



Global Antibiotic Research  
& Development Partnership

A joint DNDi / WHO initiative



Delivering on the sustainable access  
of antibiotics: moving from principles  
to practice workshop report

# Report on the workshop organised by the Global Antibiotic Research and Development Partnership in collaboration with the Medicines Patent Pool and the World Health Organization

**1-2 July 2019, Geneva, Switzerland**

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# 1. Executive summary

## Workshop aims and objectives

This two-day workshop sought to define a roadmap that fosters access and appropriate use of antibiotics for all those who need them.

Convened by the Global Antibiotic Research and Development Partnership (GARDP) in collaboration with the Medicines Patent Pool (MPP) and the World Health Organization (WHO), over 50 stakeholders from across the antibiotic research and development (R&D) value chain came together to identify practical access and stewardship interventions and ways in which these can be implemented.

Participants explored the barriers currently stalling progress and developed practical recommendations to improve access and stewardship. The aim was to define a roadmap of pre- and post-registration activities for new antibiotics that promote both access and stewardship, and identify practical ways to implement the roadmap.

Participants were assigned to one of four working sessions representing key steps in the pathway to improve the access and stewardship of antibiotics, namely: R&D; availability; manufacturing, distribution and supply; access and stewardship; and financing.

## Interventions proposed

Several practical interventions were made that span the R&D and access pathway. These include:

- Orienting R&D towards the development of new treatments by generating evidence for treatment guidelines and to support sustainable access of antibiotics in development, and establishing a framework to facilitate access and stewardship.
- Improving the availability of treatments by harmonising regulatory requirements and enabling parallel regulation processes and common dossiers with a regular update of treatment guidelines while improving the communication around existing harmonized regulatory requirements and their flexibilities.
- Supporting manufacturers of antibiotics and public health organizations on access strategies by developing practical guidance on responsible manufacturing, environmental standards, best practices for marketing, and data sharing (surveillance). The importance of a pooled procurement mechanism for antibiotics and of working on new pricing models were also suggested.
- Exploring activities to increase patient access and stewardship by developing a checklist of best practices for access and stewardship of antibiotics and the inclusion of these criteria as a requirement for public funding and for registration of a new antibiotics.



## Next steps for GARDP

The cross-cutting recommendations that emerged from the thematic discussions have informed GARDP's access and stewardship framework.

GARDP is taking the following measures forward as part of its practical, project-based approach to develop five new treatments to address the burden of antibiotic-resistant infections by 2025 with its partners:

- **Licensing:** focus on implementing in- and out-licensing strategies to support quality manufacturing, early access, affordability and responsible marketing.
- **Regulatory:** collaborate with WHO and national regulators to ensure an optimal regulatory pathway for GARDP drug candidates, including facilitating global registration and label extension; and share GARDP's experience to advocate for increasing coherence between key regulatory authorities for antibiotic drug development.
- **Public health, policy and appropriate use:** generate evidence for guidelines to ensure sustainable access for each treatment in GARDP portfolio; support monitoring programmes for the emergence of resistance; outline the basis for antibiotic stewardship; develop and support implementation of early access programmes in high burden countries.
- **Outsourcing strategies:** defining best practice in manufacturing which can then be used as a

benchmark across the industry; optimizing cost of goods of GARDP drug candidates; building and maintaining a core group of partnerships with manufacturers.

- **Procurement:** build better understanding of national needs and facilitate and advocate for cost-saving procurement mechanisms which support predictable demand.
- **Reimbursement models:** support and advocate for equitable reimbursement models that promote win-win scenarios ensuring long-term sustainable supply and appropriate use of GARDP candidate drugs.



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## 2. Introduction

### Background

The rise of antimicrobial resistance (AMR), or drug-resistant infections, is outpacing drug discovery at an alarming rate. The natural process of microorganisms evolving to survive exposure to antimicrobial drugs, as well as the lack of tools and public health interventions to counter the phenomenon, risks causing a dramatic increase in human morbidity and mortality. Each year, an estimated 700,000 people die worldwide as a result of drug-resistant infections.

