

## **Appendix:**

### Glossary

In order to clarify how certain expressions are used throughout the text and to minimize ambiguity and misunderstanding, an effort was made to provide a list of definitions of frequently used terms in a glossary below. When it was felt that particular or novel aspects of surveillance demanded a more detailed explanation, these are included in additional text boxes throughout the text.

#### *Antibiotic resistance (ABR)*

Antibiotic resistance (ABR) is usually referred to as resistance of bacteria against antibiotic drugs and chemotherapeutic agents developed to treat bacterial infections in humans and animals.

#### *Antimicrobial resistance (AMR)*

Antimicrobial resistance (AMR) is the resistance of micro-organisms to an antimicrobial drug to which they were previously sensitive. Resistant organisms can include viruses, bacteria, fungi, protozoa, but also parasitic worms and insects (although the last-mentioned are not micro-organisms in a strict sense).

#### *Burden of disease (BoD)*

This is an estimate of the societal impact of defined health problems. It measures the mortality, morbidity, and financial cost or other societal indicators. The conventional currency of BoD is the DALY, which stands for ‘disability-adjusted life year’. It combines disease-associated mortality and morbidity into a single value, adding up the number of life years lost due to premature death or disability. Thereby, the loss of healthy life in younger people will contribute proportionally more DALYs than adverse health events that strike at older age. As a result, AMR infections in low-income countries will yield relatively more DALYs than in high income countries where the burden shifts to older age. Current BoD predictions suffer from substantial limitations in that they make assumptions based on historical trends. These extrapolate the success of pharmaceutical interventions (vaccination and antibiotics) witnessed over the last 50 years. It is therefore

important to remain aware that the BoD estimates regularly published by WHO yield erroneously optimistic projections if one of the major effect modifying trends such as antimicrobial effectiveness reversed. Consequently, the most important instruments for decision-makers on national and global health issues underestimate the role of AMR among emergent and resurgent infectious diseases in the coming decades due to a paucity of data.

#### *Cosmopolitan opportunistic bacterial pathogen (COBP)*

COBPs are a common part of human microbiota, either as transient or permanent colonizers, but can also colonize other vertebrates or exist in the environment. They include for example enterobacteriaceae and the non-fermenters *A. baumannii* and *P. aeruginosa* but also *S. pneumoniae*, *H. influenza*, *S. aureus*, and enterococci. They attain a cosmopolitan distribution which spans the entire inhabited world. Every time when antibiotics are used, COBPs become indiscriminately exposed to their selective effects. Consequently, the most significant increase of ABR has been observed among this type of bacteria. COBPs are truly opportunistic pathogens. Therefore, the most vulnerable segment of societies, i.e. the young, elderly, and immune-compromised, are more often affected and suffer the gravest consequences of decaying antibiotic effectiveness. This is also the reason why the true burden of disease associated with antibiotic resistance is underestimated as mortality associated with COBPs is frequently included among other categories in cause of death statistics.

#### *Drug resistance index (DRI)*

This metric is an intuitive measure to determine the average effectiveness of available antibiotics in hospitals and primary care. The DRI is a measure for both the resistance and the availability of antibiotics, and it will be expressed as a single index which can assume a value between 0 and 1. Thus a DRI of 0.3 would mean that 30% of a defined bacterial species (or a defined infection) cannot be successfully treated with the locally available drugs. For a DRI of 0.9 this would be as much as 90%.

#### *Health care collective*

Any number of health care institutions, practitioners, or primary care trusts that refer

patients between each other at a local level. A health care collective typically consists of a large referral (often tertiary) hospital and hospitals and health care institutions that refer patients and cater for the same local catchment population.

### *High-risk clones (HiRiCs)*

High-risk clones are defined as bacteria of a specific genotype or genomic lineage that have attained particular public health importance for any of the following reasons:

1. they show an increased potential for causing disease, disability, and death,
2. they show a new or particular propensity for spread in the community, in hospitals, and/or between or within particular segments of the population. This also includes spread between different hosts (e.g. humans exposed to farm animals or their products),
3. they are difficult to treat or control using standard and/or advanced clinical management due to acquired resistance against antibiotics or disinfectants, which enhances their survival (tenacity) in tissues, hosts, reservoirs, or the environment.

### *High-risk genetic elements (HiRiEs)*

These are predominantly mobile genetic elements that can move between bacterial cells increasing their genetic repertoire, thus conferring the properties of high-risk clones.

High-risk genetic elements can consist of genes coding for virulence factors, cell adhesins, immunomodulators, and importantly in the context of this document the determinants for antibiotic resistance.

### *Occurrence*

This can be measured as incidence which is the most intuitive measure of risk, or as prevalence which is the most intuitive measure for the frequency of a health problem among a population. Importantly, all measures of occurrence require an estimate of the population size which is often difficult or impossible when the operational unit of surveillance is based on test results such as antimicrobial susceptibility tests generated in specialist diagnostic laboratories.

### *Operational unit of surveillance (OUS)*

A defined marker of health-related states, events, or determinants that can be measured and recorded, and which can be subjected to simple logical operations such as quantifying, equating, aligning, etc. and eventually tabulated and displayed as the essential surveillance information.

### *Scale, scope, and structure*

The scale determines the resolution or precision with which the objects of surveillance are ascertained in geographical and temporal dimension. The scope of a surveillance system specifies the objects of interest, i.e. what surveillance should record and what remains excluded. The structure describes how the components (surveillance sites, data bases, reference laboratories, etc.) are connected within an organizational, managerial, and data flow framework.

### *Semantic standards*

In science, engineering, and industry agreements on terms, expressions, and names for the unequivocal exchange of information using digital data transfer systems.

### *Surveillance*

As a central theme in epidemiological practice, surveillance is used for the quantification and mapping of health-related states, events, or determinants through systematic recording and reporting. Decisions to implement surveillance are based on the perceived degree of harm inflicted on individuals and society, the frequency of occurrence and variability in time and place, and the potential for spread, but also guided by the demand for information that could direct appropriate control strategies.

## List of abbreviations and acronyms

ABR antibiotic resistance

AMR antimicrobial resistance

BoD burden of disease

CLSI Clinical Laboratory Standards Institute

COBP cosmopolitan opportunistic bacterial pathogens

DALY disability-adjusted life years

EARS-Net European Antimicrobial Resistance Surveillance Network

EUCAST European Committee for Antimicrobial Susceptibility Testing

HIV Human Immunodeficiency Virus

LMIC low- and middle-income countries

MIC minimum inhibitory concentration

ReVALA Red Latinoamericana de la Vigilancia a las Resistencias Antimicrobianas

TB tuberculosis

WHO World Health Organization

WGS whole-genome sequencing