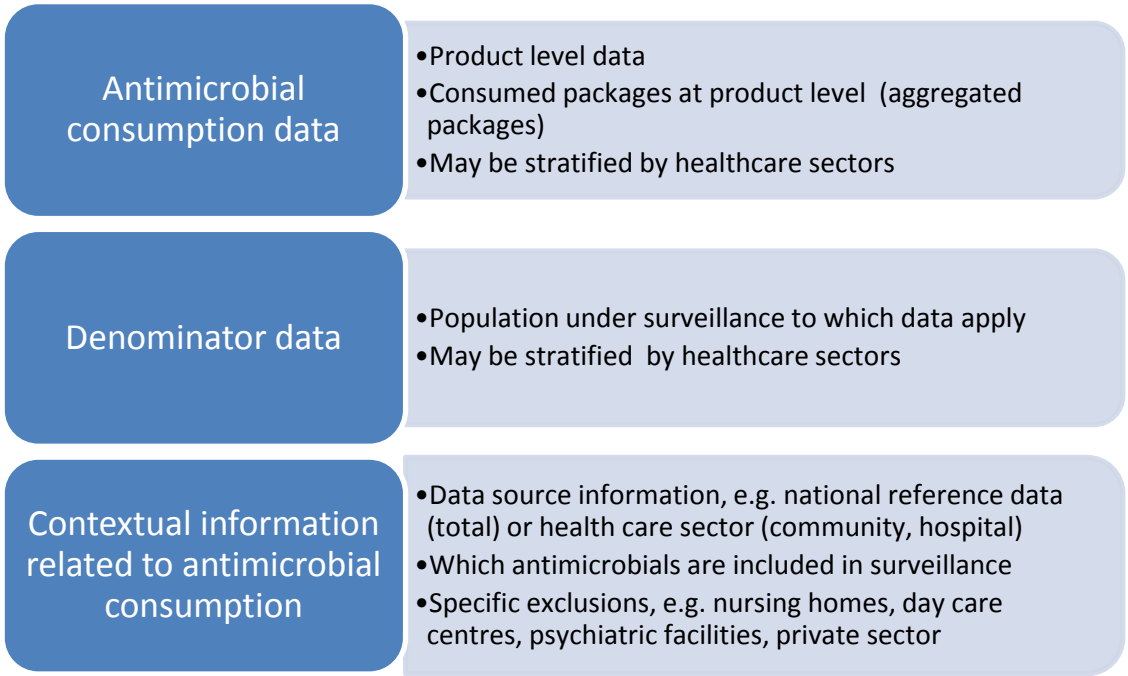

Figure 1 Elements of data collection

4.1.1. Antimicrobial consumption data

4.1.1.1. Product level data

The first step requires identification of all the products for the antimicrobial agents registered (i.e., with marketing authorization) in the country – a valid national exhaustive register of products. In some cases this will not already exist and this list of products will need to be developed. For each antimicrobial substance, this means a list of all products by formulation, strength and pack size. For commonly used products with multiple manufacturers this could mean 50 or more product lines for a single INN like amoxicillin or

ceftriaxone. The register file will need to be updated each year as new products receive marketing authorization.

4.1.1.2. Package level data

Consumption is expressed as the total numbers of packages for each product in the register of antimicrobial products that are consumed during the defined period of time. Mostly these will be annual (yearly) data. However data may be available for different time periods such as quarterly.

4.1.1.3. Substance level data

Consumption at substance level can be summarized as aggregated DDDs. As noted earlier, the numbers of DDDs is calculated as follows:

$$\textbf{Number of DDDs} = \frac{Total\ grams\ used}{DDD\ value\ in\ grams}$$

Where the total grams of the medicine used is determined by summing the amounts of active ingredient across the various formulations (different strengths of tablets or capsules, syrup formulations) and pack sizes. The DDD value is assigned by the WHO Collaborating Centre (http://www.whocc.no/atc_ddd_index/).

4.2. Data sources for consumption estimates

4.2.1. Flow of antimicrobials

Procurement and supply of antimicrobial agents at the country level may be complex. In its simplest and 'idealised' form, for a country without domestic manufacturing capacity, antimicrobials are imported (licensed imports with customs records), are supplied and distributed by licenced wholesalers and distributors to public and private hospitals, community health facilities and community pharmacies and then provided to patients based on prescriptions written by appropriately registered health care professionals. In some countries, these medicines will be reimbursed by health insurance programs, with or without the imposition of patient co-payments.

The reality in many countries is quite different. Antimicrobials may be sourced from both international and domestic producers. Imports may be subject to re-export to other countries; domestic producers may export part of their production. Orders may be placed with wholesalers or directly with manufacturers. Imported products may be used in the veterinary and agriculture sectors as well as for human use. Healthcare professionals and patients may be able to import products directly. Antimicrobials may be purchased over-the-counter as well as with prescription. Borders may be 'porous' with illegal imports and exports. Patients may buy products in neighbouring countries where products are cheaper.

4.2.2. Potential sources of information on antimicrobial consumption

There are a number of potential sources of information on consumption of antimicrobials:

- import data (using data from customs records and declaration forms)
- production records of domestic manufacturers (exclude any exports of products)
- wholesaler/distributor data – this could be data on procurement by wholesalers or records of sales by the wholesalers to healthcare facilities and pharmacies
- public sector procurement records – these exist where there is both centralised and decentralised purchasing of medicines for the public sector
- donations – this may relate to particular programs such as HIV, TB, malaria or for special populations such as migrants and refugees
- records from community and hospital pharmacies and licensed drug stores
- data from health insurance programs
- prescribing records of doctors and dispensing records of pharmacists
- information on antimicrobial use from patients themselves.

These sources provide information with differing levels of detail on the consumption and use of antimicrobials. It is important to understand the nature, scope and limitations of the data collection from each of these sources; otherwise there is a risk of under- or over-estimation of antimicrobial consumption. Table 1 summarises some of the strengths and weaknesses of each of these data sources.

The sources differ in the degree of difficulty of gathering information. There may be a single import authority in the public sector that retains records of all authorized importation, a complex array of local and multi-national manufacturers, multiple wholesalers in the public and private sectors, an insurance authority that covers only some and not all sectors of the population, and private health care providers (hospitals, clinics, health care professionals) that may be reluctant to provide information.

It will be up to governments in Member States to decide whether data collection is voluntary or mandatory across all providers and all sectors. Changes in regulation or laws might be necessary to oblige the data providers to deliver the requested information.

The data sources ‘close’ to the patient will provide the most reliable estimates of antimicrobial consumption and will be more likely to provide data on age and gender of the patient, provider details and indication for the antimicrobial prescription. However, these will also be the most sophisticated and most expensive sources of data.

