

A NATIONAL ACTION PLAN TO CONTAIN ANTIMICROBIAL RESISTANCE IN CHINA: CONTENTS, ACTIONS AND EXPECTATIONS

PROFESSOR YONGHONG XIAO, VICE-DIRECTOR, STATE KEY LABORATORY FOR DIAGNOSIS & TREATMENT OF INFECTIOUS DISEASES, THE FIRST AFFILIATED HOSPITAL, COLLEGE OF MEDICINE, ZHEJIANG UNIVERSITY, HANGZHOU, CHINA



In response to the call of the World Health Organization, the Chinese government issued its national action plan to contain antimicrobial resistance (AMR) in August 2016. The ambitious five-year plan contains detailed strategies and clear targets. The major targets include new drugs and the development of new techniques, implementation of antibiotics sale only with a prescription, optimization of surveillance, rational use of antibiotics in both the human and animal sectors, and professional education and publicity for AMR control.

Antimicrobial resistance (AMR) is a serious public health threat of international concern. Containment of AMR is a very urgent priority throughout the world and was one of many issues discussed at various high-level international political conferences. The G7 has already reached a consensus on AMR control (1); the G20 discussed AMR control and issued a communique on this in 2016 (2); and there was a special debate on AMR at the United Nations General Assembly in September 2016 (3). In 2014, the World Health Organization (WHO) adopted a resolution to develop a Global Action Plan for AMR containment. This was issued in 2015 and required all member states to develop their own action plan by 2017 (4). The week before the G20 summit in Hangzhou, the Chinese National Health and Family Planning Commission (NHFPC), together with 13 other ministries, issued the “National Action Plan to Contain AMR (2016–2020)” (hereafter referred to as the Plan). This is the official response to the WHO Global Action Plan and calls from major global political groups regarding AMR control. Considering its contents and actions, this is an ambitious plan with comprehensive coverage, integrating the concept of One Health in AMR control. The implementation of the Plan will be a great step towards global AMR control (5).

The Plan is fully integrated with the concept of One Health

The Plan fully reflects the Chinese government’s appropriate attitude toward drug resistance control. The Plan is coordinated by the NHFPC, together with 13 other ministries, and covers not only the research and development (R&D), registration, distribution and use of antimicrobial agents, but

also professional and public education. The participation of the Ministry of Finance will guarantee funding for implementation of the Plan. Although they have a unified aim, all involved parties have distinct responsibilities.

In accordance with the provisions of the Plan, health authorities will be responsible for strengthening management of the clinical application of antibacterial agents to curb bacterial resistance and will coordinate and supervise implementation of the Plan. The development and reform administrative authorities will enhance R&D and industrialization of antibacterial agents. The science and technology authorities will support studies of new agents and AMR through the relevant science and technology plans (projects and funding). The finance authorities will provide budgets for AMR control and supervise the use of related fiscal funds. The food and drug administrative authorities will strengthen management of the approval, registration, production and circulation of antibiotics, focusing on the implementation of regulations related to the sale of antibiotics with a prescription in retail pharmacy. The industry and information authorities will optimize policies of the pharmaceutical industry to promote green manufacture of antibacterial agents and industrialization of new related techniques. The traditional Chinese medicine authorities and military health administrative departments will provide antimicrobial stewardship in traditional Chinese medicine institutions and military medical institutions, respectively. The agriculture sectors will improve management of the production, sale and use of veterinary antimicrobial agents to contain antibacterial resistance arising from animal sources. The land and resources authorities will strengthen

Table 1: Goals and strategies of the National Action Plan of China

Goals

- ➔ To launch 1–2 new antibacterial agents and 5–10 new diagnostic techniques.
- ➔ To implement the sale of antibiotics only with a prescription in pharmacies across the entire country and in animal husbandry in half of the provinces.
- ➔ To optimize surveillance, to establish an evaluation system for antibacterial agent consumption and resistance in both the healthcare and animal husbandry sectors and to set up AMR reference laboratories and bacterial strain banks.
- ➔ To implement an antimicrobial stewardship programme in all hospitals.
- ➔ To discontinue the use of antibiotics as animal growth promoters.
- ➔ To educate medical staff, veterinarians, animal producers, students, and members of the public about AMR, and to set up an annual antibiotic alert week.

Strategies

- ➔ To prevent and control AMR by ensuring coordination between multiple sectors, each with its own responsibilities.
- ➔ To increase investment in antibiotic R&D.
- ➔ To strengthen security management of the supply of antibacterial agents.
- ➔ To establish and strengthen a control system for antibacterial agent use and drug resistance.
- ➔ To optimize surveillance systems for antibiotic consumption and resistance.
- ➔ To improve the professional capacity of bacterial resistance prevention and control.
- ➔ To strengthen the prevention and governance of antibiotic environmental pollution.
- ➔ To increase publicity and deliver education programmes regarding the rational use of antibacterial agents and AMR.
- ➔ To ensure communication and cooperation on an international scale.

the monitoring of antimicrobial contamination of soil. The environmental protection authorities will strengthen the prevention and governance of environmental pollution of antibiotics, environmental law enforcement and capacity-building for the monitoring of antimicrobial pollution, and accelerate the establishment of systems to evaluate antibiotic contamination. The education authorities will include content about the rational use of antimicrobial agents and AMR in health education courses for primary and middle school students. The culture and media authorities will widely disseminate information regarding AMR to the public via the major public media services.