Over the last few years, several initiatives have been launched to reinvigorate the antibiotic research and development pipeline. Despite this, we need to significantly scale-up our efforts to address the magnitude of the public health challenges we face today.

While drug resistance occurs naturally over time, there are many other contributing factors leading to the increase in drug-resistant bacteria. The challenges are wider than just the need for drug development. These include overuse and misuse of antibiotics in human and animal medicine, and in food production, poor infection prevention and control measures, and lack of affordable, globally available quality medicines. More needs to be done across the board to address the global reasons for this crisis.

No single actor or group can deliver a solution alone. A partnership approach with both the public and private sector is essential to successfully address the public health impact of AMR.

The private sector brings significant experience and innovation in the development and delivery of treatments. However, a purely market-driven approach has not delivered enough innovative antibacterial treatments. Public sector involvement is needed to identify public health needs, set priorities, inject funding and re-shape incentives for the private sector.

Public-private partnerships can leverage the best of both sectors and provide a transparent vehicle for collaboration, focused on achieving a mutually beneficial objective: new treatments for drug-resistant infections, for every person who needs them.



## Workshop objectives and approach

GARDP in collaboration with WHO and MPP, convened a two-day technical workshop bringing together key stakeholders with an interest in the promotion, access and appropriate use of new antibiotics.

Participants explored the challenges of access and stewardship in relation to antibiotics and developed practical recommendations to improve access and stewardship. The aim was to define a roadmap of pre- and post-registration activities for new antibiotics that promote both access and stewardship, and identify practical ways to implement the roadmap.

Workshop participants included technical experts from public health organizations, non-governmental organizations, industry, and government representatives from low-, middle- and high-income countries. They were assigned to one of four working sessions representing key steps in the pathway to improve the access and stewardship of antibiotics:

- R&D: identifying activities/measures that will accelerate R&D for key public health priorities while incorporating actions to facilitate access and stewardship.
- Availability: identifying activities/measures that can expedite in-country availability of new antibiotics, focusing particularly on regulatory measures.
- Manufacturing, distribution, and supply: identifying activities/measures to support best practices in terms of manufacturing, distribution, procurement and pricing to ensure rapid availability in high burden countries at the same time as supporting sustainable use.
- Access and stewardship: identifying innovator-initiated activities to increase patient access and stewardship, and manage the dynamics between these two aims.

A final plenary session on financing brought all participants together to explore how to secure the political will and appropriate financing mechanisms to support end to end R&D and how to move the recommendations on access and stewardship forward into concrete actions.



### 3. Challenges in the R&D and access value chain: Research and development

The workshop on R&D identified the main barriers and challenges currently limiting R&D in antibiotic development and how to accelerate the development of antibiotics that address global public health needs.

#### Challenges

The antibiotic R&D landscape has changed considerably. Most large pharmaceutical companies with resources to integrate the various R&D activities required to take an innovative compound from discovery through to regulatory approval and access have withdrawn from the market. However, small-medium sized enterprises (SME), who are filling the void left by pharmaceuticals do not have the same range of capabilities.

#### Discussion

*Set up expert networks to rethink the design of clinical trials taking into account developing treatments that address global health priorities, and advise on access and stewardship.*

The group agreed that the best way to promote access and stewardship in antibiotics is to integrate access and appropriate use in the research and development pathway from the beginning and to develop the right products in the right way, based on global public health needs and defined in target product profiles (TPPs). Setting priorities for R&D in antibiotics is crucial and should focus on development of treatments rather than individual drugs, and include diagnostics and vaccines as well as therapeutics.

This includes careful design of clinical trials and choice of indications. Measures to facilitate access and stewardship while a candidate drug is in

phase II or III development could include setting up expert networks specialising in clinical trial design that support the development of diagnostic strategies alongside therapeutics. Strong public health input from R&D funders is needed to drive inclusion of public health priorities.