It is very important to correctly identify the data sources used in the country. If more than one data source is used, it is important to be aware of overlaps in the information provided. If they are treated as separate estimates and summed to provide ‘total consumption’ this may overestimate actual antimicrobial consumption.

Table 1: Strengths and limitations of data sources for antimicrobial consumption

Data source	Strengths	Limitations
Import data	- Import permits issued by Government - Centralized records - Standardised reporting for customs declaration forms including product type (generic, branded), volume, port of origin, country of manufacture, batch number, expiry date) - Includes OTC medicines	- Documentation may be incomplete - May include parallel trade stock movements - Not account for smuggled goods or illegal entry of products - Volumes match import cycles not consumption patterns - Are administrative records and not formatted for research and analysis
Domestic manufacturers	- Local licensed producers should be easily identified - Can separate product volumes for local use and for export - Can request data in format suitable for analysis	- Private companies may be unwilling to provide data - Volumes reflect production not consumption patterns
Public sector procurement	- Likely to have reasonable documentation of purchases - Disaggregation of distribution data to facility types (community and hospital) and geographical location is possible - May be single (or limited number) of procurement agencies	- Only provides data for public sector - May not reflect total public sector consumption if other procurement is undertaken by hospitals, health facilities - May include stock procured but never supplied
Wholesalers	- Only legal entity able to import medicines for distribution - Can provide purchase and supply data - Supply data may be disaggregated (community/hospital; by regions, facility type) - Data collection easier where limited numbers of wholesalers - Distribution/supply data likely to be closer to actual consumption than purchase data	- Some countries medical, dental, veterinary practitioners and pharmacists can also import medicines - May be difficult to get data from private sector - Large number of wholesalers in some settings - May supply other smaller wholesalers not 'end-users' - Wholesalers may provide agriculture and veterinary sectors as well as for human use
Donations	-May be significant proportion of antimicrobials dispensed for specific clinical programs	- May be difficult to differentiate donations for local population and special populations (migrants, refugees)
Community	- Sales from pharmacies or drug	- Large number of facilities makes

Data source	Strengths	Limitations
and hospital pharmacies, drug stores *Dispensing data*	stores is closer to the actual use of antimicrobials by the patients - Can separate community and hospital sectors - Potentially can separate to public and private sectors - May include some OTC medicines	data collection resource intensive - May be difficult to collect data where only manual records exist - May be difficult to get information from private sector - Does not take account of compliance with therapy
Health insurance data	- Patient-level consumption data - May be disaggregated by patient demographic characteristics - Geographic data may be available - Disaggregation to community and hospital sectors possible - Often limited number of data providers - Data more accessible if public sector agencies	- May be difficult to get information from private sector - Only reimbursed antimicrobials reported - Selected populations covered by health insurance; may not be representative of whole population - Administrative records may not include all the variables of interest
Prescribing records of (health professionals or databases)	- May have patient characteristics, diagnosis, dose, duration, co-prescribed medicines	- Prescribed medicines may not be dispensed - Samples of prescribers may not be representative and therefore not reflect national data
Community, household survey data	- Patient-level data will be available - Most closely reflects actual consumption - Repeat surveys can provide longitudinal data	- Time-consuming and labour intensive to collect the data - Issues of representativeness of the data collected
Commercial data sources (e.g. IMS Health)	- Standardised data collection - Capacity to combine data from multiple sources including manufacturer records, hospital and pharmacy data	- Data must be purchased - May be limited data collection in some countries - May not be able to examine data at regional, local, facility or prescriber level - Use of EphMRA/PBIRG classification rather than ATC codes so may be limited information at the pharmacological or chemical subgroup level

OTC=over-the-counter

4.3. Denominator data

The total numbers of DDDs derived as consumption estimates should be adjusted for the population to which the data apply.

For national estimates of consumption, the appropriate population will be the total national population (all age and gender groups combined). WHO has standardized population estimates for all Member States. This is the default used for calculations. However, it is possible for a country to use its own national population estimates if it is believed the WHO estimate is not correct. National population estimates are available in the WHO Global Observatory (http://apps.who.int/gho/data/node.main.POP107?lang=en).

4.4. Reporting metrics

The standard reporting metric for national estimates is **DDDs/1000inhabitants/day (DID).**

The data collection template requires entry of numbers of packages for each product included in the register. These packages may be summed to give a total number of packages consumed. This will provide a crude estimate of the number of courses of treatment with antimicrobials used per year and is based on the assumption that one package = one course of treatment. This measure needs to be interpreted carefully. In some settings, a package of oral medicine will represent a course of treatment. In other settings, patients may buy small numbers of tablets or capsules or dispensing is from large containers of the medicine, in which case a package will have very little meaning. A package is not likely to be a good guide to a course of treatment with an injectable antimicrobial.

4.5. Contextual information relating to data collection

It is important to report the sources of data used, the sectors being reported, the antimicrobial agents included in the surveillance and to identify if there are any specific groups of patients or facility types that have been excluded from the calculations (e.g. nursing homes, day care centres, psychiatric facilities, rehabilitation units etc.). The worksheet tab ‘Data Availability’ collects some descriptive data. This may be supplemented by questionnaires or other surveys.

5. Data management

5.1. Data flow

Within the framework of a global WHO programme on surveillance of antimicrobial consumption, data will flow from country to the regional office and to global/ head-quarters (Figure 2).

