A joint DNDi / WHO initiative

Global Antibiotic Research & Development Partnership

BUSINESS PLAN

2017-2023

Developing new antibiotic treatments and ensuring sustainable access for all
Addressing a looming crisis

Antimicrobial resistance (AMR), also referred to as drug resistant infections, is outpacing drug discovery at an alarming rate. The fact that microorganisms can evolve to survive exposure to antimicrobial drugs is an inevitable part of nature, and, without the necessary tools to counter this phenomenon, human morbidity and mortality can drastically increase. Overuse and misuse of drugs, poor infection prevention and control, lack of quality medicines, and inadequate investment in new drug development are exponentially multiplying resistant organisms. We face a future where once treatable infections will again become life-threatening, where the medical breakthroughs against infectious diseases made in the last half-century will be in peril, and where prolonged illness, disability, and death will loom.

While, encouragingly, a number of initiatives have been launched in the past years that aim to reinvigorate the antibiotic research and development pipeline, more can and must be done to provide the necessary tools to cope with the magnitude of the public health challenges we face today.
A unique approach to R&D for new antibiotic treatments

The Global Antibiotic Research and Development Partnership (GARDP) was established in May 2016 as a joint initiative by the World Health Organization (WHO) and the Drugs for Neglected Diseases initiative (DNDi). As an important element of the WHO Global Action Plan on Antimicrobial Resistance, this not-for-profit research and development (R&D) organization addresses global public health needs by developing and delivering new or improved antibiotic treatments while endeavouring to ensure sustainable access.

VISION

GARDP’s vision is a world where patient needs-driven R&D ensures that effective, appropriate, and affordable antibiotic treatments are developed and available to all as a global public good.

MISSION

GARDP’s mission is to work in partnership with the public and private sectors to develop and deliver new treatments for bacterial infections where drug resistance is present or emerging, or for which inadequate treatment exists.
GARDP is a great initiative. GARDP benefits from decades of collective experience on the front lines of Research & Development and Antimicrobial Resistance garnered by WHO and DNDi.

— Mr Hermann Gröhe, Federal Minister of Health, Germany

The origins of GARDP

GARDP is built on the shared missions of WHO and DNDi. The new organization draws its strength from both: WHO’s mandate to drive the global response to antimicrobial resistance and set health priorities, and DNDi’s expertise in harnessing partnerships to build a pipeline for neglected diseases and deliver not-for-profit, needs-driven R&D.

A UNIQUE PARENTAGE

GARDP benefits from a unique parentage: WHO provides support in setting priorities and target product profiles, leads the Global Development and Stewardship Framework for AMR, garners Member State support, and ensures effective liaison with relevant WHO departments.

DNDi is responsible for hosting and facilitating GARDP. It provides the governance, scientific environment and input, and infrastructure, as well as support for resource mobilization, communication, finance and human resources necessary to build and launch solid R&D programmes. GARDP is led by its Director who also serves as a member of DNDi’s executive team. DNDi’s Board of Directors oversees GARDP’s activities, with expert advice from the GARDP Scientific Advisory Committee of renowned experts in the field of antimicrobial resistance and drug development.
Starting in 2014, WHO and DNDi jointly developed the concept of setting up a new product development partnership through various consultations with Member States and other stakeholders. The idea was to set up a new initiative that would eventually become a dedicated entity, similar to DNDi’s own incubation by the medical humanitarian organization Médecins Sans Frontières (MSF) in 2003. DNDi’s consultations with its founding partners and key global public health actors during the revision of its business plan identified drug-resistant infections as an important area of unaddressed patient needs, paving the way for the incubation of GARDP.

In 2015, WHO Member States adopted the GAP-AMR from which the need to ‘create new public-private partnerships for R&D of new antimicrobial agents and diagnostics’ was identified. A technical consultation was held at WHO with Member States and other key stakeholders to discuss the proposed concept of such a product development partnership. With the support emanating from this meeting, DNDi’s Board of Directors approved of the incubation of GARDP.

