

FIRST MEETING OF THE WHO ANTIFUNGAL EXPERT GROUP ON IDENTIFYING PRIORITY FUNGAL PATHOGENS

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1. Introduction

This document includes the report and the minutes of the first meeting of the antifungal expert group convened by the World Health Organization (WHO) to develop a priority pathogens list for fungal infections of public health importance and to define the research & development (R&D) priorities. To allow full participation of experts from all parts of the world, the meeting took place virtually in two parts on 7 and 9 April 2020. The Global Action Plan¹ (GAP) on Antimicrobial Resistance (AMR) objective five calls for an increase of sustainable investment in new medicines, diagnostic tools and other interventions. In response to that, in 2017 WHO developed the Priority list of antibiotic-resistant bacteria² to guide R&D of new antibiotics for drug resistant bacterial infections, including tuberculosis. Since then, WHO has been reviewing the clinical antibacterial pipeline³, and since 2019, the preclinical pipeline⁴, on an annual basis to see to what extent global R&D efforts for new antibacterial agents are responding to the antibiotic-resistance priority pathogen list (Figure 1).

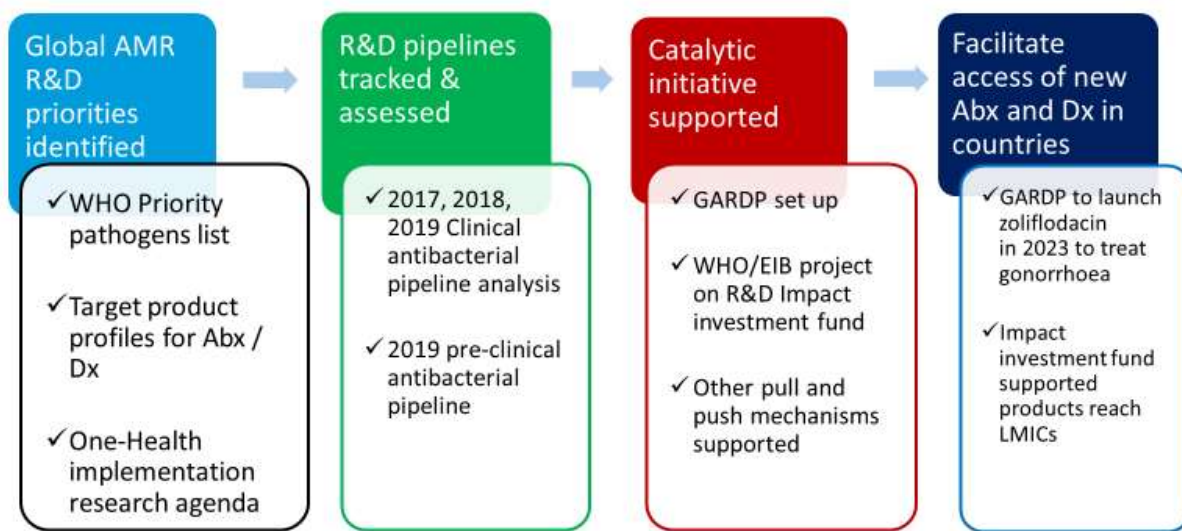


Figure 1. Presentation slide from the meeting on WHO's work on R&D priority setting for AMR

¹ Global action plan on antimicrobial resistance. Geneva: World Health Organization; 2015 <https://www.who.int/antimicrobial-resistance/global-action-plan/en/>, accessed 15/04/2020

² Prioritization of pathogens to guide discovery, research and development of new antibiotics for drug resistant bacterial infections, including tuberculosis. Geneva: World Health Organization; 2017 https://www.who.int/medicines/areas/rational_use/prioritization-of-pathogens/en/, accessed 15/04/2020

³ 2019 antibacterial agents in clinical development: an analysis of the antibacterial clinical development pipeline. Geneva: World Health Organization; 2019 <https://apps.who.int/iris/handle/10665/330420>, accessed 15/04/2020

⁴ Antibacterial agents in preclinical development: an open access database. Geneva: World Health Organization; 2019 <https://apps.who.int/iris/handle/10665/330290>, accessed 15/04/2020

Recognizing the public health threat of the global increase in burden of disease of fungal infections, coupled with existing treatability and resistance issues (both intrinsic and acquired), WHO is extending its efforts to develop a priority fungal pathogens list of public health importance and identify R&D priorities and gaps.

For several fungal diseases, effective treatment is missing altogether. Existing antifungal treatments belong to only a few classes of compounds and the pipeline for new antifungals is sparse. The process of identifying R&D gaps will also take into account possible shortcomings of the current standard of care and diagnostics. The existing treatment of certain fungal infections is challenging, including toxicity issues with long treatment courses and drug-drug interactions, amongst other concerns around the overall lack of treatment options. Availability and access to antifungal treatment and diagnostics are important components in reducing the burden of disease of fungal infections.