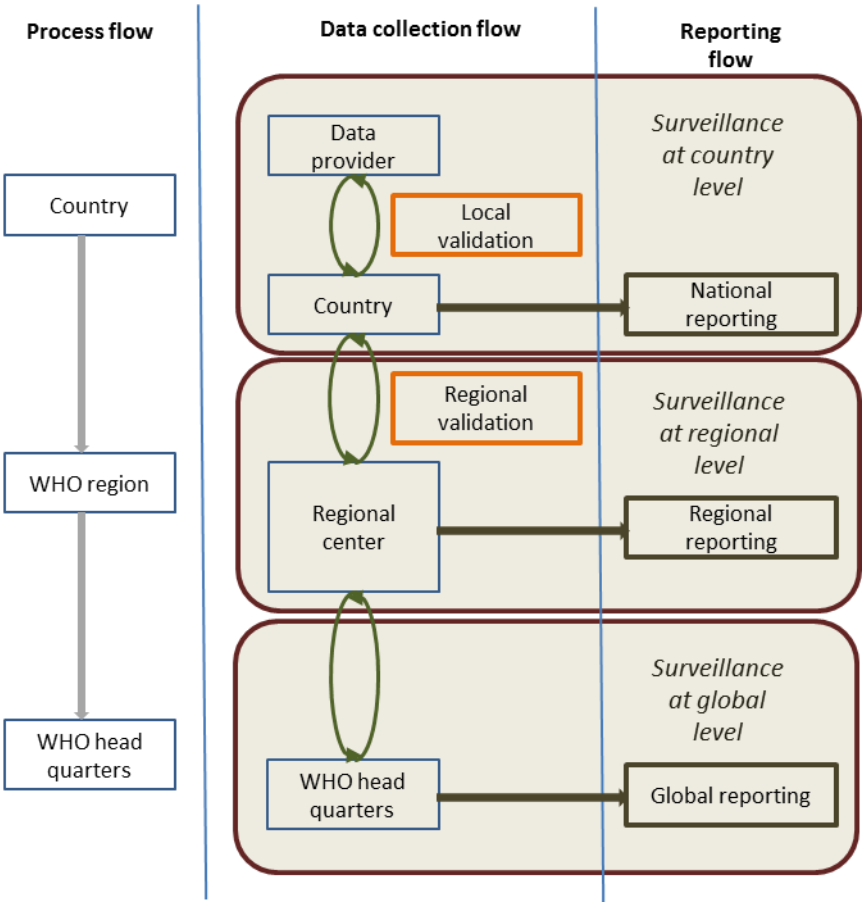

Figure 2 Flow of data between country, regional office and global/head-quarters

5.2. Data collection

Collection of data on antimicrobial consumption, population and questionnaires is the responsibility of the country and its AMC national team for the surveillance programme. At country level, protocols, forms and related documents provided by WHO might be translated into national language. If necessary, extra documents such as training materials may be produced by countries to facilitate the national data collection. The national data providers may need some training on which data to collect and how to report them to the AMC national team.

The data collection process at national level can be split into different tasks according the following points:

1. Every year, the national team sends a call for data to the data providers.
2. The data providers deliver the requested information to the national team in the agreed format.
3. The national team checks and validates the data delivered by the data provider. If there are issues with the data or clarifications are needed, the national team will contact the data providers.
4. When the data are validated, the national team prepares the data for submission to the regional office.

5.3. Data submission

Data submission involves the country, regional and global levels.

The data submission process is separated into the following steps:

1. The AMC national team submits the validated consumption data, population data and questionnaire responses to the regional office.
2. The AMC regional team collates the data from the countries.
3. The AMC regional team validates the data at regional level with issues resolved through consultation with national focal points.
4. The regional team submits the relevant validated data to the AMC global team at WHO Geneva for analysis and reporting.

5.4. Data analysis

Ideally there will be capacity developed at country level to undertake the analyses of AMC data. In the first instance, for countries new to collecting these data, the analysis will be supported by regional and global AMC teams.

5.5. Dissemination of data

While there is Member State agreement for reporting of antimicrobial consumption estimates at the global and regional level, the data are most useful at the country level. Countries should share findings with all stakeholders through dissemination workshops and other communications. There will be a need to support countries in developing appropriate dissemination tools and preparing documents relevant for decision-makers and other stakeholders.

6. Template for Data Collection

6.1. Structure of template

The Excel template for data collection has a number of worksheets:

1. Macro	These are embedded routines to assist in data checking and export.
2. Data Availability	for each category of medicine (A07AA, D01BA, J01, J02, J04, J05, P01AB, N04BB) indicate whether the data represent the total, community or hospital consumption
3. Product Data	the key worksheet for data. A separate guidance document is available to provide step-by-step advice on completing this worksheet.
4. Population Data	for each category of medicine (A07AA, D01BA, J01, J02, J04, J05, P01AB, N04BB) indicate population to which the given consumption data apply
5. ATC	list of medicines being monitored, with ATC code and ATC level.
6. DDD	the DDD assigned by the WHO Collaborating Centre with units of measurement (gram, mg, MU)
7. DDD combination	provides a list of combination medicines that have an approved DDD or approved 'unit dose' measurement
8. Conversion	a table of conversion factors from MU to grams (See Annex 4)
9. Units	a description of the units used (See Annex 5)
10. Salts	the specification of salts is only required for hexamine (hippurate or mandelate) and where erythromycin data relate to the ethylsuccinate salt.
11. RoAs	routes of administration (oral, parenteral, rectal, inhalation powder, inhalation solution). (See Annex 6)

As shown Figure 1, there are three parts to the data collection – antimicrobial consumption data, denominator data and contextual information related to antimicrobial consumption. The key spreadsheet for completion is the worksheet called **'Product Data'**. In this worksheet data are entered on the antimicrobial products (medicines register) and estimates of consumption (number of packages) that is converted into numbers of DDDs. Population data are recorded here and population-adjusted consumption estimates are automatically calculated by the macro. Contextual information related to antimicrobial consumption is entered in the worksheet called '**Data availability**'.

6.2. Variables

6.2.1. Variables for antimicrobial medicines register

Some countries will already have an electronic database of all antimicrobial products that have marketing authorization (= registered products). Where such a database exists, the relevant data can be copied into the cells of the spreadsheet.

Where there is no existing list of products, this will need to be created. This is a significant task in Year 1. For subsequent years, the data register file can be edited and new products added. The descriptions for products could be maintained (with zero consumption) and this will provide an 'historical' file of products and consumption over the years.

The product-level variables included in the register are shown in Table 2. A full description of the variables, data type, variable type, information and data rules and response options are provided in Annex 3.

Table 2: Product-level data variables for the antimicrobial register

Variable name	Content
COUNTRY	Based on ISO 3166 alpha-3 country codes
PRODUCT_ID	Unique identifier of the medicinal product package (MPP).
LABEL	Medicinal product package label
PACKSIZE	Size of the package
PACKSIZE_UNIT	Pack size unit of measurement
PAEDIATRICS_PRODUCT *	Is it a paediatric medicine product
FORM*	Pharmaceutical formulation type
ROUTE_ADMIN	Route of administration
STRENGTH	Quantity of the main ingredient of each item
STRENGTH_UNIT	Unit measurement of strength
INBASQ	Basic ingredient quantity
INBASQ_UNIT	Unit measurement of the basic ingredient quantity
ATC5	WHO ATC code at substance level (ATC5-level)
SALT *	Salt of the active substance (hexamine, erythromycin only)
COMBINATION	The WHO CC has defined DDD for combined products
PRODUCT_NAME *	Medicinal product name
INGREDIENTS *	Ingredient name: e.g. amoxicillin and enzyme inhibitor.
PRODUCT_ORIGIN *	The product can be import, donation or locally produced.
MANUFACTURER_COUNTRY	The country of the manufacturer of the product.
MANUFACTURER *	Name of manufacturer
GENERIC*	Is the product a generic?
CONV_FACTOR *(macro)*	Transform strength expressed in IU into G.
WHO_DDD *(macro)*	The DDD defined by the WHO CC for the ATC code
WHO_DDD_UNIT *(macro)*	Unit measurement of the WHO DDD (MG, G, IU, MU, UD)
DPP *(macro)*	DDD Per Package

Source: WHO antimicrobial medicines collection protocol year 2016

***optional variables for dataset; macro = calculated automatically by Excel macro**

6.2.2. Variables for consumption estimates (packages and DDDs)

The numbers of packages of each product imported/sold/dispensed are recorded. The numbers of packages can be aggregated by the desired level of ATC code and reported as total number of packages.