Initiated and incubated through close collaboration between WHO and DNDi, GARDP was launched in May 2016. Since then, GARDP has received seed funding and pledges from the governments of Germany, Netherlands, South Africa, Switzerland, and the United Kingdom of Great Britain and Northern Ireland as well as from MSF.

By early 2017, GARDP has secured EUR 6.5 million in seed funding, built a team of 10, facilitated 11 expert meetings in 6 countries on specific disease areas, regional issues, project reviews, and sustainable access. A Scientific Advisory Committee of AMR and drug development experts has been set up. With their expert review and DNDi’s Board of Directors’ validation, GARDP is ready to launch three programmes with one more in development.
The focus: unaddressed public health gaps

GARDP’s work begins with prioritizing R&D to focus **on unaddressed public health gaps**, notably for drug-resistant bacterial infections. Through partnership, collaboration, and coordination as well as the adoption of innovative business models, GARDP will ensure that R&D investment offers public health returns, delinking the cost of antibiotic treatments from the price of the products and volume-based sales. The goal is for effective antibiotic treatments to be made affordable and accessible to all in need and in a manner which minimizes the risk of inducing resistance. GARDP will work by prioritizing and then directly executing R&D programmes as well as establishing broader collaborative partnerships to deliver on its mission and vision.

**GARDP’s Objectives for the Period 2017 to 2023**

- Secure EUR 270 million to execute its R&D programmes, build a highly experienced R&D team, and establish a dedicated entity
- Develop and deliver up to four new treatments through improvement of existing antibiotics and acceleration of the entry of new chemical entities
- Build a robust pipeline of pre-clinical and clinical candidates with up to four candidates brought into pre-clinical or clinical development
- Support and advocate for appropriate use of antibiotics, sustainable access, and suitable financing of R&D for new antibiotic treatments
A prioritization process to guide R&D

To ensure that GARDP focuses its scientific portfolio towards meeting priority needs, its R&D prioritization process begins with the requirement that any programme meets at least two out of three key criteria:

1. target priority pathogens
2. address priority diseases and syndromes
3. help underserved priority patient populations.

Combining these three fields provides a decisional tool to identify priority needs. Attention will be brought to ensuring that no efforts undertaken by others are duplicated. This prioritization process capitalizes on WHO’s prior and ongoing work on:

- prioritization and review of pathogens through the Priority Pathogens List that clearly shows the need to address certain gram-negative bacteria
- priority infectious disease syndromes review that points to major evidence-base gaps particularly on paediatric populations, and
- a qualitative and quantitative review of the antibiotic R&D pipeline.

Potential programmes are then subjected to the following criteria before selection as part of the GARDP portfolio:

- global health need with clear relevance for developing countries
- gap in R&D left by existing actors
- potential for short- to medium-term fruition
- R&D opportunity and potential to partner effectively, and
- potential or ability to test and/or apply access and stewardship strategies.

Other published literature and reports, as well as stakeholder consultations, form part of this prioritization process.

GARDP will promote and stimulate diagnostic actors and funders to engage in relevant R&D for diagnostics, especially where this will contribute to improved use of drugs in GARDP programmes.

Focus on gram-negative bacteria and multidrug-resistant pathogens; certain fungal pathogens may also be considered.

e.g. Neonates and children, immunocompromised patients, marginalized and underserved populations

e.g. Sepsis, sexually-transmitted infections and potentially enteric infections

DEFINING PRIORITIES
A public health oriented scientific strategy

Building on DNDi’s experience in developing an R&D pipeline for neglected diseases, GARDP’s strategy for antibiotic drug development comprises a mix of short- and long-term approaches. GARDP will focus on drug-resistant bacterial infections, including serious infections for which adequate treatment is not available. Bacterial infections are spread globally, so GARDP will maintain a global focus, including attention to the needs of low- and middle-income countries.

