PRIORITIZATION OF PATHOGENS TO GUIDE DISCOVERY, RESEARCH AND DEVELOPMENT OF NEW ANTIBIOTICS FOR DRUG-RESISTANT BACTERIAL INFECTIONS, INCLUDING TUBERCULOSIS

World Health Organization

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ISBN 978-92-4-002643-8 (electronic version)

ISBN 978-92-4-002642-1 (print version)

This publication was originally published under WHO reference number WHO/EMP/IAU/2017.12

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Suggested citation. Prioritization of pathogens to guide discovery, research and development of new antibiotics for drug-resistant bacterial infections, including tuberculosis. Geneva: World Health Organization; 2017(WHO/EMP/IAU/2017.12). (Licence: CC BY-NC-SA 3.0 IGO..

Cataloguing-in-Publication (CIP) data. CIP data are available at http://apps.who.int/iris.

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Printed in Geneva, Switzerland

Foreword

Infectious diseases are among the top 10 causes of death and the leading cause of disability-adjusted life years worldwide. Among these, acute lower respiratory tract infections, diarrhoeal diseases and tuberculosis (TB) are responsible for significant global morbidity and mortality. The overall burden of communicable diseases is strongly linked to poverty and, as a result, the African continent still suffers from the highest mortality from infectious diseases.

The reasons for the emergence and re-emergence of infectious diseases worldwide include a breakdown of public health measures in the face of epidemic transitions, increasing international travel, immigration for political, social and economic reasons, microbe adaptation and ability to change, and transmission of several pathogens between animals and humans. Of great concern is the global emergence of resistance of infectious pathogens to many first-line medicines.

Equitable access to medicines is another major concern in many low- and middle-income countries where common, treatable infections like pneumonia and TB are still associated with high numbers of deaths, often in children. The emergence of pathogenic microbes with drug resistance, not only to the most commonly used antibiotics but also to second-line, "reserve" medicines, further increases the burden of infectious diseases. Low-income countries are particularly vulnerable because of conditions that enable the spread of these diseases, such as poor sanitation, lack of control of and guidance on antibiotic use, inadequate health-care services and systems, and limited or inadequate infection control measures.

Middle- and upper-middle-income countries are not free of the burden of drug resistance, however. BRICS countries (Brazil, Russian Federation, India, China and South Africa) and several European countries face major epidemics of multidrug-resistant infections caused by common Gram-negative bacteria and multidrug-resistant-TB (MDR-TB), with devastating public health and economic consequences. Sadly, the pipeline for new antibiotics currently includes only a small number of novel compounds in development. In the past 20 years, only two new antibiotic classes, both active only against Gram-positive bacteria, have received global regulatory approval by international regulatory agencies. In the same time period, no new antibiotics against Gram-negative bacteria have been approved. In addition, only two completely new drugs for MDR-TB treatment (bedaquiline and delamanid) have reached the market in over 70 years.

In 2016, at the high-level meeting of the UN General Assembly on antimicrobial resistance, Heads of State directed an unprecedented level of attention to curbing the spread of infections that are resistant to antimicrobial medicines. They reaffirmed their commitment to stopping the misuse of antimicrobial medicines in human health, animal health and agriculture, and recognized the need for stronger systems to monitor drug-resistant infections and the amounts of antimicrobials used in humans and animals. In the wake of the increasing global awareness of the need for new antibiotics, Member States highlighted market failures, and called for new incentives for investment in research and development of new, effective and affordable medicines, rapid diagnostic tests, and other important therapies to replace those that are losing their effectiveness. In response to this and in line with the Global Action Plan on Antimicrobial Resistance to support the identification of pathogens of greatest concern, WHO developed a priority list of antibiotic-resistant bacteria to underpin renewed efforts for the research and development of new antibiotics.

2016 was also the first year of implementation of the WHO End TB Strategy, which was adopted by the World Health Assembly in 2014 and aimed at attaining universal access to TB prevention, diagnosis and treatment. Global TB care and control measures saved an estimated 49 million lives between 2000 and 2015, yet widespread MDR-TB threatens to reverse the gains made from decades of effort to contain the TB epidemic. MDR-TB was declared a global crisis by WHO in 2014, 21 years after TB had been declared a global emergency (in 1993) and despite greatly improved cure rates in patients with drug-susceptible TB. The TB emergency prompted the establishment of new financing mechanisms to support countries in tackling the TB epidemic, most notably the Global Fund and Unitaid. However, investment in research and development for TB has major gaps in the funding needed to develop new tools that would help achieve the targets of the WHO End TB Strategy.

The overall goal of the following report is to present the priority pathogens to be targeted for research and development of new antibiotics to treat drug-resistant bacterial infections and TB. It is acknowledged that viral, fungal and parasitic infections may well need a similar strategy in the near future. The development of new antibiotics to tackle the serious problem of drug-resistant infections needs to be prioritized in the global political agenda of world leaders and health policy-makers. It also needs to be linked to the development of appropriate health-care delivery services and to proper stewardship to safeguard the use of current and future medicines. This challenge cannot be simplified in a "one size fits all" approach. The only possible defence against the threat of antimicrobial resistance and the (very real) possibility of a post-antibiotic era is a global and coordinated effort by all stakeholders. This document reflects the commitment and contribution of WHO and its partners to help establish priorities for critically needed research and development on new antibiotics against drug-resistant bacterial infections and TB, in line with our mission of ensuring health for all.

Dr Tedros Adhanom Ghebreyesus
WHO Director-General

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Acknowledgements

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The report comprises two main sections.

Section 1 describes the current situation with respect to TB and was prepared by Karin Weyer (WHO, GTB).

Sections 2 reports the methods and results of the multi-criteria decision analysis used to prioritize other antibiotic-resistant bacteria and was prepared by Evelina Tacconelli (Tübingen University Hospital, DZIF Partner Center, Germany), and Nicola Magrini (WHO EMP) in collaboration with members of the WHO Priority Pathogens List (PPL) coordinating, advisory and working groups. The contributions of the following individuals are gratefully acknowledged:

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