ACTIVITY REPORT 2020

EXECUTIVE SUMMARY

Global Antibiotic
Research & Development
Partnership

GARDP

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EXECUTIVE SUMMARY

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MESSAGE

FROM THE EXECUTIVE DIRECTOR & BOARD CHAIR

2020 was an extremely challenging year for all of us. COVID-19 has brought tragic loss, suffering and disruption to every corner of the world. And it will do so until we finally contain this virus.

We would like to thank our partners, supporters and colleagues for their unwavering commitment to **GARDP** and its vital work against this extraordinary backdrop of adversity. Thanks to their courage and enthusiasm 2020 was a year in which we were able to make remarkable progress despite the many challenges.

If 2020 reminded us of one crucial fact, it is that infectious diseases have no regard for national borders. And, ideally, neither should drugs or vaccines. The only way to contain COVID-19 and ensure we are more prepared for future pandemics will be through a coordinated global effort—no country nor sector will succeed by going at it alone. And just as pandemic preparedness has become a priority for countries, so awareness has grown of the need to tackle the slower-moving, silent pandemic of antibiotic resistance.

GARDP is calling on the world to support the delivery of five new treatments by 2025 to tackle the drug-resistant infections that pose the greatest threat to global health. We are seeking €500 million to develop these treatments and ensure their responsible use and sustainable access.

Your support will allow us to develop new and lifesaving treatments. It will fund critical work to enable access to antibiotics for every person who needs them and to ensure treatments remain effective for as long as possible.

We at **GARDP**, together with our partners from the public and private sectors, will redouble our efforts to ensure that antibiotic resistance never paralyzes the world as the COVID-19 pandemic has this past year. As we begin to look forward to life beyond this global health crisis, we and the whole team are looking forward to the next chapter of our work in tackling another great health challenge of our time.

Professor Ramanan Laxminarayan
GARDP BOARD CHAIR

Dr. Manica Balasegaram
GARDP EXECUTIVE DIRECTOR

HIGHLIGHTS

2020 MILESTONES

GARDP's Activity Report highlights our key achievements in 2020, an extremely challenging year in light of the COVID-19 pandemic, which brought suffering, disruption and economic hardship to virtually every corner of the globe.

We are proud of the progress we made in 2020 towards building our antibiotic portfolio and achieving our 5 BY 25 goal: to deliver five new treatments to tackle drug-resistant infections that pose the greatest threat to health by 2025.

2020 MILESTONES

1. Completed a landmark observational study on neonatal sepsis and finalised a clinical study report on the pharmacokinetic clinical trial assessing the safety and dosing of fosfomycin in newborns.
2. Successfully identified one potential antibiotic combination of fosfomycin-amikacin to treat neonatal sepsis.
3. Signed first agreement of GARDP's Serious Bacterial Infections programme and started the first project to bring a new drug to market.
4. Continued patient enrolment, including a new site in The Netherlands, as part of our phase 3 trial of a new treatment f or gonorrhoea.
5. Organized 17 REVIVE webinars and launched a new online Antimicrobial Encyclopaedia.
6. Screened over 24,000 compounds from five different partners. Daiichi Sankyo joined the GARDP-led Antimicrobial Resistance Screening Consortium alongside Eisai and Takeda.

CHILDREN'S ANTIBIOTICS

DEVELOPING NEW AND IMPROVED TREATMENTS FOR CHILDREN

In July, following a minimal pandemic-related delay, GARDP locked the database on Neo-AMR Observational Study (NeoOBS), one of the largest global observational studies on the care of newborns with sepsis. This study, which involved more than 3,200 newborns at 19 sites across 11 countries, will provide the evidence we need to fill knowledge gaps, improve treatments and save lives. The full results of this landmark observational study will be published once the analysis is complete. The results from the NeoOBS study will also inform the design of a large strategic public health clinical trial—slated to commence in 2022—that will evaluate the potential of antibiotic combinations in treating neonatal sepsis.

Over **5 million** babies are diagnosed with neonatal sepsis annually.[1]

GARDP finalised a clinical study report on the pharmacokinetic clinical trial in Kenya assessing the safety and dosing of fosfomycin in newborns, which completed enrolment in 2019. Results from this study, run in partnership with the KEMRI-Wellcome Trust Research Programme, Centre for Tropical Medicine and Global Health at the University of Oxford, Medical Research Council Clinical Trials Unit at University College London and St George's University of London, will inform the dosing of future work to develop effective treatments for neonatal sepsis.