The number of packages of each product is also multiplied by the number of DDDs per package to calculate the total numbers of DDDs for each product. The numbers of DDD are aggregated by at the desired ATC code level to give total number of DDDs.

Consumption data may also be reported by sector – total consumption data disaggregated to hospital and community (ambulatory care) data, or to public and private sector.

The consumption variables included in the spreadsheet are shown in Table 3. A full description of the variables, data type, variable type, information and data rules and response options are provided in Annex 3.

Table 3: Consumption data variables

Variable name	Content
Consumption by packages	
TOTAL_PACKAGES	Total number of packages consumed during the year
COMMUNITY_PACKAGES	Total number of packages consumed in community during the year
HOSPITAL_PACKAGES	Total number of packages consumed in hospital sector during the year

Source: WHO antimicrobial medicines collection protocol year 2016
DDD = Defined Daily Doses

6.2.3. Variables for population estimates

The total population may be based on WHO national population estimates for the relevant year or local estimates if there are reasons to believe WHO estimates are inaccurate.

6.2.4. Variables for population-adjusted estimates

The total numbers of packages and DDDs are divided by population estimates and the estimates adjusted to express consumption as numbers of packages/inhabitants/year (PIY) or numbers of DDDs/1000 inhabitants/day (DID).

6.3. Contextual information

Additional information obtained my questionnaire or survey may help with interpretation of the consumption estimates.

The worksheet tab **'Data Availability'** should be completed. This reports the country (3-digit code), year of data collection, and for each class of antimicrobials under monitoring whether the data are for total, community or hospital use.

7. Glossary

Admitted patient	A patient who receives hospital services and undergoes a hospital's formal admission process, and is thus accepted by a hospital for inpatient care. This includes hospital-in-the-home care.
Anatomical Therapeutic Chemical (ATC) Classification System	An international system, controlled by the World Health Organization Collaborating Centre for Drug Statistics Methodology, that categorizes all medicines into one of fourteen anatomical groups, each of which is divided into therapeutic uses and further subdivided into chemical subgroups.
Antimicrobial	An antimicrobial is a medicine that selectively destroys or inhibits the growth of susceptible microorganisms. Sometimes referred to as an 'antimicrobial agent'. Examples include antibiotics (also known as antibacterials) antiviral and antifungal agents.
Antibiotic resistance	A property of bacteria that confers the capacity to grow in the presence of antibiotic levels that would normally suppress growth or kill susceptible bacteria.
Antimicrobial resistance (AMR)	The ability of a microorganism to grow or survive in the presence of an antimicrobial at a concentration that is usually sufficient to inhibit or kill microorganisms of the same species and that exceeds concentrations achievable in the human/animal/patient.
Antimicrobial stewardship	The use of co-ordinated interventions to improve and measure the use of antimicrobials by promoting optimal drug regimen, dose, duration and route. The aim is for optimal clinical outcome and to limit selection of resistant strains. This is a key component of a multi-faceted approach to preventing antimicrobial resistance.
Broad-spectrum antibiotics	These are effective against a wide range of bacteria. For example, meropenem is a broad-spectrum antibacterial.
Carbapenems	Carbapenems are broad-spectrum antibiotics, often used as the last line of treatment for hard to treat human infections caused by Gram-negative bacteria.
Carbapenemases	These are enzymes produced by bacteria which destroy carbapenems and other beta-lactam antibiotics.
Cephalosporins	Types of broad-spectrum antibiotics.
Cephalosporins – third-generation	Cephalosporins like cefotaxime and cefixime are particularly active against Gram-negative bacteria.

Coverage	Penetration of an intervention into the targeted population and extent to which they access the intervention.
Disaggregated	Statistics that are based on individual (that is, ungrouped) variables — for example, separating the data by gender, age, disease state etc.
Episode of care	A period of health care with a defined start and end.
First-line treatment	The preferred initial treatment of a patient at a particular stage of their medical condition.
Generic (name)	The accepted or official nonproprietary name (not a chemical formula or a brand) by which a medicine is identified.
Gram-negative bacteria	Those bacteria that do not retain crystal violet dye in the Gram-staining procedure. They can cause many types of infection and include E. coli and Pseudomonas aeruginosa.
Gram-positive bacteria	These are bacteria that are stained dark blue or violet in the Gram-staining procedure. They include Staphylococcus aureus and Clostridium difficile.
Healthcare Associated Infections (HCAI)	Infections acquired via the provision of healthcare in either a hospital or community setting. Also referred to as nosocomial infections
Multi-drug resistant	Resistance to two or more antibiotics from different classes.
Meticillin-resistant Staphylococcus aureus (MRSA)	A strain of *Staphylococcus aureus* that is resistant to beta lactam antibiotics which include penicillins (e.g. 25ethicillin and oxacillin) and almost all cephalosporin antibiotics. Also called *multiresistant S. aureus*
'One-Health' approach	Describes a coordinated, collaborative, multi-disciplinary and cross-sectoral work at local, national, and global levels to attain optimal health for people, animals and the environment.
Pathogen	An infectious agent (bug or germ), a microorganism such as a virus, bacterium, or fungus that causes disease in its host.
Prevalence Also referred to as point prevalence	The number of events of interest in a given population at a given point in time, usually expressed as a prevalence rate i.e. as a proportion of the defined population size at that time. It includes all the events of interest, both new and long standing cases.
Primary care	Services provided by GP practices, dental practices, community pharmacies and high street optometrists.

Quinolones	A family of antibiotics, includes broad-spectrum agents like ciprofloxacin.
Responsible prescribing	The use of antimicrobials in the most appropriate way for the treatment or prevention of infectious disease.
Secondary care	Covers acute healthcare, either elective care (planned specialist medical care or surgery, usually following referral) or emergency care.
Selection (of resistant bacteria)	The process whereby exposure to an antibiotic kills or inhibits sensitive bacteria, allowing resistant bacteria to increase in number relative to the sensitive bacteria.

8. Annexes

Annex 1: Introduction to ATC and DDD methodology

Categorization of medicines

The Anatomical Therapeutic Chemical (ATC) classification system is the most commonly used method for aggregation of medicines data and allows flexibility in reporting by medicine or groups of medicines. The classification of a substance in the ATC/DDD system is not a recommendation for use, nor does it imply any judgements about efficacy or relative efficacy of drugs and groups of drugs.