To support WHO's efforts on fungal infection R&D priority setting, a WHO expert group on fungal infections has been established for 2020-2021. The aim of the expert group together with WHO is to:

- develop a priority list of fungal pathogens of public health importance;
- define related R&D priorities to align R&D investments with the identified public health needs; and
- review regularly the clinical antifungal pipeline to track trends and guide R&D priorities.

This first (virtual) meeting of the antifungal expert group took place on 7 and 9 of April 2020 to discuss the methodology, pathogen selection and available evidence to begin the prioritization of fungal pathogens of global public health importance for which there is an urgent need for R&D for new treatments.

2. Summary of the meeting proceedings

Two virtual meetings took place with an identical agenda (Annex I). Following a short roundtable of introductions by the participants (Annex II), the meeting began with opening remarks delivered by Haileyesus Getahun (Director of WHO/AMR/GCP). He highlighted WHO's long term vision to enhance its response to address fungal infections of public health importance in the context of drug-resistance, including to guide and stimulate R&D for new treatments, diagnostics and other critical public health interventions.

Peter Beyer (senior advisor, WHO/AMR/GCP) presented the outcome of the assessment of the declaration of interests of the participants. All experts and observers were allowed to participate fully in the meeting (Annex III). The declaration of interest form of Arnaldo Colombo was outstanding; thus his participation was provisional subject to its subsequent assessment. Peter Beyer then presented an overview of WHO's work in R&D priority setting on AMR in accordance

with the Global Action Plan on AMR strategic objective five and outlined the overall aim of the informal expert group on fungal infections.

Following the opening session, two rounds of discussion took place on 1) the methodology, including criteria for the prioritization exercise of fungal pathogens of public health importance that require R&D for new treatments, and 2) the preliminary pathogen selection. At the beginning of each discussion session Laura Jung (Intern, WHO/AMR/GCP) provided a brief presentation, and Sarah Paulin (technical advisor, WHO/AMR/GCP) chaired the discussions and input by experts.

Overview

The aim of the discussion was to seek the views of the experts on the most appropriate methodology to develop a fungal pathogen priority list to guide priority setting for R&D into new treatments. To start the discussion, WHO presented one possible option: to base the exercise on the methodology that was used for the WHO bacterial priority pathogens list⁵ and adapt it to the specificities of fungal infections. This approach used a multi-criteria decision analysis (MCDA)⁶, which utilizes a list of criteria and combines evidence-based data and expert opinion. The following background work was undertaken by the WHO team in preparation for the meeting and was presented to provide a starting point for the expert group discussion:

Initial literature review: a literature review was conducted by the WHO team in January 2020 which identified the absence of any existing global prioritization with regard to R&D for fungal infections. It was noted that three fungal infections were included in the CDC priority threat list (2019)⁷.

Preliminary selection of fungal pathogens: an initial selection of fungal pathogens was developed by the WHO team for discussion with the experts. This selection focused on pathogens that cause invasive fungal infections and was based on the CDC Antibiotic Resistance Threats Report (2019) and expert opinion from different internal WHO departments.

Draft selection of criteria for prioritization: based on the criteria of the priority pathogens list for antibiotic-resistant bacteria, six criteria were initially chosen by the WHO team with relevance to fungal infections:

- a. mortality;

⁵ Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. Geneva: World Health Organization; 2017 https://www.who.int/medicines/publications/WHO-PPL-Short_Summary_25Feb-ET_NM_WHO.pdf, accessed 15/04/2020

⁶ Tacconelli E., Carrara E., Savoldi A., Harbarth S., Mendelson M., Monnet D. L. Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis. *Lancet Infect Dis.* 2018 Mar;18(3):318-327, accessed 15/04/2020

⁷ Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019 <https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf>, accessed 15/04/2020

- b. community burden;
- c. health-care burden;
- d. proof / prevalence of resistance;
- e. transmissibility; and
- f. treatability.

In addition, a criterion for the R&D pipeline analysis was suggested, to be completed once the initial list has been agreed with the experts.

Data extraction and synthesis: for the preliminary list of fungal pathogens and criteria, the WHO team reviewed the existing published literature and international treatment guidelines and summarized the evidence in a performance matrix, which was provided to the experts ahead of the meeting (Annex IV).

Through two subsequent sets of discussions, the participants were asked to comment on 1) the draft methodology, and 2) the selection and prioritization of fungal pathogens of public health importance.

In the first set of discussions the participants were asked to comment on the initial approach presented for the methodology and the appropriateness of MCDA with regard to fungal pathogens. The participants were also invited to provide comments on the initial list of criteria, in particular the comprehensiveness of the criteria, as well as the possibilities of weighing and stratifying the criteria.

During the second set of discussions the participants were invited to comment on a preliminary selection of fungal pathogens and to evaluate the significance of the chosen pathogens for global public health that would require urgent R&D treatments, taking into account existing resistance and treatability issues. In addition, experts were asked to suggest any additional pathogens that should be considered for inclusion in the long list from which the priorities will be identified, and how the prioritization process should be conducted.

Summary of discussion points on the methodology

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