**Short- to medium-term strategy:**
GARDP identifies and builds on short-term opportunities to help improve and extend the use of existing antibiotics and accelerate the entry of pipeline products for relevant public health needs. This also serves as a ‘bridge’ until novel antibiotics become available.

**Long-term strategy:** GARDP will explore and advance early-stage, needs-based R&D activities unpursued by other actors.

GARDP will employ a portfolio approach, ensuring that projects begin with the end-goal in mind and are driven by target product profiles that define the key characteristics for a treatment and keep patients’ needs at the centre of decision making. GARDP will implement comprehensive programmes, each comprising specific projects that may start at any stage of the R&D pipeline – from discovery to implementation. Projects will be pushed through the pipeline until treatments reach patients.

**R&D INTERVENTIONS**

GARDP will consider whether there is a valid entry point for an identified priority based on three major types of interventions. The choice of these interventions is based on consultation with external stakeholders and DNDi’s experience over the last 13 years.

- **Optimizing the use of antibiotics** by improving dosing, treatment duration, formulation, drug repurposing, and new combinations (with old, new, and non-antibiotics) to improve treatment for important and drug-resistant bacterial infections
- **Accelerating, re-starting, and recovering** the development of new and abandoned drug candidates that address public health priorities and vulnerable populations (e.g. people living with sexually-transmitted infections (STIs), newborns)
- **Exploring novel and innovative drug development approaches** with a longer-term view towards meeting patients’ needs.
Portfolio selection process for initial business plan

At the heart of the portfolio selection process are Target Product Profiles (TPPs) which provide an overview of the ideal characteristics of a treatment or product being considered for inclusion into the GARDP portfolio. They guide the development, use, and impact of a product or treatment. They are also an important tool in go/no-go decision-making within a programme.

Guided TPPs are developed very early on the lifetime of every GARDP programme to manage the specific project and required work, serve as a communication tool internally and to the outside, and play a key role in discussions with regulatory bodies.
A Portfolio of R&D Programmes for 2017-2023

Programme 1: Neonatal Sepsis
While significant achievements have been made in reducing mortality in children under the age of five, mortality remains a burden in children less than one month of age with antimicrobial resistance posing a particular threat. This programme, which has established two target product profiles, aims to develop:
- an alternative first-line treatment for clinically diagnosed cases of sepsis (delivered by 2023)
- a new treatment for confirmed multidrug-resistant pathogens (in clinical development or delivered by 2023)

Programme 2: Sexually-transmitted Infections
A significant sexually-transmitted infection (STI), Neisseria gonorrhoeae is threatening to soon become untreatable due to its resistance to all available classes of antimicrobials. This programme will accelerate the entry of new antibiotics and explore the use of combinations, including old and new antibiotics, while focusing development on specific public health needs (e.g. confirmed drug-resistant, extragenital, and complicated cases of gonorrhea). This programme, which has established a short- and long-term target product profile, aims to develop:
- a new treatment for gonorrhea, including multidrug-resistant cases (delivered by 2023)
- a combination treatment to be integrated for syndromic management of STIs (in clinical development)

Programme 3: Paediatric Antibiotic Platform
This programme aims to optimize current treatments and accelerate development of pipeline/new antibiotics for children through improvements in dose, duration of treatment, and formulation, or through combinations. Depending on the outputs of the initial scoping exercise to be undertaken over 2017/18, at least two projects are anticipated. This programme aims to develop:
- an optimized paediatric antibiotic treatment (delivered by 2023)
- 1-2 additional paediatric projects (in clinical development by 2023)