*Build centres of excellence in clinical trials to run trials on an ongoing basis and ensure that drugs being tested meet local health needs.*

The group recommended building centres of excellence in clinical trials where they are not yet present, with the aim of running trials on an ongoing basis to ensure that drugs being tested meet local health needs. These centres need to be located close the relevant patient populations in high burden areas. The inclusion of national healthcare authorities is also important to understand the needs of different countries. Engaging authorities early in the development of new antibiotics is crucial.

Although some priorities have been defined, such as developing antibiotics effective against extended-spectrum beta-lactamase bacteria, more work needs to be done on prioritising antibiotics in need of development, as well as develop an R&D plan that includes appropriate endpoints for drugs that will be approved and prescribed. WHO has already developed and published a priority pathogen list of bacteria that pose the greatest threat to human health to guide the R&D of new antibiotics. WHO has particular expertise and the ability to act as a high-level coordinating hub. The challenge is to find effective measures that link prioritised profiles to incentives.

*Build better collaboration, coordination and cooperation between the different players involved in antibiotic development, namely between different funders, and between regulators and payers.*



Of importance is the need to improve collaboration and coordination between different players involved across the entire R&D process including between funders, and between regulators and payers. This may help streamline the various steps in antibiotic development; develop a clear list of priorities for novel antimicrobials and diagnostics; improve coordination and address gaps in the pipeline; and share information earlier in drug development. Collaboration could also facilitate agreement on new clinical end-points for non-traditional antibiotics and paediatric plans.

*Streamline regulatory approval approaches, as far as possible, to reduce time between regulatory approval and clinical use across multiple countries*

In terms of supporting SMEs to build in provisions for access and stewardship, a useful measure could include harmonising regulatory frameworks that acknowledge global health priorities. This has the potential to reduce the time between regulatory approval and clinical use, making products available to patients sooner. It would also give companies clear guidance on priorities beyond a single country. It could also be helpful to set up a global organisation able to provide SMEs with access to relevant expertise, tools and resources to assist with regulation.

*Create new incentives and a sustainable commercial plan.*

In contrast to drugs for HIV, where funding and mechanisms have been developed to encourage the development of new drugs and support access in developing countries, the situation is very different for antibiotics. Similar funding and mechanisms are lacking for R&D in antibiotics, although organisations such as GARDP and CARB-X are starting to move them forward.

The group acknowledged that it is essential to ensure there is a sustainable path for commercialisation otherwise companies working to develop new antibiotics will not survive. This will not be a 'one size fits all' approach so it is important to explore a range of options relevant to non-for-profits and companies. Approaches could include new ways to create a market for antibiotics, incentives based on the future accrual of profit and exploring private investment funding. One suggestion was to motivate shareholders' investment by promoting corporate social responsibility.

### Summary of recommendations

- Set up expert networks to rethink the design of clinical trials that consider developing treatments that address global health priorities, and advise on access and stewardship.
- Build centres of excellence in clinical trials in high burden contexts to run trials on an ongoing basis and ensure that drugs being tested meet local health needs.
- Build better collaboration, coordination and cooperation between the different players involved in antibiotic development.
- Streamline regulatory approval approaches, as far as possible, to reduce time between regulatory approval and clinical use across multiple countries.
- Create new incentives and a sustainable commercial plan.

### 3. Challenges in the R&D and access value chain: Availability

The workshop explored the factors that currently limit in-country availability of new antibiotics and what measures could help to expedite availability, focusing particularly on regulatory measures needed.

#### Challenges

Accelerating access to antibiotics across a broad geographic area is challenging and requires understanding the different approaches to registration that can facilitate availability, as well as considering the feasibility of developing a pathway that allows the same data to be accepted globally.

