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Follow-up to the high-level meetings of the United Nations General Assembly on health-related issues

Antimicrobial resistance

Report by the Director-General

1. This report provides an update on the implementation of resolution WHA68.7 (2015), the global action plan on antimicrobial resistance and United Nations General Assembly resolution 71/3, "Political declaration of the high-level meeting of the General Assembly on antimicrobial resistance," which was adopted in October 2016, and key ongoing challenges and emerging threats.

2. The political declaration reaffirmed the global action plan and its five overarching objectives, which were developed by WHO in collaboration with, and subsequently adopted by FAO and OIE.

3. The sections below provide a summary of WHO's actions at all three levels of the Organization, as well as through collaboration with FAO, OIE and other stakeholders to support the implementation of the commitments made in the political declaration and in resolution WHA68.7.

COUNTRY-LEVEL PROGRESS IN COMBATING ANTIMICROBIAL RESISTANCE

4. Based on guidance and tools jointly developed by WHO, FAO and OIE, Member States have developed and started implementing their national action plans for combating antimicrobial resistance. As of October 2018, 112 countries have finalized their national action plans and another 65 are in the process of developing theirs; these countries represent all regions and all levels of income and development.

5. To gauge progress, an annual country self-assessment survey has been jointly administered by WHO, FAO and OIE since 2016, with questions structured around the strategic objectives of the global action plan. In 2018, 154 out of WHO's 194 Member States, representing 91% of the world's population, responded to the survey, while nearly 40% have progressed to implementing their action plans after receiving government approval, establishing monitoring arrangements, engaging all relevant sectors and identifying specific funding for implementation. Responses from the surveys are published in an open-access database, offering scope for in-country review with civil society and other stakeholders.

6. Key findings of the antimicrobial resistance country self-assessment survey 2018 include:

(a) Some 50% of responding countries have established a multisectoral antimicrobial resistance working group, with representatives from the human, animal and plant health, food

safety, food production and environment sectors; these working groups are functional in 53 countries;

(b) While 125 countries have conducted awareness campaigns about the risks of antimicrobial resistance in human health, more nationwide efforts are needed; in the animal health and other non-human sectors, one third of countries have conducted awareness campaigns;

(c) Although 105 (68%) countries report that they have a national antimicrobial resistance surveillance system for some common bacterial pathogens in humans, not all of these countries are currently enrolled in the Global Antimicrobial Surveillance System (GLASS); the animal sector and food sector show close to 40% of countries conducting surveillance;

(d) A total of 90 countries report that they have a national infection prevention and control programme, with national guidelines; in the non-human sectors, the number of countries reporting national programmes for infection prevention and control are much smaller;

(e) While 123 countries have policies requiring a prescription for antibiotic use in humans, 64 countries have limited the use of critically important antimicrobials (human and animal) for growth promotion in animal food production.

7. Although these self-assessment surveys have limitations, when their results are compared with data from the Joint External Evaluations of the International Health Regulations (2005) conducted between 2016 and 2018, the scores are broadly consistent. In the context of strengthening global health security, one of the key technical areas being evaluated in the Joint External Evaluations is whether Member States have a functional system for the national response to combat antimicrobial resistance through a One Health approach.

PROGRESS IN IMPLEMENTING THE GLOBAL ACTION PLAN

Objective 1. Improve awareness and understanding of antimicrobial resistance through effective communication, education and training

8. Every November since 2015, World Antibiotic Awareness Week has been a major campaign in all regions to improve awareness of antimicrobial resistance and urge action. FAO and OIE also actively participate in this week-long campaign on the standing theme “Antibiotics: Handle with Care.” In 2017, 131 countries from all six regions participated in the campaign and there was significant media attention.

9. Technical consultations with behaviour change experts to share knowledge on changing behaviour around the use of antibiotics were held in 2017 and 2018, with the active participation of staff from FAO and OIE. Based on these consultations, a number of country-based pilot projects will be defined and developed in 2019.

10. WHO is also liaising with FAO and OIE to develop, adapt and disseminate cross-sectoral educational materials that address antimicrobial resistance at the human–animal interface, including inappropriate use of antimicrobials in food production. A training module on the role of infection prevention and control to combat antimicrobial resistance is being finalized for dissemination.