The first level of the code indicates the anatomical main group and consists of one letter. There are 14 main groups as follows:

ATC Main Groups

A	•Alimentary tract and metabolism
B	•Blood and blood forming organs
C	•Cardiovascular
D	•Dermatologicals
G	•Genito-urinary system and sex hormones
H	•Systemic hormonal preparations, excluding sex hormones and insulin
J	•Anti-infectives for systemic use
L	•Antineoplastic and immunomodulating agents
M	•Musculo-skeletal system
N	•Nervous system
P	•Anti-parasitic products, insecticides and repellants
R	•Respiratory system
S	•Sensory organs
V	•Various

The structure and nomenclature used in the ATC classification system is illustrated for the anti-diabetic medicine, metformin, and is shown in A1**.**

There are a number of challenges with the use of the ATC system. In some cases, a medicine can be used for different indications and this is not always reflected in the ATC code. In some cases, medicines will have several different ATC codes depending on the use of the product, for example for systemic use or topical use.

Medicinal products containing two or more active ingredients are considered combinations in the ATC system and have a different ATC code to the single components.

In addition, there are regular revisions of the ATC code to deal with new drugs and changes in use of products. It is important to be aware of changes in ATC codes that may have occurred over time when interpreting trends over time.

Box A1: The Anatomical Therapeutic Chemical (ATC) Classification system

In the Anatomical Therapeutic Chemical (ATC) classification system, the active substances are divided into different groups according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties.
Drugs are classified in groups at five different levels. The drugs are divided into fourteen main groups (1st level), with pharmacological/therapeutic subgroups (2nd level). The 3rd and 4th levels are chemical/pharmacological/therapeutic subgroups and the 5th level is the chemical substance. The 2nd, 3rd and 4th levels are often used to identify pharmacological subgroups when that is considered more appropriate than therapeutic or chemical subgroups.
The complete classification of metformin illustrates the structure of the code:

A	Alimentary tract and metabolism (1st level, anatomical main group)
A10	Drugs used in diabetes (2nd level, therapeutic subgroup)
A10B	Blood glucose lowering drugs, excl insulins (3rd level, pharmacological subgroup)
A10BA	Biguanides (4th level, chemical subgroup)
A10BA02	Metformin (5th level, chemical substance)

Thus, in the ATC system all plain metformin preparations are given the code A10BA02.

Nomenclature

International nonproprietary names (INN) are preferred. If INN names are not assigned, USAN (United States Adopted Name) or BAN (British Approved Name) names are usually chosen.
WHO's list of drug terms (Pharmacological action and therapeutic use of drugs - List of Terms) is used when naming the different ATC levels.

ATC Codes for antimicrobial agents

The WHO Collaborating Centre for Drug Statistics Methodology has developed coding rules for all medicines. In relation to antimicrobials, the 2016 guidelines state (http://www.whocc.no/filearchive/publications/2016_guidelines_web.pdf)

J01 ANTIBACTERIALS FOR SYSTEMIC USE

This group comprises antibacterials for systemic use, except antimycobacterials, which are classified in J04. The antibacterials are classified according to their mode of action and chemistry.

Combinations of two or more systemic antibacterials from different third levels are classified in J01R, except combinations of sulfonamides and trimethoprim, which are classified at a separate 4th level, J01EE.

Combinations of antibacterials with other drugs, including local anesthetics or vitamins, are classified at separate 5th levels in the respective antibacterial group by using the 50-series. Common cold preparations containing minimal amounts of antibacterials are classified in R05X.

Inhaled antiinfectives are classified here based on the fact that preparations for inhalation cannot be separated from preparations for injection.

Application of the ATC classification system

The anti-infective agents for systemic use are classified under ATC Main Group J (level 1).

Level 1 (Main group): ATC Main Group J (Anti-infective for systemic use)

Level 2 (pharmacological/therapeutic subgroups):

J ANTIINFECTIVES FOR SYSTEMIC USE

J01 Antibacterials for systemic use
J02 Antimycotics for systemic use
J04 Antimycobacterials
J05 Antivirals for systemic use
J06 Immune sera and immunoglobulins
J07 Vaccines

Level 3 (chemical/pharmacological/therapeutic subgroups):

J01 ANTIBACTERIALS FOR SYSTEMIC USE

J01A Tetracyclines
J01B Amphenicols
J01C Beta-lactam antibacterials, penicillins
J01D Other beta-lactam antibacterials
J01E Sulfonamides and trimethoprim
J01F Macrolides, lincosamides and streptogramins
J01G Aminoglycoside antibacterials
J01M Quinolone antibacterials
J01R Combinations of antibacterials
J01X Other antibacterials

Level 4 (chemical/pharmacological/therapeutic subgroups):

J01C BETA-LACTAM ANTIBACTERIALS, PENICILLINS

J01CA Penicillins with extended spectrum
J01CE Beta-lactamase sensitive penicillins
J01CF Beta-lactamase resistant penicillins
J01CG Beta-lactamase inhibitors
J01CR Combinations of penicillins,
J01CR Combinations of penicillins, incl. beta-lactamase inhibitors

Level 5 (chemical substance):

J01CA PENICILLINS WITH EXTENDED SPECTRUM

ATC Code	Name	ATC Code	Name
J01CA01	ampicillin	J01CA12	piperacillin
J01CA02	pivampicillin	J01CA13	ticarcillin
J01CA03	carbenicillin	J01CA14	metampicillin
J01CA04	amoxicillin	J01CA15	talampicillin
J01CA05	carindacillin	J01CA16	sulbenicillin
J01CA06	bacampicillin	J01CA17	temocillin
J01CA07	epicillin	J01CA18	hetacillin
J01CA08	pivmecillinam	J01CA19	aspoxicillin
J01CA09	azlocillin	J01CA20	combinations
J01CA10	mezlocillin	J01CA51	ampicillin, combinations
J01CA11	mecillinam		

Some examples of ATC codes

(i) **Amoxicillin** is ***J01CA04*** and classified as follows:

J ANTIINFECTIVES FOR SYSTEMIC USE (Level 1)
J01 ANTIBACTERIALS FOR SYSTEMIC USE (Level 2)
J01C BETA-LACTAM ANTIBACTERIALS, PENICILLINS (Level 3)
J01CA Penicillins with extended spectrum (Level 4)
J01CA04 Amoxicillin (Level 5)

Note: J01CA04 applies to amoxicillin in all its formulations – oral, parenteral, syrup formulations for children etc.