The Plan fully reflects the concept of One Health and integrates related sectors such as the health, agriculture, and environmental protection departments. All parties will take actions related to the occurrence and spread of AMR, the use of antibiotics in healthcare and agriculture will be regulated, and the possible environmental hazards of antibiotics will be governed. All the actions are completely in line with the global action plan of the WHO (4).

In addition to the medical field, agriculture and animal husbandry is another important sector for antibiotic consumption. Antibiotic use in the healthcare and animal husbandry sectors and environmental pollution affect

antibacterial resistance. An investigation in China revealed problems or weaknesses in the management of antimicrobial agents that need to be regulated. Environmental pollution of antibacterial agents is serious, the use of antibacterial agents in the animal husbandry sector is relatively high and resistance can spread between animals and humans. AMR is not only harmful to human health, but also potentially threatens animal health and food safety (6, 7, 8). Whole chain management of antibacterial agents and AMR is the only way to control drug resistance.

A macro-strategy framework and detailed actions

The Plan establishes a good management framework, clarifies the national macro-policy and outlines specific provisions for its implementation.

It defines multisectoral collaborative mechanisms, however, the NHFPC will be responsible for the coordination of all work and the formation of a working group of the various ministries with distinct roles. Local government departments also need to take appropriate actions in accordance with the Plan. It emphasizes the need to accelerate the registration of innovative products, strengthen the management of drug circulation, strictly implement the sale of antibiotics with a prescription, promote industrial upgrading, encourage the green manufacture of antibacterial agents, enforce the rational use of antimicrobial agents and generate separate lists of antibiotics for human and animal use.

The Plan proposes clear five-year targets, which include launching one to two innovative drugs, marketing five to 10 new diagnostic techniques and controlling the main resistant pathogens in both the healthcare and animal husbandry sectors.

It contains substantial details regarding financial investment, construction of facilities and scientific research linked with AMR control. The Plan describes the importance of basic research and technology development for AMR control and clearly indicates the need to improve surveillance systems and establish an AMR reference laboratory and strain bank. The essence of science and technology infrastructure for AMR control provides the foundation for the implementation of the Plan.

The Plan describes the direction of scientific research and technology development and proposes requirements for the evaluation of the actions. Studies will cover basic research, drug development, diagnosis, vaccine innovation, exploration into animal growth-promoting alternatives, clinical investigations of the rational use of antibacterial agents and establishment of systems to evaluate antibiotic environmental pollution. Implementing these studies will not only greatly enhance China's standing in the field of AMR control, but will also

positively contribute to international AMR containment.

The Plan focuses on capacity building of human resource for AMR control and the promotion of public awareness. In China, the public has long held misconceptions regarding antibiotics and mistakenly believes they are general antimicrobial agents, leading to patients placing excessive pressure on clinicians. These misconceptions must be corrected (9). For AMR control, it is also essential to educate animal feeding practitioners in order to change how animals are fed in China and gradually reduce the consumption of antibiotics as growth promoters (10).

The Plan advocates international cooperation and promises active participation in international actions related to AMR control. The Chinese government will not only actively participate in international programmes and activities concerning AMR control, but is also willing to provide active assistance to other countries and regions as needed.

Financial and resource guarantees to ensure AMR containment

In addition to the actions and targets, the Plan also provides financial and resource guarantees to ensure its implementation. It provides financial support to increase security measures and some articles clearly describe the responsibility of the Ministry of Finance to allocate provisions. These provisions reflect the determination of the Chinese government to control AMR. Financial support is a key element stressed by WHO (3, 4).

An advisory committee will be established for scientific management, comprising a wide range of professionals selected on their professional strengths. The committee will provide advice, consultations and recommendations regarding the management of antimicrobial agents and AMR control. At the same time, all localities will be able to set up their own advisory committees by referring to the organization of the national advisory committee.

The Plan clarifies the targets and responsibilities of all sectors and outlines a reward and punishment system; departments and individuals who fail to implement or violate the relevant provisions will face disciplinary measures.

Designed in accordance with the WHO's Global Action Plan

The WHO Global Action Plan has five strategies (4): (1) to improve understanding and awareness of antibacterial resistance, (2) to strengthen surveillance and research, (3) to strengthen infection control and thereby reduce infections, (4) to promote the rational use of antibiotics in the healthcare and animal husbandry sectors, and (5) to ensure continuous investment and R&D of new technology. China's Plan goes beyond this with more specific and comprehensive aims; in

addition to the use of antibacterial agents in humans and animals, it includes articles on a range of other issues including prevention of environmental pollution, industrial development of antibiotics and drug policies. Moreover, international cooperation is included as a key aspect of the strategies.