#### Discussion

##### *Improving communication on regulatory requirements*

While regulators have updated information on regulatory requirements for developing antimicrobials, group members recognised that there remains a lack of information and confusion, particularly among SMEs, around regulatory requirements and flexibilities and with regard to public health trials.

Several suggestions on how this could be improved were made, including:

- Developing publications on harmonized development pathways with regulators around the globe, with a potential role for the International

Coalition of Medicines Regulatory Authorities (ICMRA).

- Inclusion of updated information on regulatory requirements on regulators' and public-private partnerships' websites.
- Providing regulatory guidance by meeting companies more frequently.
- Hosting more public workshops and scientific meetings to inform companies on current requirements and advancements in the science of drug development.

##### *Supporting the update of treatment guidelines in a timelier manner*

Treatment guidelines in many countries are currently not updated on a regular basis, which can cause problems in proving the need for products. At the same time, there is a perceived challenge for SMEs to provide public health data that demonstrates product differentiation, and where their products fit in treatment guidelines.

To overcome these challenges, measures should be developed to support countries update treatment guidelines in a timelier manner. The group recognised that updating guidelines on the antibiotic use is complex given the number of drugs available to treat lots of conditions, in contrast to HIV where guidelines are updated regularly by a central mechanism. They suggested starting work on a group of priority indications, such as pneumonia or sexually-transmitted infections, noting that WHO has already started discussions on these.

### *Harmonising regional approaches to drug development*

Harmonization at the regional level was considered an achievable goal as it builds on the commonality of approaches that often exists within regions. The aim would be to develop a route for drug developers to apply for regional registration, which could speed up market entry and help a company access a whole region at the same time. A starting point would be to review examples of what has already been done in regional drug registration, such as work by the Economic Community of West Africa States experience in Ebola, and drawing on use of the EMA's Article 58 procedure. Practicalities such as fees and centralisation of activities, including pharmacovigilance and packaging, would need addressing to ensure success.

### *Enabling a parallel regulation process and the use of common dossiers by building on existing coherence between regulatory bodies*

Finished pharmaceutical products (FPPs) that are WHO-prequalified have been evaluated and inspected according to international standards. But they must still be approved for use by the national medicines regulatory authorities (NMRAs) of the countries for which market entry is sought. Repeating assessment and inspection of those FPPs not only consumes scarce regulatory resources but also extends the time needed to make them available to patients. WHO has therefore designed a collaborative procedure that both enables NMRAs to make use of work already carried out by WHO and to strengthen their own regulatory oversight processes, in line with international best practices. Of greatest interest to manufacturers is that application of the procedure enables faster registration.

The procedure (Collaborative Procedure between the World Health Organization Prequalification of Medicines Programme and National Medicines Regulatory Authorities in the Assessment and Accelerated National Registration of WHO-prequalified Pharmaceutical Products) is open to NMRAs in all WHO Member States and holders of prequalified FPPs, on a voluntary basis, and its principles are a model for other regulatory collaborative initiatives.

### **Summary of recommendations**

- Address misconceptions regarding regulatory requirements, particularly for SMEs by improving access to information and advice.
- Support update of treatment guidelines in a timelier manner.
- Harmonise regional approaches to drug development.
- Adopt WHO's collaborative procedure to enable a parallel regulation process.

### 3. Challenges in the R&D and access value chain: Manufacturing, distribution, and supply

Workshop participants considered how to support best practices in terms of manufacturing, distribution, procurement and pricing to ensure availability in high burden countries while at the same time supporting sustainable use.

#### Challenges

Manufacturing and distribution are key components of the supply chain that should be adapted to low- and mid-income countries to facilitate sustainable access to essential antibiotics, and regulated to ensure appropriate use. Standards and initiatives all play an important role in improving stewardship.

Manufacturers in some countries are not currently regulated in accordance with good manufacturing practices and/or do not meet internationally accepted quality standards. This creates a major imbalance in the standards different manufacturers are required to work to. There is also a gap in regulations on the environmental impact of antibiotic manufacturing.