(ii) **Ceftriaxone** is ***J01DD04***

J ANTIINFECTIVES FOR SYSTEMIC USE (Level 1)
J01 ANTIBACTERIALS FOR SYSTEMIC USE (Level 2)
J01D OTHER BETA-LACTAM ANTIBACTERIALS (Level 3)
J01DD Third generation cephalosporins (Level 4)
J01DD04 Ceftriaxone (Level 5)

(iii) **Amoxicillin + clavulanic acid** is ***J01CR02***

J ANTIINFECTIVES FOR SYSTEMIC USE (Level 1)
J01 ANTIBACTERIALS FOR SYSTEMIC USE (Level 2)
J01C BETA-LACTAM ANTIBACTERIALS, PENICILLINS (Level 3)
J01CR Combinations of penicillins including beta-lactamase inhibitors (Level 4)
J01CA02 Amoxicillin and enzyme inhibitor (Level 5)

Changes of ATC Codes and new codes

ATC codes can change over time as more experience is gained with the medicine and more products become available. The WHO ATC/DDD website provides information on alterations to ATC codes since 1982 (http://www.whocc.no/atc_ddd_alterations__cumulative/atc_alterations/

New ATC codes can also be found on the website (http://www.whocc.no/atc/lists_of_new_atc_ddds_and_altera/new_atc/).

Antimicrobials with multiple ATC codes

There are some antimicrobials that are classified under more than one ATC code, for example metronidazole and vancomycin, reflecting their use in different clinical situations.

Metronidazole

A01AB17	Alimentary tract and metabolism, *Antiinfectives and antiseptics for local oral treatment*
D06BX01	Dermatologicals, *Other chemotherapeutics*
G01AF01	Genitourinary system and sex hormones, *Imidazole derivatives*
J01XD01	Antiinfectives for systemic use, *Imidazole derivatives*
P01AB01	Antiparasitic products, insecticides and repellants, *Nitroimidazole derivatives*
P01AB51	Antiparasitic products, insecticides and repellants, *Nitroimidazole derivatives, metronidazole combinations*

Vancomycin

A07AA09	Alimentary tract and metabolism, *Intestinal antiinfectives*
J01XA01	Antiinfectives for systemic use, *Other antibacterials, Glycopepeptide antibacterials*

To determine total use of each of these antimicrobials, it will be necessary to include all the relevant ATC codes.

Defined Daily Dose (DDD)

The most commonly used measure for reporting of drug utilization is numbers of Defined Daily Doses (DDDs) where the DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. A DDD is only assigned for drugs that already have an ATC code. Converting aggregate quantities to DDDs allows a rough estimation of the potential treatment days of the pharmaceutical are procured or consumed. The DDD, however, is only a *technical unit of use* and does not necessarily reflect the recommended or average prescribed dose.

The DDDs for the anti-infectives are as a main rule based on the use in infections of moderate severity. However, some anti-infective are only used in severe infections and their DDDs are assigned accordingly.

Generally, DDDs assigned are based on daily treatment. However, in the case of antimicrobial agents there are rules to guide calculation of the DDD based on the duration of the treatment.

For anti-infective given in a high initially starting dose followed by a lower daily "maintenance" dose, the DDDs are based on the "maintenance" dose if the total duration of the treatment course is more than one week.

If, however, the treatment course is 7 days or less, the DDDs are assigned according to the average daily dose i.e. the total course dose divided by the number of treatment days.

Example of calculation of DDD for antimicrobial agent

Substance M: 1000mg on the first day, then 500mg daily. Duration of therapy: 14 days

DDD is 500mg

Substance M: 1000mg on the first day, then 500mg daily. Duration of therapy: 5 days

DDD is 600mg ((1000 + 4x500)/5 = 600mg)

Note: the DDD is a technical unit of measurement and it may or may not reflect the doses that are prescribed and used in practice. The prescribed daily dose (PDD) is the average daily dose prescribed and is obtained from a representative sample of prescriptions.

The DDD remains a useful metric as it is a standardized measure and can be applied to all data. It is important to think about possible differences with prescribed daily doses when interpreting the results of the analysis.

Returning **J01CA Penicillins with extended spectrum,** the DDD values assigned in 2016 are:

ATC Code	Name	DDD	Unit of DDD	Administration route
J01CA01	ampicillin	2	g	O
		2	g	P
		2	g	R
J01CA02	pivampicillin	1.05	g	O
J01CA03	carbenicillin	12	g	P
J01CA04	amoxicillin	1	g	P
		1	g	O
J01CA05	carindacillin	4	g	O
J01CA06	bacampicillin	1.2	g	O
J01CA07	epicillin	2	g	O
		2	g	P
J01CA08	pivmecillinam	0.6	g	O
J01CA09	azlocillin	12	g	P
J01CA10	mezlocillin	6	g	P
J01CA11	mecillinam	1.2	g	P
J01CA12	piperacillin	14	g	P
J01CA13	ticarcillin	15	g	P
J01CA14	metampicillin	1.5	g	O
		1.5	g	P
J01CA15	talampicillin	2	g	O
J01CA16	sulbenicillin	15	g	P
J01CA17	temocillin	2	g	P
J01CA18	hetacillin	2	g	O
J01CA19	aspoxicillin	4	g	P
J01CA20	combinations			
J01CA51	ampicillin, combinations			

DDD = defined daily dose; g = gram; O=oral; P=parenteral

Note that there are three DDD values for ampicillin, and two each for amoxicillin, epicillin and metampicillin. In this case, the DDDs remain the same for oral and parenteral administration although this is not the case for all antimicrobials.

Some examples of where the DDD changes according to the formulation are shown in the following table:

ATC Code	Name	DDD	Unit of DDD	Administration route
J01CR02	amoxicillin and enzyme inhibitor	1	g	O
		3	g	P
J01FA01	erythromycin	1	g	O
	erthyromycin ethylsuccinate	2	g	O
		1	g	P
J01MA02	ciprofloxacin	1	g	O
		0.5	g	P
J01GB01	tobramycin	0.112	g	Inhal. powder
		0.3	g	Inhal. solution
		0.24	g	P
P01AB01	metronidazole	2	g	O
P01AB01	metronidazole	2	g	R
J01XD01	metronidazole	1.5	g	P

DDD = defined daily dose; g = gram; O=oral; P=parenteral; inhal=inhalation; R=rectal

Notes:

1. The DDD for amoxicillin and enzyme inhibitor is the same as the DDD for amoxicillin alone. The DDD for the combination is based on the main active ingredient.
2. Erythromycin ethylsuccinate has a special code for salt (ESUC) in the data collection template so that the correct DDD is applied.
3. The different DDD values for ciprofloxacin, tobramycin and metronidazole are assigned in the template according to whether the product is for oral, parenteral, inhalation or rectal administration.
4. In the case of metronidazole, J01 only includes the forms for parenteral administration. For total use of metronidazole, it will be necessary to use all the relevant ATC codes. Data for P01AB01 are included in the AMC template.