GARDP has successfully identified three existing antibiotics - fosfomycin, flomoxef, and amikacin - as potential alternative treatments to ampicillin-gentamicin, the WHO standard of care for neonatal sepsis in most settings. Together with partners we have completed the assessment of fosfomycin-amikacin and fosfomycin-flomoxef combinations using a hollow fibre infection model to assess the pharmacokinetic and pharmacodynamic properties of the combinations as well as their ability to prevent the emergence of resistance. This work is ongoing for the third combination of flomoxef and amikacin.

Following the agreement signed between **GARDP** and Venatorx Pharmaceuticals, one of the first compounds we are examining is cefepime-taniborbactam, which is currently undergoing a phase 3 trial for use in adults. **GARDP** will seek regulatory approval for the use of cefepime-taniborbactam in children and newborns.

Up to **40% of bacterial infections** in hospitalized babies are resistant to standard treatments.[2]

[1] *Rudd K E, Johnson S C, Agesa K M, Shackelford K A, Tsoi D, Kievlan D R et al. 'Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study'. The Lancet. 2020;395(10219):200–211*
[2] *WHO. https://www.who.int/mediacentre/commentaries/antibiotic-resistant-bacteria/en/*

SEXUALLY TRANSMITTED INFECTIONS

DEVELOPING A NEW TREATMENT FOR GONORRHOEA DURING A GLOBAL PANDEMIC

As part of GARDP's partnership with Entasis Therapeutics to develop zoliflodacin, a novel antibiotic to treat resistant strains of gonorrhoea, patient recruitment was well underway at US sites in early 2020. Preparations to activate sites in The Netherlands, South Africa and Thailand were also quite advanced.

However, as the COVID-19 pandemic unfolded, it soon became clear that we would be unable to continue the trial in a way that guaranteed the safety of everyone involved while also managing the logistical issues the crisis created. Although we were forced to place the trial on hold in March, we immediately focused our attention on creating a strategy that would enable us to safely re-launch the study. Thanks to that hard work, we have already been able to resume patient recruitment in the US and enrol our first Dutch patients at our site in The Netherlands. Furthermore, we successfully managed to activate our sites in South Africa and Thailand in early 2021. The trial aims to enrol approximately 1,000 adults with urogenital gonorrhoea from clinical trial sites in the four countries.

In Q4 2020, **GARDP** initiated a consultation process with key experts around zoliflodacin to identify the evidence necessary to understand public health need, optimize clinical management and support optimal use. We expect to finish the process by end 2021.

Activities are already progressing to understand the prevalence of gonorrhoea in priority countries (including Kenya, South Africa and Thailand) and the levels of antibiotic resistance in the relevant bacteria.

10,000 people are infected with gonorrhoea every hour.[3]

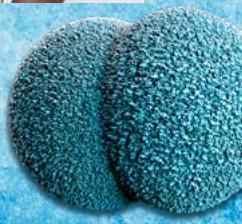
In November 2020, **GARDP** partnered with the Foundation for Innovative New Diagnostics (FIND) and the World Health Organization (WHO) to explore joint initiatives, with an initial priority focus on STIs, that could improve sustainable access to antibiotics and protect them against the emergence of antimicrobial resistance.

We will work on a joint project to roll out and scale up the use of a point-of care test along with zoliflodacin treatment for improved clinical management, stewardship and public health value. This will generate the evidence required to strengthen national and international treatment guidelines and implementation strategies.

