

Paediatric Antibiotics

Antimicrobial resistance (AMR) is a major and rapidly growing global public health threat. Responsible for more than 700,000 deaths a year, it poses a significant threat¹ to the attainment of the UN Sustainable Development Goals (SDGs), in particular SDG3, which aims to ensure healthy lives and promote wellbeing for all.²

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 their sustainable access.

Initiated by the World Health Organization (WHO) and the Drugs for Neglected Disease *initiative* (DNDi) in May 2016, GARDP is an important element of WHO's Global Action Plan on Antimicrobial Resistance that calls for new public-private partnerships to encourage R&D of new antimicrobial agents and diagnostics. Following a successful incubation period, GARDP became an independent legal entity in 2019.

GARDP's programmes incorporate access and stewardship strategies to ensure treatments are affordable and available to all those who need them.

Partnerships are central to GARDP's model and include WHO, pharmaceutical and biotechnology companies, academia, governments, health authorities, philanthropic organisations and civil society from across the world.

Infectious diseases, including pneumonia and sepsis, are a leading cause of death and disability in children under 5-years-old; responsible for more than three million childhood deaths a year.³ Increasing drug resistance is making them harder to treat.

Children are highly vulnerable to the impact of AMR. In Europe, drug-resistant infections are responsible for 2,300 disability-adjusted life years (DALYs)⁴ per 100,000 people each year. Infants under the age of 1-year-old bear the vast majority of the burden,⁵ which is expected to be even more severe in many LMIC settings.

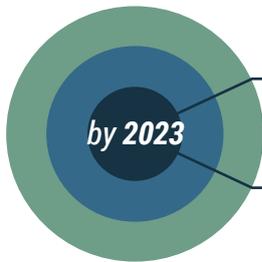
Children who are prescribed antibiotics more than any other medicine⁶, need treatments adapted to their specific needs, in terms of dosing, formulation and regimen type. This is particularly true for babies and young infants. However, scarce evidence means appropriate treatment options are often limited. Evaluation of antibiotics for use in children, only occurs many years after treatments are approved for use-in-adults, if it happens at all. The few active clinical trials are often limited in scope, do not recruit enough patients, and/or do not focus on the areas of greatest need.



GARDP'S PAEDIATRIC ANTIBIOTICS PROGRAMME

GARDP is working to accelerate the development of new, improved and adapted antibiotics to treat serious bacterial infections in children. The paediatric antibiotics programme is building research capacity and expertise across the world, to ensure new treatments meet public health needs and standards for regulatory approval.

OBJECTIVES



- Develop and deliver up-to-two paediatric antibiotic projects into clinical development
- Deliver one improved paediatric antibiotic treatment ready for use-in-patients

TO DATE, GARDP HAS

- Identified polymyxin B as a priority antibiotic for paediatric development, and developed and submitted a paediatric investigation plan to the European Medicines Agency (EMA). Initial registration in Europe will help facilitate access to polymyxin B in other parts of the world, including countries with a high burden of drug resistance in Africa and Asia.
- Started a collaboration with Novartis' generic division, Sandoz, to accelerate the development and availability of antibiotic treatments for children in LMIC settings. In particular to develop heat-stable child-appropriate formulations.
- Supported and contributed to academic research to increase the evidence base for children's antibiotics, including a review of global consumption patterns. The data generated helps to inform national action plans on AMR.

GLOBAL CHILDREN'S ANTIBIOTIC PLATFORM

GARDP and the paediatric research network, Penta,⁶ are developing a global children's antibiotic platform supported by a network of experts and trial sites from high-income and LMIC settings, which will carry out clinical and pre-clinical activities wherever they are needed.

The platform's activities include to:

- Develop master protocols and streamlined paediatric plans acceptable to regulatory authorities
- Use innovative trial designs to maximise the information that can be gained from each trial.
- Start trials in children as early as possible to fast-track development and registration of antibiotic treatments.
- Develop registration and access strategies to ensure treatments are affordable and available, as fast as possible.

LOOKING AHEAD

- A multi-country clinical trial to establish the correct dose of polymyxin B in children-of-all-ages, and evaluate its safety – will be set up in early 2020.
- Up-to-two further drug candidates towards improved children's antibiotics, will be identified by the end of 2019. These may come from drugs that have been recently registered for use-in-adults or that are in late-stage clinical development and/or may include efforts to re-purpose older antibiotics.
- Further research will be conducted and published, and ongoing activities will support the build and development of the global children's antibiotic platform.

A GLOBAL COLLABORATION



The paediatric antibiotics programme, including the global children's antibiotic platform, incorporating Penta's network, has partners and/or trial sites in:

Bangladesh	Thailand
Brazil	Uganda
China	United Kingdom
Greece	Vietnam
India	Zambia
Italy	Zimbabwe
SouthAfrica	

For a full list of partners see gardp.org/partners

- 1 O'Neill, J. (Chair) Antimicrobial Resistance: *Tackling a crisis for the health and wealth of nations*: The Review on Antimicrobial Resistance, 2016
- 2 The *2030 Agenda for Sustainable Development*, 2015.
- 3 Liu L et al (2015) *Global, regional, and national causes of child mortality in 2000-13* – The Lancet 385; 430-40
- 4 WHO describes one DALY as being equal to "one lost year of healthy life," with the sum of DALYs across a population or disease burden measuring the gap between current health status and a situation where people live free of disease and disability
- 5 Cassini, A. et al (2018) *Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015* Lancet Infect Dis. 2019 Jan;19(1):56-66
- 6 Penta has more than 100 clinical centres globally and has sponsored more than 20 major trials involving more than 3,500 children. Penta co-ordinates the pan-European clinical trial network *connect4children* and is paediatric partner for the European Clinical Research Alliance on Infectious Diseases (ECRAID). www.penta-id.org