Objective 2. Strengthen the knowledge and evidence base through surveillance and research

11. GLASS, which was launched in October 2015, provides a standardized approach to the collection, analysis and sharing of antimicrobial resistance data by countries for selected bacteria that cause infections in humans; it seeks to monitor the status of existing or newly developed national antimicrobial resistance surveillance systems. As of July 2018, 68 countries (10 low-income countries, 16 lower-middle-income countries, 15 upper-middle-income countries, 27 high-income countries) provided data to GLASS, 67 of which included information on their national antimicrobial resistance surveillance systems, while 44 also provided antimicrobial resistance data. Compared with 2017, GLASS has seen a 57% increase in country enrolment in 2018 and almost twice the number of countries have submitted antimicrobial resistance data.

12. GLASS is providing support and developing tools, especially for countries with limited resources. It has also facilitated synergies between WHO surveillance initiatives related to antimicrobial resistance. New modules within the GLASS information technology platform are being built to facilitate further integration of analysis and reporting. In addition, the GLASS Emerging Antimicrobial Resistance Reporting (GLASS-EAR) component was launched in 2018 to support the detection, early warning and risk assessment capacities of national antimicrobial resistance surveillance programmes and to strengthen global health security.

13. Next year, at the end of the initial phase (2015–2019), GLASS will be revised. New targets and datasets, including data from molecular testing, will be included, while emerging threats such as carbapenem-resistant Enterobacteriaceae will be addressed in a more comprehensive manner.

14. WHO is also engaged in developing, promoting and coordinating the implementation of a global protocol for integrated surveillance of antimicrobial resistance in humans, the food chain and the environment, using appropriate indicators (e.g., the extended spectrum beta-lactamases *E.coli* tricycle project). This work is based on the guidance of the WHO Advisory Group on Integrated Surveillance of Antimicrobials Resistance. Whole genome sequencing as a tool to strengthen foodborne disease surveillance and response is also being promoted. Discussions are also under way to collaborate with FAO and OIE on the development of a single portal linking data on antimicrobial resistance rates and antimicrobial consumption from human, animal and agricultural sectors. In collaboration with FAO, WHO is also contributing to the revision and further development of the relevant Codex Alimentarius standards and related texts to reduce antimicrobial resistance in the food chain by providing evidence-based guidance to the Codex Alimentarius Commission.

15. WHO, in collaboration with other relevant United Nations agencies, is engaged in improving the understanding of the role of inadequate water, sanitation and hygiene (WASH) facilities and environmental contamination with residues and resistant bacteria as drivers of antimicrobial resistance and its impact on health. In this regard, WHO supports the Global Sewage Surveillance Project and the publication of results. Technical assistance is also being provided to facilitate the integration of environmental surveillance modalities into GLASS.

Objective 3. Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures

16. Prevention of infections is critical to reducing the need for antibiotics and controlling the spread of resistant microorganisms. Following the issue of the new WHO evidence-based recommendations on core components of effective programmes on infection prevention and control in 2016, further specific

technical guidelines have been issued in 2017 on the prevention and control of carbapenem-resistant Enterobacteriaceae, Acinetobacter baumannii and Pseudomonas aeruginosa in health care facilities.[1] To bridge the gap in implementation and monitoring of programmes and practices on infection prevention and control demonstrated by various surveys, a broad range of practical tools and resources have been produced building on evidence and country examples.[2] Over the last year, intensive support has been provided through collaboration across the three levels of WHO to more than 40 countries for the assessment and implementation of core components of infection prevention and control, including strong linkages to antimicrobial resistance, WASH and health emergencies national action plans, and to quality of care improvement in the context of universal health coverage.

17. WHO is providing technical support on strengthening environmental components within national action plans for tackling antimicrobial resistance, with a focus on monitoring and strengthening the availability of basic WASH services in health care facilities, wastewater treatment, health care waste management and surveillance. Based on evidence gathered in the WHO/UNICEF Joint Monitoring Programme Report in 2017, the report on WASH services in health care facilities and other studies, the linkage between WASH and antimicrobial resistance has been highlighted in the new WHO WASH Strategy 2018–2025. There will be greater collaboration with UNEP and other United Nations agencies on these issues.

Objective 4. Optimize the use of antimicrobial medicines in human and animal health

18. In its most recent Model List of Essential Medicines (2017), WHO adopted a new classification for antibiotics to guide better use and reduce resistance, comprising three groups:

(a) **Access** antibiotics (for common infections): these should be available at all times, affordable and quality-assured;

(b) **Watch** antibiotics (including most of the highest priority critically important antimicrobials for human medicine): recommended only for specific, limited indications;

(c) **Reserve** antibiotics: for situations when all alternative antibiotics have failed.