[3] *WHO. https://www.who.int/news-room/fact-sheets/detail/multi-drug-resistant-gonorrhoea*

SERIOUS BACTERIAL INFECTIONS

NEW PARTNERSHIP TO TREAT HOSPITAL INFECTIONS



In LMICs, **10% of hospitalized patients** will develop an infection, including one in two people in intensive care units.[4]

In April, **GARDP** signed a collaboration agreement with Venatorx Pharmaceuticals, the first partnership of our new Serious Bacterial Infections programme. We are working with Venatorx to accelerate the development of cefepime-taniborbactam, a new compound that shows activity against two of WHO's three priority pathogens for which we urgently need to develop new drugs due to their growing resistance to existing antibiotics - *Enterobacterales* and *Pseudomonas aeruginosa*. We are supporting a phase 3 Venatorx-sponsored trial to test the efficacy and safety of cefepime-taniborbactam in patients with complicated urinary tract infections (cUTI). This pivotal trial will pave the way for the initial new drug registration and eventual approval of cefepime-taniborbactam by the FDA and EMA.

Our collaboration with Venatorx includes an observational study that will examine the frequency, treatment methods and outcomes in patients with carbapenem-resistant bacterial infections. Since such infections are particularly prevalent in India and South Africa, the sites involved in the observational study will be located in these two countries and are likely to participate in a future interventional trial of cefepime-taniborbactam in serious carbapenem-resistant bacterial infections.

[4] *WHO Healthcare-associated infections fact sheet. https://www.who.int/gpsc/country_work/gpsc_ccisc_fact_sheet_en.pdf*
[5] *WHO Healthcare-associated infections fact sheet. https://www.who.int/gpsc/country_work/gpsc_ccisc_fact_sheet_en.pdf*

In high-income countries, **7% of all hospitalized patients** will contract an infection, including one in three people in intensive care units.[5]

Despite delays due to COVID-19, crucial preparatory and mitigating steps have been undertaken, enrolment for the cUTI trial is to be completed in 2021, and we will begin recruiting for the observational study in early 2022.

Cefepime-taniborbactam has the potential to address a significant unmet need as a new treatment for antibiotic-resistant infections in adults and children, and we will work closely with Venatorx to make it available to everyone who needs it, wherever they live.

*"Our partnership with **GARDP** is vital for safeguarding our ability to advance cefepime-taniborbactam through phase 3 clinical trials and afford access to patients, including children, who are more susceptible to hard-to-treat bacterial infections."*

CHRISTOPHER J. BURNS
Ph.D., PRESIDENT AND CEO OF VENATORX PHARMACEUTICALS

ADVANCING ANTIOBITIC R&D

RESTORING OUR ANTIBIOTIC PIPELINE & KNOWLEDGE SHARING

ASSET EVALUATION AND DEVELOPMENT

We evaluated 10 new assets by conducting systematic reviews and meta-analyses of antibiotic combinations used on carbapenem-resistant pathogens. In 2021, **GARDP** aims to confirm a development asset that could address those difficult-to-treat resistant infections in children not covered by our current portfolio.

DISCOVERY AND EXPLORATORY RESEARCH

As part of **GARDP**'s Discovery and Exploratory Research activities, over 24,000 compounds from five different partners were screened in 2020. Daiichi Sankyo joined the Antimicrobial Resistance (AMR) Screening Consortium led by **GARDP** and contributed a chemical library from their proprietary collection for screening in **GARDP**-designed antibacterial assays performed by the Institut Pasteur Korea.

SCIENTIFIC AFFAIRS

Due to the COVID-19 pandemic, we transitioned entirely to online conferences and webinars in 2020. This move did not hinder the ongoing success of the online platform REVIVE, which promotes the retention and sharing of knowledge among the antimicrobial R&D community. We reached over 3,800 people from more than 100 countries through 17 REVIVE webinars last year, with the platform's overall content library now available worldwide. We also organized 3 corporate webinars and one with the Union for International Cancer Control (UICC) on AMR and cancer. The new online Antimicrobial Encyclopaedia was launched in time for World Antimicrobial Awareness Week in November. In 2021, a new webinar series, AMR Discussions, will be launched.

LEARNING THE LESSONS OF COVID-19

The COVID-19 pandemic has brought into sharp focus the impact of pandemics, in which more than three million people have died, trillions of dollars have been lost, expenditures cut and international efforts to achieve the Sustainable Development Goals put in jeopardy.

In a November 2020 report[6], **GARDP** called on governments around the world to work with both the public and private sectors on bringing the lessons of COVID-19 to bear on drug-resistant infections. This silent pandemic existed before and will endure beyond the crisis that stopped the world in 2020—and may yet turn out to be even more devastating.