Some manufacturers may not be subject to controls on manufacturing effluents, risking the creation of environmental reservoirs of resistant microbes. Other challenges include incentivizing manufacturers/distributors to take a licence for an antibiotic whose use will be restricted as part of good stewardship, controlling marketing practices to avoid companies inappropriately promoting new antibiotics.

#### Discussion

*Developing practical guidance for manufacturers on responsible manufacturing, environmental standards, stewardship and best practices for promotion*

The group agreed on the need to develop clear guidance, for countries and manufacturers, on manufacturing standards, environmental standards, marketing practices (including inappropriately promotion of watch or reserve antibiotics) and stewardship. Companies belonging to the Antimicrobial Resistance Roadmap (from the AMR Industry Alliance) have developed and implemented an Antibiotic Manufacturing Framework. However, not all antibiotic manufacturers, including generic companies belong to the Roadmap.

One recommendation was to develop practical guidance that include public health input and it was suggested that discussions could take place within the context of WHO's development and stewardship framework.

Measures should also be explored to support responsible promotion of new antibiotics. One suggestion was to separate promotional and educational activities, placing the responsibility for educating healthcare professionals on independent organizations, such as ministries of health. Another proposal was to develop an industry code of practice for responsible promotion of antibiotics that decouples incentives from volume.

The group considered the difficulty in defining permissible buyers for new Access, Watch or Reserve antibiotics but suggested developing guidance that



certain AWARE antibiotics should only be made available under specific conditions. Conditions could include who has the capacity to use these drugs appropriately and the restriction of some antibiotics for hospital use.

The group suggested that governments, WHO and UN Environment should take the lead in developing such guidance with the input of public health organizations and manufacturers.

Companies (and public health organizations) involved in the development and manufacturing of antibiotics should consider incorporating such guidance into their access and stewardship plans.

Such guidance should also be incorporated into licensing agreements, with provisions that reflect best practices on how the licensed antibiotic is to be manufactured, supplied, priced and promoted in order to support access and stewardship. Licensing, as done by the Medicines Patent Pool, could be a way to facilitate access in LMICs with appropriate stewardship-related terms and conditions.

The next AMR Benchmark report by the Access to Medicines Foundation will be published in January 2020 and will include information on what companies are doing in terms of access and stewardship.

The group suggested that it would be helpful to convene a meeting with relevant stakeholders to review the findings, evaluate what is working, and discuss what seem to be the best approaches to achieve access and stewardship. This could inform guidelines on best practices.