Programme 4: Exploratory/Upstream/Memory Recovery
Through this early-stage programme, GARDP will explore and support alternative upstream R&D approaches to address gram-negative pathogens that cause serious bacterial infections as well as possibly fungal infections. While directly supporting existing GARDP programmes and/or providing impetus for new ones, it also aims to contribute to the broader antibiotic R&D community.
A key component is the Antimicrobial Memory Recovery Initiative (AMRI) which aims to recover and bring together the knowledge, experts, data, and assets of forgotten, abandoned, or withdrawn antibiotics. AMRI will also identify possible pre-clinical and clinical candidates. Additionally, an antibiotic drug combination platform may be developed to optimize regimens consisting of existing/new antibiotics and non-antibiotic drugs. Depending on the number and quality of drug candidates identified, this programme aims to:
- bring one candidate to lead optimization and one new chemical entity to late-stage clinical development (by 2023)
GARDP’s role within the global AMR R&D landscape

- Priority Target Product Profiles (TPPs): GARDP works with WHO to develop specific TPPs for key programmes
- Supporting the R&D ecosystem: GARDP helps build tools and resources that will support drug developers, especially in academia and small and medium-sized enterprises (SMEs) (e.g. see Exploratory/Upstream/Memory Recovery Programme, page 9)
- R&D implementation: GARDP will develop and execute programmes for key global health AMR priorities receiving insufficient investment (e.g. see Neonatal Sepsis Programme and Sexually-Transmitted Infections Programme, page 9)

**PARTNERSHIP MODELS**

GARDP will work largely as a virtual R&D organization through direct partnerships and multi-stakeholder collaborations, including with academia, industry, international organizations and governments. Working with patented and non-patented drug candidates, GARDP will follow DNDi’s access-driven intellectual property policy in its agreements.1 While maintaining a clear focus and strategy for all its programmatic interventions, GARDP will develop partnership models tailored to the capacity and ability of actors involved: in certain programmes, GARDP will need to be actively driving and implementing R&D programmes, while in others, equitable partnerships will be sought whereby GARDP brings in the appropriate amount of funding, direction, and support. All GARDP funding will be linked to the need to develop and make available affordable products that answer to public health needs.


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Active R&D programmes driven, sponsored and directly executed by GARDP:
- developed with key partners, covering areas of acute need
- very few external actors playing a role

Equal partnerships to which GARDP brings appropriate funding, direction, and support:
- GARDP may seek out or receive request for partnership
- GARDP works to ensure sustainable access is embedded and global public health needs are met through appropriate business models
A comprehensive and sustainable approach to access

For GARDP, a comprehensive and sustainable approach to access necessarily comprises innovation, access, and stewardship of antibiotic treatments. It also implies that the stewardship of antibiotic treatments is framed within an access-oriented approach and not vice versa. Considering its broad geographical scope, country income contexts, varying product characteristics, target populations, and collaboration agreements, GARDP will develop targeted access approaches for every R&D project.

GARDP’s access approach will include a range of different activities. For example, registration will be prioritized for countries with highest burden or need. Beyond the regulatory route, a ‘public health’ pathway will also be taken, including studies essential for public health use. Data from all studies and programmes will be made accessible to inform solid evidence-based policies and drive timely guideline change. Specific focus will also be given to the way products are packaged and distributed, and pilot implementation programmes will be developed to ensure rapid patient access to treatments. Supporting, piloting, and seeking to effectively adapt incentive mechanisms that can facilitate the scaling up of treatments will be considered. The principle of delinking the costs of R&D from price of products and volume-based sales will be applied ensuring affordability as well as sustainable quality production.

This work will consider and factor in ongoing work on the WHO Global Development and Stewardship Framework.