WHO anticipates that the introduction of the "AWaRe" framework will reduce the use of "Watch" Group and "Reserve" Group antibiotics, while the accessibility of Access antibiotics will expand.

19. The first WHO Report on Surveillance of Antibiotic Consumption, published in November 2018, presents data on the consumption of systemic antibiotics from 65 countries. The report describes WHO's approach to monitor antimicrobial consumption and its methodology for data collection and highlights challenges and future steps in monitoring antimicrobial consumption. To assist countries in making better use of existing antibiotics, WHO has developed a toolkit to implement antimicrobial stewardship in hospitals in low- and middle-income countries, covering the core elements needed to enable stewardship activities, options for hospital interventions and education and training.

[1] See http://www.who.int/infection-prevention/publications/focus-amr/en/ (accessed 23 November 2018).

[2] See http://www.who.int/infection-prevention/en/ (accessed 23 November 2018).

20. To advance the establishment of a Global Framework for Development and Stewardship to Combat Antimicrobial Resistance, the Tripartite (WHO, FAO, OIE) in collaboration with UNEP, held a second consultation with Member States, relevant international organizations and non-State actors on 1 and 2 October 2018. A concept for the overarching framework was presented and discussed. Member States noted the need for additional consultations to move the process forward.

21. WHO updated and published the WHO list of Critically Important Antimicrobials (CIA List, 2017) for human medicine and will also disseminate guidelines for the appropriate use of the antimicrobials important for human medicine in food producing animals. Technical input will also be provided to Good Manufacturing Practice guidance on waste and wastewater management for production of Critically Important Antimicrobials.

Objective 5. Develop the economic case for sustainable investment that takes account of the needs of all countries and increases investment in new medicines, diagnostics tools, vaccines and other interventions

22. The Global Antibiotic Research and Development Partnership, a joint initiative of WHO and the Drugs for Neglected Diseases Initiative, aims to develop new treatments for bacterial infections. Since its incubation, the Partnership has launched programmes addressing sepsis in newborns through an observational study in 11 countries and a partnership to develop a new first-in-class treatment for drug-resistant gonorrhoea that is entering clinical phase 3. Another programme focuses on recovering knowledge, data and assets of forgotten or abandoned antibiotics and identifying new treatments.

23. In 2017, WHO published a global priority list of antibiotic-resistant bacteria that pose the greatest threat to human health. This list is to guide research, discovery and development of new antibiotics and is a factor in prioritizing new vaccine development. WHO will update the prioritization of pathogens to further catalyse public and private funding for research and development, and to accelerate global research and development strategies for the discovery of new antibacterial agents to treat multi-drug resistant tuberculosis and drug-resistant bacterial infections.

24. WHO published a comprehensive analysis of the clinical antibacterial and anti-tuberculosis pipeline,[1] which reviews all new antibacterial treatments that are currently being developed and assesses to what extend they are expected to have some activity against at least one WHO priority pathogen.

25. WHO is also engaged in encouraging the development of new diagnostics tools relevant to antimicrobial resistance. A landscape analysis of available technologies and promising products for low and middle-income countries is being conducted.

Antimicrobial resistance: Tuberculosis, malaria, HIV, neglected tropical diseases and sexually transmitted infections

26. According to the Global Tuberculosis Report 2018, drug-resistant tuberculosis continues to be a public health crisis. The best estimate is that, worldwide in 2017, 558 000 people developed tuberculosis that was resistant to rifampicin, the most effective first-line drug, of whom 82% had multidrug resistant tuberculosis. Among cases of multidrug resistant tuberculosis in 2017, 8.5% were estimated to have extensively drug-resistant tuberculosis. In July 2018, the latest evidence of the treatment of drug-resistant tuberculosis was reviewed by an independent panel of experts convened by WHO. A rapid

[1] WHO review: "Analysis of the clinical antibacterial and anti-tuberculosis pipeline." The Lancet https://doi.org/10.1016/S1473-3099(18)30513-9 (accessed 23 November).

communication on key changes to recommendations for the treatment of multidrug- and rifampcin-resistant tuberculosis was issued by WHO in August 2018 and outlined the reprioritization of medicines used in treatment, including the use of bedaquiline and replacing toxic injectables, with all-oral regimens as the standard of care.

