ANTIBACTERIAL AGENTS IN PRECLINICAL DEVELOPMENT

an open access database



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Discussion and conclusions

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Executive summary

This is the World Health Organization's first comprehensive overview of the preclinical antibacterial pipeline to date based on publicly available data on each included project. This report and the respective WHO database capture 252 antibacterial agents in development targeting the pathogens on the WHO priority pathogens list (Annex I), *Mycobacterium tuberculosis* and *Clostridioides difficile*. The preclinical pipeline is dynamic and scientifically diverse, with agents being developed in many parts of the world to prevent and treat drug-resistant bacterial infections:

- 252 agents are being developed by 145 individual institutions that target the WHO priority pathogens, *M. tuberculosis* and *C. difficile*.
- The review captures research projects from institutions with a wide geographical distribution, 66 (45.5%) institutions in the European Region, 51 (35.2%) in the Region of the Americas, 22 (15.2%) in the Western Pacific Region, 5 (3.4%) in the South-East Asia Region and 1 (0.7%) in the African Region.
- 108 (42.9%) are direct-acting small molecules (single agents) and 90 (35.7%) are nontraditional products that include phages, anti-virulence agents, immunomodulators, microbiome-modifying therapies and potentiators, among others.
- 100 (39.7%) agents target a single pathogen, of which 43 target *M. tuberculosis*.
- Almost 1/3 of the agents target cell wall synthesis or act directly on the membrane.
- Approximately 2-5 direct-acting small molecules and 1 nontraditional product may make it to the market in the next 10 years.
- The preclinical pipeline is dominated by small and medium-sized enterprises (n = 104, 71% of all institutions that submitted data).
- This is the first review of the preclinical pipeline that makes all of the drug development projects and institutions available through a public database.

The WHO database of the preclinical pipeline reflects approximately 84% (252 out of 304) of preclinical pipeline projects that were published in a recent anonymized preclinical review¹ based primarily on data from confidential funding sources. The review captured 407 products from the hit to lead to CTA/ IND (Clinical Trial Application/Investigational New Drug Application) enabling studies phases. Of these products, 304 had entered the lead optimization or CTA/IND-enabling studies phase (the scope of this current report).

The data at the product level is available and downloadable on the WHO Global Observatory on Health R&D (https://www.who.int/research-observatory/monitoring/processes/antibacterial_products_preclinical/en).

WHO will continue to review the preclinical and clinical antibacterial pipeline and make the data available on a regular basis to promote innovation, collaboration and transparency as well as to track evolution of the pipeline and see how the antibacterial research and development ecosystem is responding to the priority pathogens list. The ultimate aim is to collectively move forward in developing antibacterial treatments that can treat drug-resistant bacterial infections.

If you have comments or have products that should be included in this review, please contact antibacterialpipeline@who.int.

¹ Theuretzbacher U, Outterson K, Engel A, Karlén A. The global preclinical antibacterial pipeline. Nat Rev Microbiol. 2019. doi:10.1038/ s41579-019-0288-0.

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