Foreseeing challenges in implementing the Plan

With its comprehensive scope, substantial content, excellent design and clear targets, exciting achievements will be made once the Plan is implemented. However, it may also face major challenges and obstacles.

The occurrence of antibacterial resistance involves multiple links and domains from production to the use of antibacterial agents and AMR control also requires the joint actions of multiple sectors, as anticipated in the WHO Global Action Plan and described in China's Plan. China is a developing country with a large population and limited social and economic development. How the relationship among the 14 ministries is coordinated will have a large impact on the efficiency with which the Plan is implemented. Although the role of the NHFPC to provide overall coordination is clearly defined, challenges may arise because all ministries in China provide equivalent support to each other and the NHFPC lacks super-ministerial coordinating power. If coordination between the various departments is good, the Plan will be implemented successfully, as seen with the ongoing reform of China's medical and healthcare system (11). Coordination between various departments is not part of the action plans for AMR control in some other countries; however, these plans are based on the orders of heads of state or government leaders (3, 12, 13, 14).

China has a large population and a large demand for food. There are many animal feeding facilities, farming methods are still relatively primitive and antibiotic use for animal disease prevention and growth promotion is fairly common. To comply with the Plan, farming methods must be changed, hygienic animal feeding must be implemented and the use of antimicrobial agents as growth promoters must be reduced or even eliminated. To advocate the concept of One Health for AMR control, the animal husbandry, environment, and healthcare sectors must each take measures to reach the targets set. Interactions between and mutual restraints on these three sectors will influence the efficiency with which the Plan can be implemented. A single sector cannot achieve the ultimate goal of AMR control by itself (4).

Strengthening of security measures and an adequate budget are key for implementation of the Plan. It is a five-year programme and financial investment should be put in place in a timely manner to ensure that its actions can be performed rapidly. This will be key to the success or failure of the Plan (3, 4). ■

Funding: This work was supported by the by a Key Research and Development Program from Zhejiang Province (2015C03032).

Professor Yonghong Xiao, MD, PhD, drafted the National Action Plan to Contain AMR in China. He is Vice-Director of the State Key Laboratory for Diagnosis & Treatment of Infectious Diseases at the First Affiliated Hospital, College of Medicine, Zhejiang University,

Hangzhou, China. Professor Xiao's areas of expertise include infectious diseases, basic and clinical research into antimicrobial agents, bacterial resistant surveillance and mechanisms, clinical pharmacology and the rational use of antibiotics. He is the founder & leader of the Ministry of Health's national antibacterial resistant investigation net (Mohnarin), which has more than 1,300 member hospitals.

References

1. http://www.bmg.bund.de/fileadmin/dateien/Downloads/G/G7-Ges.Minister_2015/G7_Health_Ministers_Declaration_AMR_and_EBOLA.pdf (accessed Jan 30, 2017)
2. <http://www.globaltimes.cn/content/927294.shtml> (accessed Jan 30, 2017)
3. Laxminarayan R, Amabile-Cuevas CF, Otto C, et al. UN high-level meeting on antimicrobials—what do we need? *Lancet*. 2016;388(10041): 218-220
4. http://www.who.int/drugresistance/global_action_plan/en/ (accessed Jan 30, 2017)
5. National Health & Family Plan Commission of China, National plan for the containment of antibacterial resistance (2016-2020). <http://www.nhfpc.gov.cn/yzygj/s3593/201608/f1ed26a0c8774e1c8fc89dd481ec84d7.shtml> (accessed Jan 30, 2017)
6. Liu YY, Wang Y, Walsh TR, et al. Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. *Lancet Infect Dis*. 2015;16(2):161-168
7. Zhang QQ, Ying GG, Pan CG, et al. Comprehensive evaluation of antibiotics emission and fate in the river basins of China: source analysis, multimedia modeling, and linkage to bacterial resistance. *Environ Sci & Technol*. 2015; 49:6772-6782
8. Zhu YG, Johnson TA, Su JQ, et al. Diverse and abundant antibiotic resistance genes in Chinese swine farms. *PNAS*. 2013;110(9):3435-3400
9. Currie J, Lin WC, Zhang W. Patient knowledge and antibiotic abuse: Evidence from an audit study in China. *J Health Economics*. 2011;30(5):933-949
10. Boeckel TP, Brower C, Gilbert M, et al. Global trends in antimicrobial use in food animals. *PNAS*. 2015; 112(18): 5649-5654
11. Yip WCM, Hsiao W, Chen W, et al. Early appraisal of China's huge and complex health-care reforms. *Lancet*. 2012;379(9818):833-842
12. Department of Health, Department for Environment Food & Rural Affairs. UK five year antimicrobial resistance strategies 2013 to 2018. Sept. 2013.
13. https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf (accessed Jan 30, 2017)
14. <http://www.jpiamr.eu/jpiamr-and-french-ministry-of-health-to-host-collaborative-talks-between-european-ministries-agencies-and-funding-bodies-in-the-field-of-amr/> (accessed Jan 30, 2017)