27. The Global Technical Strategy for Malaria 2016–2030 calls on countries and global malaria partners to monitor the efficacy of antimalarial medicines so that the most appropriate treatments can be selected for national policies. Monitoring the efficacy of antimalarial drugs has resulted in regular policy updates in countries affected by resistance; these reviews are outlined in the annual WHO status reports on artemisinin resistance and efficacy of artemisinin-based combination therapy. WHO continues to update the Global database on antimalarial drug efficacy and resistance database, which serves as the source for the therapeutic efficacy studies summary tables, the Malaria Threats Map and the WHO World Malaria Report.

28. The elimination of AIDS as a public health threat calls for expansion of the coverage and quality of treatment and antiretroviral therapy services. This expansion needs to be balanced by efforts to ensure that the risks and impact of HIV drug resistance (HIVDR) are minimized. WHO's HIVDR report 2017 highlights concerning trends in the levels of HIVDR across several regions. Pretreatment HIV drug resistance, detected in people starting antiretroviral therapy, is increasing in low- and middle-income countries. The Global Action Plan on HIV drug resistance 2017–2021, launched in 2017, outlines key actions for country and global stakeholders to prevent, monitor and respond to HIV drug resistance and to protect ongoing progress towards achieving the global targets for epidemic control by 2030. In July 2018, WHO released a report summarizing progress and remaining challenges in implementing the Global Action Plan achieved during the first year (2017 to 2018). The monitoring of early warning indicators for HIVDR[1] will also be further strengthened. WHO has also linked the results of the reports of increasing pre-treatment HIV drug resistance to new treatment guidelines which support the use of Dolutegravir rather than Efavirenz as part of the three-drug first-line treatment for HIV.[2]

29. The Working Group on Monitoring of Neglected Tropical Diseases Drug Efficacy was established in 2011 due to the high treatment coverage rates for neglected tropical diseases in sub-Saharan Africa and South-East Asia. This is expected to eventually contribute to the emergence of resistance to anthelminthic medicines, and the Working Group's seventh meeting in 2018 articulated such concerns in relation to resistance to treatment for soil-transmitted helminthiases. While anthelmintic resistance is problematic within the veterinary sector, the full scope of the problem in human helminthiasis is being studied; however, alternative anthelminthic medicines (to be used either alone or in combination) are needed to prevent resistance developing.

30. Each year, an estimated 357 million new infections occur of the following four curable sexually transmitted infections: chlamydia (131 million), gonorrhoea (78 million), syphilis (5.6 million) and trichomoniasis (143 million). Resistance of sexually transmitted infections, in particular gonorrhoea, to antibiotics has increased rapidly in recent years and has reduced treatment options. The emergence of decreased susceptibility of gonorrhoea to the last-line treatment option (oral and injectable cephalosporins), together with antimicrobial resistance already shown to penicillins, sulphonamides, tetracyclines, quinolones and macrolides, make gonorrhoea a multidrug-resistant organism. WHO has

[1] See http://apps.who.int/iris/bitstream/handle/10665/246219/9789241511179-eng.pdf?sequence=1 (accessed 23 November 2018).

[2] See http://www.who.int/hiv/pub/guidelines/ARV2018update/en/ (accessed 23 November 2018).

issued new treatment guidelines for syphilis, gonorrhoea and chlamydia to address the problem of resistance to antibiotics.[1]

MULTISECTORAL COLLABORATION: FAO, OIE, WHO (the Tripartite)

31. The members of the Tripartite (FAO, OIE, WHO) have worked together since 2010 and strengthened their collaboration after 2016 to implement the five strategic objectives of the global action plan, including in the areas of: communication and raising awareness; strengthening the evidence base and surveillance; infection prevention and control measures; monitoring the consumption of antimicrobials; optimizing the use of antimicrobials in human, animal and plant health; national regulations and policies; development of a global stewardship framework; monitoring progress in countries through surveys; development of a global monitoring and evaluation framework; and support for research and development in new medicines, diagnostic tools, vaccines and other interventions.

32. To formalize the collaboration, the heads of agencies of the Tripartite signed a memorandum of understanding in May 2018. This was followed by the development of a joint Tripartite workplan for 2019–2020, which has five focus areas and about 20 specific outputs. The joint workplan also recognized the need for the UNEP to join the collaboration (subsequently known as "Tripartite Plus") in order to help address the various environmental issues associated with the emergence and spread of resistance pathogens.