There are vital lessons to learn from this public health tragedy. Now more than ever, governments have the opportunity to make robust and comprehensive investments into the way they prepare and respond to pandemics. This has the potential to translate into long-term, interlinked health and economic benefits for people and countries.

Unless we successfully tackle the spread of antibiotic resistance, even common infections will become significantly more difficult to treat. Better access to the right antibiotics will, therefore, be vital in ensuring that we are prepared for future pandemics and in tackling the silent pandemic of drug-resistant infections.

[6] https://gardp.org/news-resources/learning-covid19-antibiotic-resistance/

*"The COVID-19 pandemic has brought into sharp focus the impact of pandemics and the importance of preparedness. It has demonstrated that addressing the silent pandemic of drug-resistant infections can only be achieved through greater international cooperation and investment. As host country, Switzerland recognizes the major role **GARDP** plays at the global level in the fight against antibiotic resistance."*

ALAIN BERSET
FEDERAL COUNCILLOR, HEAD OF THE FEDERAL DEPARTMENT OF HOME AFFAIRS (FDHA), SWITZERLAND

A NEW ACCESS MODEL FOR ANTIBIOTICS

The global health threat of poor access to antibiotics urgently requires us to develop new concepts and mechanisms to improve the availability and affordability of these life-saving drugs. To that end, **GARDP** has developed an access strategy that focuses on four pillars - evidence generation, early introduction, regulatory, and sustainable manufacturing and commercialisation. **GARDP** is working with WHO and other international organizations on a new initiative called SECURE that will examine new access models for essential antibiotics, particularly for countries with a high-burden of drug-resistant bacterial infections.

Besides helping countries fight drug-resistant infections, **GARDP** expects this endeavour to benefit the global public health community by ensuring antibiotic security, a key component of pandemic preparedness.

*" **GARDP** has shown great progress in driving forward global health goals in such a challenging year. The UK is proud to partner with them in leading the fight against antimicrobial resistance."*

LORD BETHELL
UK MINISTER FOR INNOVATION

PARTNERS

A WORD OF THANKS

GARDP's lifesaving work is possible through smart, effective partnerships. **GARDP** brings together governments, the pharmaceutical and biotech industry, academia, and civil society to build an antibiotic portfolio and deliver 5 new treatments by 2025 for drug-resistant infections that pose the greatest threat to health.

Partnerships are at the heart of our success in developing new and improved treatments. We would like to sincerely thank the more than 60 partners in 22 countries that are helping us achieve our social mission.

GARDP is extremely grateful for the commitment of all its partners in helping us address the silent pandemic of antibiotic resistance. Thank you for your loyal support.

*"Antibiotic research and development needs an urgent boost now more than ever, and **GARDP** is part of the solution. As a **GARDP** Board Observer, I am honoured to support **GARDP** in its efforts to ensure that new and effective treatments against drug-resistant infections are made accessible to all."*

PROFESSOR HANAN H. BALKHY
ASSISTANT DIRECTOR-GENERAL FOR ANTIMICROBIAL RESISTANCE
WORLD HEALTH ORGANIZATION

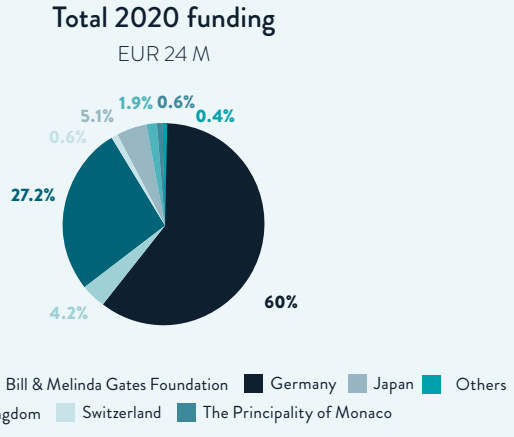
FINANCE

INCOME

NEW AND RENEWED FUNDING SHOWS COMMITMENT TO GARDP MISSION

GARDP's income grew by 27% between 2019 and 2020. Germany's Federal Ministry of Education and Research (BMBF) and the UK's Department of Health and Social Care (DHSC) increased their financial support to **GARDP** in 2020 by contributing a further EUR 5M and £2.5M respectively. The Leo Model Foundation also extended its support to **GARDP** with an additional USD 50,000. New funding of $1.8M was received from the Japanese Ministry of Health, Labour and Welfare, with a pledge for a further $7.2M over the next four years, bringing the total amount of funding in 2020 to EUR 24M. By the end of 2020, **GARDP** had secured a total of EUR 97 million in commitments (91M) and pledges (6M).