If there is no ATC code available or there is no DDD assigned for product, contact the Regional AMC team for advice.

Annex 2: List of ATC sub-groups under surveillance

Code	Name	Core set
A07AA	Antibiotics	Mandatory
D01BA	Antifungals for systemic use	Optional
J01AA	Tetracyclines	Mandatory
J01BA	Amphenicols	Mandatory
J01CA	Penicillins with extended spectrum	Mandatory
J01CE	Beta-lactamase sensitive penicillins	Mandatory
J01CF	Beta-lactamase resistant penicillins	Mandatory
J01CG	Beta-lactamase inhibitors	Mandatory
J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors	Mandatory
J01DB	First-generation cephalosporins	Mandatory
J01DC	Second-generation cephalosporins	Mandatory
J01DD	Third-generation cephalosporins	Mandatory
J01DE	Fourth-generation cephalosporins	Mandatory
J01DF	Monobactams	Mandatory
J01DH	Carbapenems	Mandatory
J01DI	Other cephalosporins and penems	Mandatory
J01EA	Trimethoprim and derivatives	Mandatory
J01EB	Short-acting sulfonamides	Mandatory
J01EC	Intermediate-acting sulfonamides	Mandatory
J01ED	Long-acting sulfonamides	Mandatory
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	Mandatory
J01FA	Macrolides	Mandatory
J01FF	Lincosamides	Mandatory
J01FG	Streptogramins	Mandatory
J01GA	Streptomycins	Mandatory
J01GB	Other aminoglycosides	Mandatory
J01MA	Fluoroquinolones	Mandatory
J01MB	Other quinolones	Mandatory
J01RA	Combinations of antibacterials	Mandatory
J01XA	Glycopeptide antibacterials	Mandatory
J01XB	Polymyxins	Mandatory
J01XC	Steroid antibacterials	Mandatory
J01XD	Imidazole derivatives	Mandatory
J01XE	Nitrofuran derivatives	Mandatory
J01XX	Other antibacterials	Mandatory
J02AA	Antibiotics	Optional
J02AB	Imidazole derivatives	Optional
J02AC	Triazole derivatives	Optional
J02AX	Other antimycotics for systemic use	Optional

J04AA	Aminosalicylic acid and derivatives	Optional
J04AB	Antibiotics	Optional
J04AC	Hydrazides	Optional
J04AD	Thiocarbamide derivatives	Optional
J04AK	Other drugs for treatment of tuberculosis	Optional
J04AM	Combinations of drugs for treatment of tuberculosis	Optional
J05AA	Thiosemicarbazones	Optional
J05AB	Nucleosides and nucleotides excl. reverse transcriptase inhibitors	Optional
J05AC	Cyclic amines	Optional
J05AD	Phosphonic acid derivatives	Optional
J05AE	Protease inhibitors	Optional
J05AF	Nucleoside and nucleotide reverse transcriptase inhibitors	Optional
J05AG	Non-nucleoside reverse transcriptase inhibitors	Optional
J05AH	Neuraminidase inhibitors	Optional
J05AR	Antivirals for treatment of HIV infections, combinations	Optional
J05AX	Other antivirals	Optional
P01AB	Nitroimidazole derivatives	Optional
P01BA	Aminoquinolines	Optional
P01BB	Biguanides	Optional
P01BC	Methanolquinolines	Optional
P01BD	Diaminopyrimidines	Optional
P01BE	Artemisinin and derivatives, plain	Optional
P01BF	Artemisinin and derivatives, combinations	Optional
P01BX	Other antimalarials	Optional
N04BB	Adamantane derivatives	Optional

Annex 3: Variables of the register and consumption datasets

WHO is providing an excel file for collecting the antimicrobial consumption data to the participating countries. The excel file contains all the variables mentioned below plus two additional ones, “Status” and “Status Message”. The excel file contains macros than will automatically populate some of the variables (including the “Status” and “Status Message”) when the macro ‘Validate Products’ is run. For each of the variables listed below, it is mentioned if they are automatically filled in by the macro. If the participants do not use the provided excel file, they have to populate all variables manually.

Variables for the ‘Product data’ worksheet	
Variable	**COUNTRY**
Description	Three letter code uniquely identifying the reporting country.
Data type	Coded Value
Variable type	Mandatory
Information	List of country codes based on the ISO3166 alpha-3 country codes list (ref: https://en.wikipedia.org/wiki/ISO_3166-1_alpha-3)
Variable	**PRODUCT_ID**
Description	The national code of the Medicinal Product Package. The code uniquely identifying the medicinal product package (MPP) for the country.
Data type	Text
Variable type	Mandatory
Information	The Product_ID should not change over time. When a MPP is no longer available on the market or is no longer registered, its Product_ID should not be attributed to another MPP in order to identify the old MPP for historical purposes (prescription history). If no code exists for a MPP, the country should provide one arbitrary code that should uniquely identify the MPP.
Variable	**LABEL**
Description	The label of the MPP. The label should contains if possible name of the medicinal product, package size, strength and pharmaceutical form
Data type	Text
Variable type	Mandatory
Information	The label is an important variable as it is the only information that allows cross check of the medicinal product package for an external reviewer.
Variable	**PACKSIZE**
Description	The package size of the MPP. The size of the MPP can be reported as a number of pieces in the MPP or as a number of mL.

Data type	Number
Variable type	Mandatory
Information	For MPP that are administrated as liquid form (i.e. syrup), the package size should be reported as mL of final reconstituted product. For all other pharmaceutical forms, the package size must be reported as a number of pieces. For instance, for vials, the package size must be reported as a number of vials in the package and not as the volume of reconstituted product.
Variable	**PACKSIZE_UNIT**
Description	The unit of the package size of the MPP.
Data type	Coded Value (see Measurement Unit List in annex)
Variable type	Mandatory
Information	The measurement unit in which is expressed the package size of the MPP.
Variable	**PAEDIATRIC_PRODUCT**
Description	The MPP is a paediatric MPP
Data type	YES/NO
Variable type	Optional
Information	The product is a paediatrics product or not.
Variable	**FORM**
Description	The pharmaceutical form of the MPP.
Data type	Text
Variable type	Optional
Information	
Variable	**ROUTE_ADMIN**
Description	The route of administration of the MPP.
Data type	Coded Value (see Administration route List in annex)
Variable type	Mandatory
Information	The route of administration is used to attribute a DDD to the MPP and to report consumption according to the route of administration.
Variable	**STRENGTH**
Description	The strength of the substance of each item as defined by PACKSIZE. For multi-ingredient products this field should contain the strength in which the DDD is expressed.
Data type	Number
Variable type	Mandatory
Information	For some specific substances used in combination with others, the WHO CC has defined some rules such as to only take into account the antimicrobial substance and not the combined substance (e.g. amoxicillin/clavulanic acid). For products with multiple antimicrobial substances, the WHO CC has defined DDD for combined products. In this case, the strength should be reported in the same unit as the DDD for the corresponding combined