### *Developing a pooled procurement mechanism*

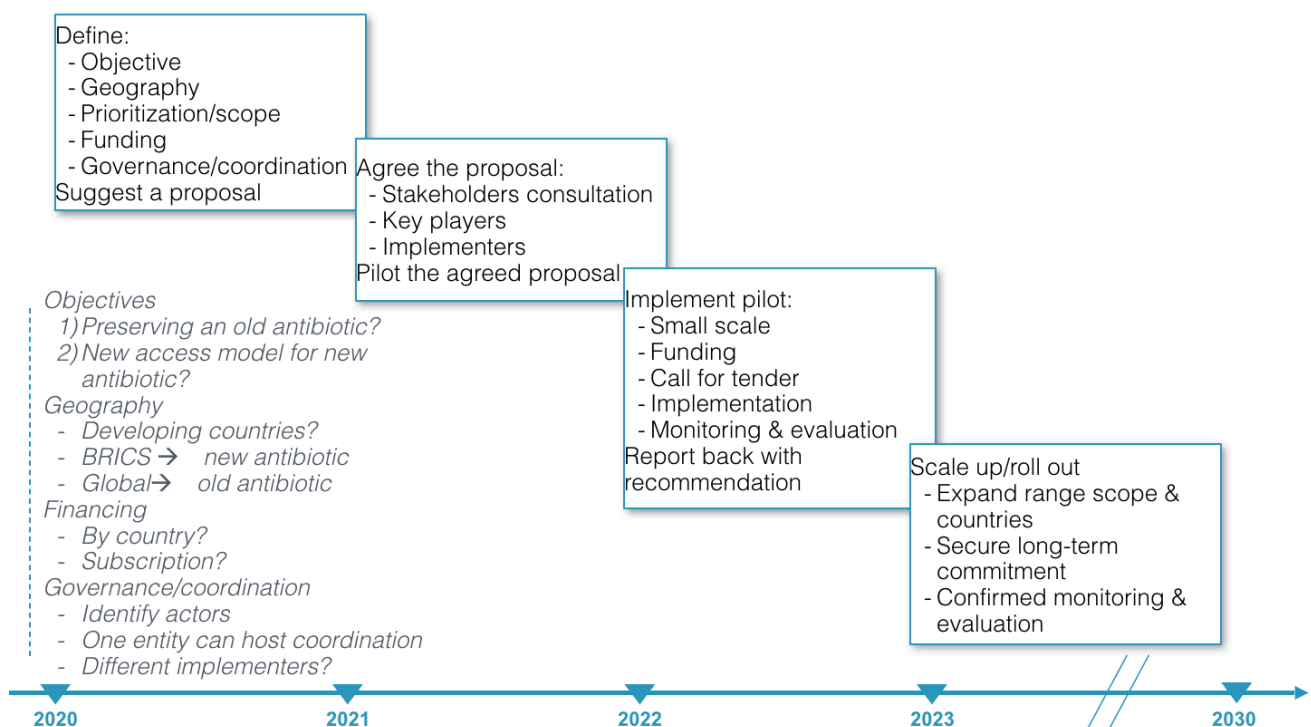
There was discussion around the benefit of having a pooled procurement mechanism to help ensure continuity of supply and to help provide a return on investment to drug developers. This mechanism would fulfil several functions including help pool or aggregate demand, assist in forecasting, minimise transaction costs for suppliers, and help with other issues such as registration waivers. Such a mechanism would need to be linked to public health needs and TPPs defined by WHO. It was also felt this could be one way to achieve a form of harmonisation of stewardship, as rules on stewardship would be part of the pooled procurement contract.

Discussion on a pooled procurement mechanism included whether a new body was needed to develop and manage this process or whether existing ones could incorporate this as part of its responsibilities. There was also discussion on whether the mechanism should be one, large centralised process, comprise various coordinated sub-regional processes (such as the Association Africaine des Centrales d'Achats de Médicaments Essentiels (ACAME) and the Pan American Health Organization (PAHO) strategic fund), or a mixture of both allowing countries that are not part of a region to participate.

As a first step, some recommended an analysis and assessment of what a pooled procurement mechanism should look like in the specific context of new antibiotics (figure 1); what would be required from a pooled procurement mechanism; the potential challenges; and a feasibility analysis. This would provide information that is currently lacking as such a mechanism has not been explored in relation to antibiotics.

### 3. Challenges in the R&D and access value chain: Continued

#### Pool procurement mechanisms



The group also considered it important to understand the range of challenges around supply and demand, so recommended a feasibility study assessing these issues in relation to new antibiotics in low- and middle-income countries (LMICs). This would enable assessment of the measures best suited to address the supply and demand gaps identified.

## Pricing

The groups agreed that addressing the issue of pricing of new antibiotics was difficult without a context, such as discussing a specific product and/or the access strategy being considered. However, it was agreed that current economic models are clearly not working in relation to the development and use of new antibiotics. New pricing/ reimbursement/ procurement models should be explored for antibiotics, with a view to ensure a sustainable market to enable access and long-term use.

Some of the models currently being explored, such as subscription models, could be part of the answer, at least for certain countries. Subscription models with upfront payments for access tied to public health criteria, as opposed to payments based on volume of products used by a health system, could act as an incentive for companies to invest in R&D by offering companies a defined revenue scheme for developing drugs that may be held in reserve, while ensuring sustainable supply to the health system.