FUNDER	%	IN M EUR
Germany (BMBF & BMG)	60 %	14.5 M
Netherlands (VWS)	4.2 %	1.0 M
United Kingdom (DFID, DHSC - GAMRIF and NIHR)	27.2 %	6.5 M
Switzerland (FOPH)	0.6 %	0.1 M
Japan (Ministry of Health, Labour & Welfare)	5.1 %	1.2 M
Bill and Melinda Gates Foundation	1.9 %	0.5 M
The Principality of Monaco	0.6 %	0.1 M
Others (South African MRC, Leo Model Foundation, Ministry of Health, Luxembourg)	0.4 %	0.1 M
Total		24 M



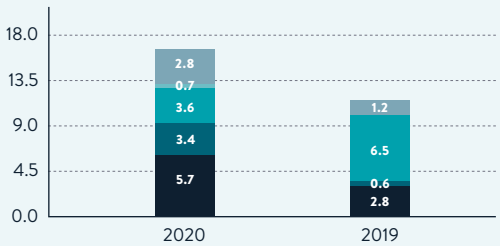
FINANCE

EXPENDITURE

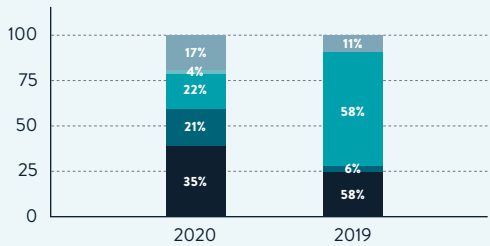
R&D EXPENDITURE

R&D spending per programme increased by EUR 5M in 2020 compared to 2019, with the largest proportion being spent within the Children's Antibiotics programme - Neonatal Sepsis (EUR 5.7 M), followed by the Sexually Transmitted Infections programme (EUR 3.6 M).

R&D expenses per programme
(In million EUR)

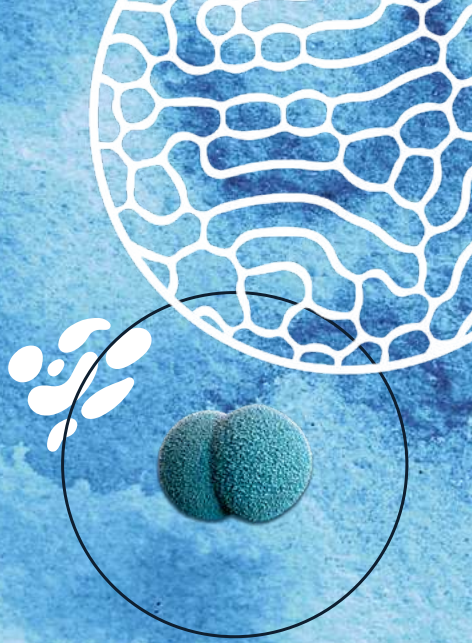


R&D expenses per programme
(In %)



Children's Antibiotics - Neonatal Sepsis
Children's Antibiotics - Paediatric Development
Sexually Transmitted Infections
Advancing Antibiotic R&D*
Serious Bacterial Infections

** - Previously called Antimicrobial Memory Recovery and Exploratory/Discovery & Exploratory in 2019 report*
*** Extracted from the unaudited "2020 Finance & Performance Report". The full report, audited by Deloitte, will be available in July 2021 on www.gardp.org*



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The Global Antibiotic Research and Development Partnership (GARDP) is a Swiss not-for-profit organization developing new treatments for drug-resistant infections that pose the greatest threat to health. GARDP was created by the World Health Organization (WHO) and the Drugs for Neglected Diseases initiative (DNDi) in 2016 to ensure that everyone who needs antibiotics receives effective and affordable treatment. We aim to develop five new treatments by 2025 to fight drug-resistant infections.


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