For each of these aspects of sustainable access, GARDP envisages varying degrees of involvement, from promotion and support to direct financing and project management. In addition, GARDP will work with a range of different partners, including local civil society organizations, universities, international organizations and agencies, funding bodies, as well as the private sector.
• Training & education on use
• Capacity building
• Pilot implementation programmes
• Auditing practice around initial implementation
• Country sponsor

• Labelling of product
• Appropriate packaging
• Drug quality & manufacturing standards
• Distribution plan
• Prioritizing country registration according to need

• Obtain appropriate indications and geographical scope in licenses
• Ensure affordable & equitable pricing strategy in place

• Link and pilot push and pull incentives, including milestone prizes
• Promote drug stewardship and scale up facility to support country procurement and use of new ‘specialized’ antibiotics
• Ensure coherence between local and global policies/guidelines
• Monitor adherence to policies/guidelines
• Evidence-based policy and guideline change
• Appropriate phase IIIb and IV trials that can establish optimal use, indication extension
• Pharmacovigilance and safety studies
• Monitor appropriateness of uptake

GARDP  Business Plan 2017-2023
Investing in Antibiotic R&D

Failing a worldwide response, the financial impact of drug-related infections will be daunting which is why it is important to ensure that investment in and gains by global initiatives like GARDP are realized and sustained.

The price tag to cover the costs of implementing GARDP’s initial programmes over the next seven years is slated at EUR 270 million which includes support to introduce up to four treatments and bring up to four candidates to pre-clinical and clinical development. Currently, EUR 6.5 million has been secured.

This initial business plan budget is being used to mobilize a skilled and experienced scientific team to carry out R&D projects, a stable management team to give direction, and the resources needed to build the capacity, human resources, and infrastructure required to support the projects, access activities, and administration. By 2023, GARDP anticipates having 55 full time equivalent (FTE) staff, 70% of whom will be dedicated to R&D. As per February 2017, GARDP has a core staff of 10 people, with additional staff support from DNDi.

The base used for this budget calculation includes industry standards for the duration of antibiotics product development, together with DNDi’s incurred financial costs per drug development phase, and considering industry and DNDi experience of attrition rates. This is then factored into estimates of the number and timing of R&D programmes and projects as well as staff needs, and is, importantly, based on GARDP’s and DNDi’s partnership model. The growth in the budget for the period 2018-2020 is based on GARDP’s objective to commence two Phase III trials as part of the initial programmes with growth stabilizing in the second part of the business plan period. As a not-for-profit R&D organization, private, public and in-kind contributions will be valuable to GARDP’s success while securing funding for its key programmes is vital.

Such growth is largely possible thanks to DNDi’s hosting and facilitating of GARDP in its start-up phase, providing the governance, scientific environment and input infrastructure as well as support for resource mobilization, communication, finance and human resources necessary to build and launch solid R&D programmes in a timely manner.
Governance and structure

GARDP is led by its Director who also serves as a member of DNDi’s executive team. DNDi’s Board of Directors oversees GARDP’s activities, with expert advice from the GARDP Scientific Advisors.

A NETWORK OF EXPERTS, GARDP INITIAL SCIENTIFIC ADVISORS:

- Jutta Heim, Professor of Biotechnology, University of Basel, Switzerland
- Chair, GARDP Scientific Advisory Committee
- Karl-Heinz Altmann, Professor, Swiss Federal Institute of Technology, Switzerland
- Rashmi H. Barbhaiya, Managing Director, Advinus Therapeutics, India
- Graeme Bilbe, R&D Director, DNDi, Switzerland
- Anthony Coates, Professor of Medical Microbiology at St George’s, University of London, UK
- Patrice Courvalin, Professor Emeritus de Classe Exceptionnelle, Antibacterial Agents Unit, Institut Pasteur, France
- George L. Drusano, Director, Institute for Therapeutic Innovation of the University of Florida, USA
- Mark J. Goldberger, Former Divisional Vice President, AbbVie, USA
- Herman Goossens, Professor of Microbiology, University Hospital, Antwerp, Belgium
- Robert Gurny, Professor Emeritus, Department of Pharmaceutics & Biopharmaceutics, University of Geneva, Switzerland
- Nicola Magrini, Secretary, WHO Expert Committee on the Selection and Use of Essential Medicines, Geneva, Switzerland
- Shabir A. Madhi, Executive Director, National Institute for Communicable Diseases, South Africa
- Lúcia Martins Teixeira, Professor, Institute of Microbiology, Federal University of Rio de Janeiro, Brazil
- Marc Mendelson, Professor of Infectious Diseases and Head of the Division of Infectious Diseases & HIV Medicine, Groote Schuur Hospital, University of Cape Town, South Africa
- Malcolm Page, Formerly Roche, Switzerland & Wisdom Professor of Medicinal Chemistry and Chemical Biology, Jacobs University, Bremen, Germany
- David Shlaes, Former Professor of Medicine, Case Western Reserve University, Ohio, USA
- Kazuhiro Tateda, Professor, Department of Microbiology and Infectious Diseases, Faculty of Medicine, Toho University, Japan
- Kamini Walia, Senior Scientist, Epidemiology & Communicable Diseases Division, Indian Council of Medical Research, India
- Nicholas White, Professor of Tropical Medicine, Mahidol University, Thailand
- Yonghong Xiao, Professor, Vice-director, State Key Laboratory of Diagnosis & Treatment of Infectious Diseases, School of Medicine, Zhejiang University, China

