Every year, drug-resistant infections are responsible for the loss of 700,000 lives worldwide. Without the development of new, lifesaving antibiotics, the numbers will continue to increase. The Global Antibiotic Research & Development Partnership (GARDP) works with partners to discover, research and develop new treatments to address this critical need.

Our discovery and exploratory research activities play a vital role in finding novel antibiotic substances (compounds). Once identified and optimized, these compounds may enter preclinical development and feed into the global antibiotic pipeline and possibly be future candidates for GARDP’s clinical programmes focused on difficult-to-treat infections, high priority pathogens, and vulnerable populations.

THE GAP IN ANTIBIOTIC R&D

Antibiotics have been used so extensively since their discovery that many species of bacteria have become resistant to them. While new antibiotics have been discovered, the pace of moving these from the test tube to the patient has been slow. Discovering new antibiotics that overcome resistant bacteria can be scientifically challenging, but the lack of economic incentive to develop new drugs is the main problem. Newly approved antibiotics usually have short treatment durations, with restrictions on their use to slow the emergence and spread of drug resistance. With limited prospects of return on investment, many in the private sector have left this field of research.

Today, the best chance to fill this void and secure an antibiotic pipeline for the future is through public-private partnerships, with all stakeholders working together.

BUILDING AN ANTIBIOTIC DISCOVERY PIPELINE

At GARDP we drive innovative research to deliver antibiotic treatments that will have the greatest public health impact, focusing on neglected areas of research.

Discovery is the first stage of antibiotic R&D, which seeks substances that have the potential to become treatments. The process of identifying new targets for antibiotics and screening compound libraries, to having optimized lead compounds ready for preclinical development can take many years of research, requiring significant investment and resources. However, these activities lay the essential foundations of discovery research and are necessary to secure much needed novel antibiotics for the future.

In South Africa (2018), the bacterium most often isolated from patients with bloodstream infections is Klebsiella pneumoniae, which is usually resistant to common antibiotics (—68% resistant to extended spectrum beta-lactams). One in 12 isolates were also resistant to carbapenems, a class of antibiotics used to treat multidrug-resistant infections.1

Department of Health Republic of South Africa. Antimicrobial Resistance.

PRIORITY PATHOGENS

Drug-resistant infections caused by Gram-negative bacteria1 are a significant concern and have been identified as a critical priority for new treatments by the World Health Organization (WHO).

GARDP’s discovery and exploratory research activities currently focus on two Gram-negative bacterial species (Klebsiella pneumoniae and Acinetobacter baumannii) on WHO’s critical priority list - these often cause difficult-to-treat hospital-acquired infections, including bloodstream infections.

1Gram-negative bacteria cause infections including pneumonia, bloodstream infections, wound or surgical site infections, and meningitis in healthcare settings. Gram-negative bacteria can be resistant to one or many drugs and are increasingly resistant to most available antibiotics. Bacteria are often easily able to become drug-resistant and can pass along many drug-resistance genes to other bacteria so that they too become drug-resistant.

2Department of Health Republic of South Africa. Antimicrobial Resistance.
WHAT IS GARDP DOING?

To date, GARDP has screened over 100,000 compounds or extracts of bacteria containing natural product antimicrobial substances and evaluated more than 10 chemical series for antibacterial activity. Four of these have moved to further hit expansion evaluation.

- GARDP established the AMR Screening Consortium; this currently comprises three Japanese pharmaceutical companies - Eisai, Takeda and Daiichi Sankyo - to access and screen libraries from the companies’ proprietary chemical compound collections that have not previously been tested for antibiotic activity. Based on a strategy developed by GARDP, three libraries were screened at the Institut Pasteur Korea, an infectious disease-focused research institute.
- GARDP has partnered with the U. S. non-profit translational research institute Calibr at Scripps Research to screen its ReFRAME compound library for compounds that potentiate the activity of a clinically useful antibiotic increasingly affected by drug-resistance.
- GARDP has partnered with Germany’s Helmholtz Institute for Pharmaceutical Research Saarland to screen its natural products library, and further isolate and characterize new natural product entities with activity against Klebsiella and Acinetobacter.

GARDP is also exploring opportunities for the discovery of novel antibiotics active against under-exploited targets in bacterial cells.

“Eisai strongly identifies with GARDP’s efforts to discover novel antibiotics to treat drug-resistant infections, which have become a threat to humans. We are pleased to provide our compound library for screening. We hope new medicines will be discovered through this partnership to realize a world in which lives are no longer lost to drug-resistant bacteria.”

DR KAPPEI TSUKAHARA
HEAD OF TSUKUBA RESEARCH LABORATORIES, EISAI

“The world needs global cooperative action to prevent a post-antibiotic era. This work, instigated by GARDP, is an active response to this urgent global demand that connects Institut Pasteur Korea’s resource with the technology of global pharmaceutical companies.”

CEO OF INSTITUT PASTEUR KOREA
DR WANGSHICK RYU