33. To finance the implementation of the joint workplan for 2019–2020, the Tripartite Plus is exploring the establishment of a trust fund mechanism. Without sustained and reliable additional resources, the majority of the outputs listed in the workplan cannot be effectively implemented.

34. WHO and the Tripartite support the work of the WHO Secretariat in managing the activities of the ad hoc inter-agency coordination group established by United Nations General Assembly resolution 71/3 on antimicrobial resistance. The Secretariat facilitates a platform for inputs into the processes and deliverables of the ad hoc group, including from Member States, civil society and the private sector, as they prepare to provide practical recommendations to ensure sustained effective action to address antimicrobial resistance.

35. The Tripartite Plus will work together to deliver the first biennial global antimicrobial resistance report in 2019, as well as contribute to the Secretary General's report to the United Nations General Assembly on the implementation of the commitments made in the high-level meeting on antimicrobial resistance.

ONGOING CHALLENGES

36. The key country-level challenges to the effective implementation of national action plans to combat antimicrobial resistance that have been identified in the past two years and that have an impact on the global response are:

(a) **Prioritization and implementation.** In middle and low-resource settings, implementing action at scale even in a few areas of national plans will be a major challenge due to scarce

[1] See http://www.who.int/en/news-room/detail/30-08-2016-growing-antibiotic-resistance-forces-updates-to-recommended-treatment-for-sexually-transmitted-infections (accessed 23 November 2018).

technical and financial resources; hence careful prioritization based on risk/reward analysis will be essential in each country;

(b) **Multisectoral working and the One Health approach.** While many countries have established a multisectoral antimicrobial resistance working group, additional strategic guidance, technical support and resources are necessary to make this coordination group functional and to help implement and monitor national action plans. This will help to strengthen the One Health approach in countries and drive support for non-human sectors so that they can attain the same level of participation and interest as in the human health sector;

(c) **Monitoring.** It is a challenge to implement a robust monitoring framework with indicators that are valid, reliable, operational, affordable and comparable and can be used across the various sectors in low- and middle-income countries. A global monitoring and evaluation framework is being published by end-2018, and countries will need assistance to develop the systems and processes needed to produce information consistently and support national and global-level monitoring;

(d) **Maintaining country-level political buy-in.** It remains a challenge to sustain political buy-in in countries for tackling antimicrobial resistance, while balancing health and broader development interests and allocating scarce national resources. Developing an economic case for sustainable investment in tackling antimicrobial resistance is therefore a top priority; this needs to be complemented by continued advocacy;

(e) **Enhancing civil society, private sector and stakeholder engagement.** Given the multisectoral nature of tackling antimicrobial resistance, a clear need has been identified to develop a comprehensive civil society, private sector and stakeholder engagement strategy, with specific activities and platforms to encourage their full participation. WHO and the Tripartite Plus will address this need in the joint workplan for 2019–2020 and will work towards developing a shared goal and vision for the global response to antimicrobial resistance.

EMERGING THREAT

37. One of the most significant threats to public health associated with antimicrobial resistance, which is already prioritized by WHO and recognized by many countries, is the carbapenem-resistant gram-negative bacteria, including carbapenem-resistant Enterobacteriaceae. These bacteria are very difficult to treat due to extremely limited remaining treatment options, and infections caused by them are associated with high mortality. They also have the potential for widespread transmission of resistance via mobile genetic elements.

38. Addressing this emerging threat will require that antimicrobial resistance be considered a cross-cluster platform, as highlighted in the Thirteenth General Programme of Work, 2019–2023. This threat necessitates the engagement and coordination of relevant departments within WHO, at all three levels, including by strengthening health systems in the context of UHC, strengthening core country capacity to identify and deal with emerging high-threat infectious pathogens as a health emergency, and addressing the social and environmental determinants of health and the impact of non-human sectors through a multisectoral approach. Coordinated efforts are needed to monitor the threat in all countries, scale up more targeted measures for infection prevention and control, invest in the development of new medicines and support effective measures to optimize the consumption of antibiotics.

ACTION BY THE EXECUTIVE BOARD

39. The Board is invited to note the report and to focus its discussions on providing further guidance on:

- moving forward with the global development and stewardship framework;
- accelerating Member States' implementation of national action plans for combating antimicrobial resistance;
- strengthening linkages at country level between plans for combating antimicrobial resistance and plans for universal health coverage, health security, and multisectoral action.

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