It is still too early to decide which is the best economic model for antibiotics. More information is needed on whether these models work, how they work, and where and when they might work, if at all. One way to understand how the different models might work in practice is to run a pilot for each model and evaluate the results. This could be done alongside reviewing and documenting the current market. Understanding why companies are failing is important.

A discussion on the need for frontloading focused on two aspects: frontloading the costs of R&D and

frontloading investment in the product itself once it reaches the market. If an antibiotic only makes a profit several years after registration, finding a way to provide an immediate return to help ensure the supplier can continue manufacturing is critical.

Differential pricing was also discussed. Most of the group thought it made sense to have different pricing or subscription structures for different contexts, such as differentiating between commercial markets and access-type countries. However, implementing this approach would be complex and no consensus was reached on how to do this in practice.

## Summary of recommendations

- Develop practical guidance for manufacturers on responsible manufacturing, environmental standards, stewardship and best practices for promotion, based on WHO's Framework on Development & Stewardship.
- Promote a pooled procurement mechanism for antibiotics.
- Explore new reimbursement models that consider sustainability to enable access and long-term use.

### 3. Challenges in the R&D and access value chain: Access and stewardship

The workshop explored innovator and developer-initiated activities (including GARDP) to increase patient access and stewardship at the same time as managing the dynamics between these two aspects.

#### Challenges

Finding the right balance between access and stewardship is essential. Addressing barriers to access without considering appropriate use ultimately creates the greatest challenge – the emergence of antibiotic resistance. Joining efforts with multiple stakeholders to develop realistic global and national interventions is an important step towards designing new solutions. Stewardship is multifaceted, with activities such as access, education and training all having an impact.

#### Discussion

*Develop a checklist of criteria for access and stewardship required for registration of new antibiotics*

To ensure access and stewardship are effectively incorporated into the registration of new antibiotics, a recommendation was made to define access and stewardship criteria within a globally applicable checklist. Meeting the defined criteria could be included as a requirement for registration of new antibiotics. The checklist could also be used by countries to promote access and stewardship, as part of national action plans and to determine the collection of relevant surveillance data. It could also

be used by funders of R&D activities who can support or condition funding on the activities required within the checklist.

*Ensure appropriate promotion of new antibiotics by redirecting promotional funds to publicly-supervised training programmes*

Some in the group suggested one way to ensure appropriate promotion of a new antibiotic programme could be to redirect companies' promotional funds to publicly supervised education and training, and to support developing and updating guidelines. These activities could be managed by an independent public body at the national level. Piloting in a few countries to check this approach was considered feasible and was suggested to commence.

*Outline an ideal access and stewardship programme by piloting the introduction of an old antibiotic not yet registered in a given country*

The group felt the best approach to strike a balance between access and stewardship was to pilot the introduction of an 'old' antibiotic in a country it was not yet registered in. This would include building capacity for access and stewardship.

Conducting a pilot for old antibiotics as a basis to determine an access and stewardship programmes offers several advantages:

- It is likely to be easier to start building access and stewardship for an 'old' antibiotic, particularly as the price is likely to be lower, so offers an economical approach to conducting a feasibility study that can be adapted to the future launch of new antibiotics.



- A number of different ideas could be tested simultaneously, providing guidance for building capacity and testing out what is possible within healthcare systems.

- It could also provide a country access to a previously unavailable antibiotic.

A proposed roadmap to conduct a pilot for the introduction of an old antibiotic could include the following steps:

- Seek buy-in from the ministries of health of selected countries.

- Develop a shortlist of drugs and countries using drugs already listed on the AWaRE categorization on WHO's Essential Medicines List.

- Select quality assured manufacturers of the shortlisted drugs willing to participate and with a stable market to avoid shortages.

- Conduct a scoping exercise in selected countries that includes reviewing the following: existing antibiotics, availability, burden of disease, AMR data, existing healthcare infrastructures.