A formal GARDP Scientific Advisory Committee will be in place by the end of May 2017.

Over the course of 2017/18, a longer-term executive and governance structure will be developed to accommodate GARDP’s growing portfolio and size. In the meantime, being hosted in DNDi offers a unique opportunity to leverage existing networks and build a new, dedicated entity for AMR through:

- **Starting** within an existing governance structure allows time to build a strategy, programmes/projects and a longer-term governance
- **Utilizing** existing support structures of DNDi that ensure our funding is directed to start up of core R&D business
- **Extensive** regional presence and networks to help implement trials with 7 regional offices in high-, middle- and low-income countries
- **Building** strong links with AMR networks, including microbiology and trial networks in high-income countries

DNDi BOARD OF DIRECTORS:

- Marcel Tanner, Chair; University of Basel, Switzerland
- Els Torreele, Secretary; Médecins Sans Frontières (MSF)
- Derrick Wong, Treasurer; non-profit management consultant, France
- Noor Hisham Abdullah, Ministry of Health, Malaysia
- Rashmi Arora, Indian Council of Medical Research (ICMR), India
- Jorge Bermudez, Fundação Oswaldo Cruz, Brazil
- Christian Bréchot, Institut Pasteur, France
- Abul Faiz, Patient representative; Sir Salimullah Medical College, Bangladesh
- Joanna Liu, Médecins Sans Frontières (MSF)
- Alwyn Mwinga, Patient representative; Zambart, Zambia
- Bernards Ogutu, Kenya Medical Research Institute (KEMRI), Kenya
- Bennett Shapiro, PureTech Ventures, formerly with Merck & Co., USA
- John Reeder, WHO – TDR, Permanent Observer of the Board
The rise of antimicrobial resistance is a severe threat that is rendering more and more life-saving medicines useless. WHO together with DNDi has set up GARDP as a proactive initiative, within a larger global response, that can bring new products into the R&D pipeline.

― Dr Margaret Chan, Director-General World Health Organization

The Global Antibiotic Research and Development Partnership (GARDP) is a not-for-profit research and development organization that addresses global public health needs by developing and delivering new or improved antibiotic treatments while endeavouring to ensure sustainable access.

Initiated and incubated through close collaboration between the World Health Organization and the Drugs for Neglected Diseases initiative (DNDi), GARDP is part of the implementation of the Global Action Plan on Antimicrobial Resistance that calls for new public-private partnerships for encouraging research and development of new antimicrobial agents and diagnostics.

GARDP’s mission is to work in partnership with the public and private sectors, to develop and deliver new treatments for bacterial infections where drug resistance is present or emerging or for which inadequate treatment exists.

GARDP is currently hosted and facilitated by DNDi which provides the scientific environment, necessary personnel, governance, and infrastructure to ensure an effective start-up phase.