	product.
Variable	**STRENGTH_UNIT**
Description	The unit of the strength of the MPP.
Data type	Coded Value (see Measurement Unit List in annex)
Variable type	Mandatory
Information	The measurement unit in which is expressed the strength of the MPP.
Variable	**INBASQ**
Description	The basic ingredient quantity (INBASQ) used for describing concentration of fluids (e.g. 200 mg/10 ml). In syrups and solutions INBASQ describes the denominator part of the strength. In all other cases (including perfusion fluids or ampullas), the INBASQ should be set to 1.
Data type	Number
Variable type	Mandatory
Information	The default value is 1 when the package size is not expressed in ML
Variable	**INBASQ_UNIT**
Description	The unit of the INBASQ of the MPP.
Data type	Coded Value (see Measurement Unit List in annex)
Variable type	Mandatory
Information	The measurement unit in which is expressed the basic ingredient quantity of the MPP.
Variable	**ATC5**
Description	The WHO ATC code at substance level (ATC 5th level) of the MPP
Data type	Coded Value
Variable type	Mandatory
Information	Each ATC code is linked to its product main therapeutic use. The ATC5 variable is used to attribute a DDD to the MPP and to report antimicrobial consumption according to the ATC classification. See ATC classification at ATC 4th level in annex.
Variable	**SALT**
Description	The code of the salt associated to the active substance.
Data type	Coded Value
Variable type	Optional
Information	It is only valid for methenamin (J01XX05) and erythromycin (J01FA01), for all other substances, the salt should not be specified. The reason is that the WHO CC has defined DDD depending on the salt for these two substances only.
Variable	**COMBINATION**
Description	The code of the combined product of the MPP
Data type	Coded Value (see Combined Product List in annex)
Variable type	Optional

Information	If the MPP is a combined product with a corresponding entry in the Combined Product list, the variable must be set in order to attribute the correct DDD to the MPP. In addition if the variable is set, the strength unit should be reported in Unit Doses.
Variable	**PRODUCT_NAME**
Description	The name of the product.
Data type	Text
Variable type	Optional
Information	The name of the product. The name should be common to all MPPs of the same product.
Variable	**INGREDIENTS**
Description	The name of the ingredients in the MPP, not only the antimicrobial substances.
Data type	Text
Variable type	Optional
Information	INN names should be used to report the ingredients.
Variable	**PRODUCT_ORIGIN**
Description	The source of the product.
Data type	Coded Value
Variable type	Optional
Information	The source of the product can be import, donation, locally produced.
Variable	**MANUFACTURER_COUNTRY**
Description	Three letter code uniquely identifying the country of manufacturing.
Data type	Coded Value
Variable type	Optional
Information	See COUNTRY variable
Variable	**MANUFACTURER**
Description	The name of marketing authorization number of the MPP.
Data type	Text
Variable type	Optional
Information	
Variable	**GENERICS**
Description	The MPP is a generic.
Data type	YES/NO
Variable type	Optional
Information	
Variable	**CONV_FACTOR**
Description	the conversion factor to transform strength expressed in IU into strength expressed in G.
Data type	Number
Variable type	Macro enters data in this cell automatically

Information	If there is no need to convert from IU to G, CONV_FACTOR must be set to 1. See Conversion Factor List for the list of existing conversion factors. If strength is expressed in IU and DDD in G and no conversion factor exists, no DDD per MPP will be calculated and no consumption for this MPP will be reported. See Conversion factor list in annex.
Variable	**PACKCONTENT**
Description	The content of active substance the MPP.
Data type	Number
Variable type	Macro enters data in this cell automatically
Information	The package content of the MPP is calculated by multiplying the package size by the strength and dividing by the INBASQ.
Variable	**PACKCONTENT_UNIT**
Description	The unit of the package content of the MPP.
Data type	Coded Value (see Measurement Unit List in annex)
Variable type	Macro enters data in this cell automatically
Information	The measurement unit in which is expressed the package content of the MPP.
Variable	**ARS**
Description	A code combining the ATC code (A), the route of administration code (R) and the optional Salt code (S)
Data type	Character
Variable type	Macro enters data in this cell automatically
Information	The ARS code identified uniquely the DDD to be assigned to the product. Note that when a combination code is entered, the DDD for this product will be picked up using the combination code.
Variable	**WHO_DDD**
Description	The official WHO DDD of the MPP.
Data type	Number
Variable type	Macro enters data in this cell automatically
Information	The WHO DDD is assigned according to the ATC5, ROUTE_ADMIN, COMBINATION and SALT variables. Some MPP will not have corresponding WHO DDD. In this case, if no national DDD exists, no DDD per MPP will be calculated and no consumption for this MPP will be reported.
Variable	**WHO_DDD_UNIT**
Description	The unit of the WHO DDD of the MPP.
Data type	Coded Value (see Measurement Unit List in annex)
Variable type	Macro enters this cell automatically
Information	The measurement unit in which is expressed the WHO DDD of the MPP.
Variable	**DPP**

Description	The number of calculated DDD in the MPP.
Data type	Number
Variable type	Macro enters data in this cell automatically
Information	If a CALC_DDD has been assigned, the DPP will be calculated for the MPP. The overall number of sold DDD for the MPP will be calculated by multiplying the DPP by the number of packages sold.
Variable	**TOTAL_PACKAGES (previously T_PACKAGES)**
Description	The total number of packages of the MPP / Product_ID
Data type	Number
Variable type	
Information	
Variable	**COMMUNITY_PACKAGES (previously C_PACKAGES)**
Description	The number of packages of the MPP / Product_ID for community use.
Data type	Number
Variable type	
Information	
Variable	**HOSPITAL_PACKAGES (previously H_PACKAGES)**
Description	The number of packages of the MPP / Product_ID for hospital use.
Data type	Number
Variable type	
Information	

Annex 4: Conversion factor List

ATC5	Administration Route	From	To	Factor
J01CE01	P	MU	G	0.6
J01CE02	O	MU	G	0.625
J01FA02	O	MU	G	0.3125
J01CE08	P	MU	G	0.6
J01CE09	P	MU	G	1

Annex 5: Administration Route List

Code	Name
O	Oral
P	Parenteral
R	Rectal
IP	Inhalation powder
IS	Inhalation solution

Annex 6: Measurement Unit List

Code	Name
MG	Milligram
G	Gram
IU	International unit
MU	Millions of international unit
UD	Unit dose
PCS	Piece
ML	Millilitre