- Facilitate registration through a collaborative system with a common dossier.

- Develop guidelines including stewardship training and post-marketing surveillance and pharmacovigilance.

- Clearly position the antibiotic in the healthcare system, namely for community or healthcare facility use.

- Consider the value of a pooled procurement mechanism to ensure sustainable access.

### Summary of recommendations

- Develop a checklist of criteria for access and stewardship required for registration of new antibiotics.

- Ensure appropriate promotion of new antibiotics by redirecting promotional funds to publicly-supervised training programmes.

- Outline an ideal access and stewardship programme by piloting the introduction of an old antibiotic not yet registered in a given country.

### 3. Challenges in the R&D and access value chain: Financing

The financing section of the workshop discussed how to move the recommendations on access and stewardship forward into concrete actions. Participants answered the following questions through voting pads.

#### Challenges

There is a serious market failure in antibiotics, with current economic systems generally supporting overuse of existing antibiotics. Reducing inappropriate use at the same time as ensuring access is challenging, particularly in low- and mid-income countries, as there is no global funding to support measures to address AMR. Even with a major effort to improve stewardship of current antibiotics, new antibiotics will inevitably be needed so supporting a viable pipeline is essential. Moreover, while the cost of developing new antibiotics increases, their commercial viability is severely limited as novel antibiotics are reserved for use when all other antibiotics fail. Therefore, novel financing approaches are needed to make the production / distribution of existing antibiotics and the development of new antimicrobials viable.

#### Discussion

Most workshop participants considered that a global entity is needed to pilot access and stewardship measures discussed during the workshop. However, it was noted that governments need to be engaged

and take responsibility for implementation and national action plans are essential to make progress. Momentum for AMR issues needs to be driven at the highest level and kept on national and international health agendas. Having a newly created assistant director-general on AMR position at WHO will help to push this issue at a global level.

There was recognition that engaging organisations to fund access and stewardship activities for antibiotics is challenging, as there are no examples to draw from that show a way forward. Conducting a pilot, within a short timescale, that demonstrates visible and measurable results may be helpful to attract funding. The most effective way of achieving this is by different organisations working together.

Most participants considered funding should be broad based, and include government funding, in recognition that there is no global health market and that the antibiotic market cannot function sustainably. Some ideas discussed included:

- The critical need to educate senior officials working in government treasury and health departments on the impact and importance of AMR, and that antibiotics are critical, life-saving drugs used for relatively short courses. This means companies do not make the return on investments compared to drugs used to treat long-term chronic illnesses.
- Identifying where governments have core funding responsibilities, such as implementing national action plans and supporting innovations, access, stewardship and regulation.

In parallel, it is important to explore private sector incentives that support innovation in antibiotics. A key challenge here is enabling access in LMICs or high burden countries not seen as an attractive commercial market, and how to put value to new antibiotics in developed markets. The preferred approach would be to assess the global healthcare value but this is currently not adopted for antibiotics, which are economically undervalued despite the fact they are life-saving.

There was strong support for piloting new financial mechanisms for R&D activities, with preference for a subscription scheme or milestone prize as opposed to a market entry reward or transferable exclusivity.

Participants agreed there is a need to do more to incentivise the development of antibiotics from early stage trials through to patient care. However, it was recognised there is no 'one size fits all' solution and that considering a menu of options that are potentially flexible is important, including subscription models that are currently being piloted by a few countries.

One suggestion was to link incentives to global access measures, such as only providing transferable exclusivity vouchers to companies that completely fulfil all the AMR measures required, including global access.

## Summary of recommendations

- Broad-based, multilateral funding is required to support access and stewardship activities and partnerships that both public and private entities can benefit from.
- Governments should contribute to funding innovation, access and stewardship for antibiotics in parallel with measures to encourage investment by the private sector.
- Pull mechanisms should be piloted for R&D activities, exploring a range of approaches including subscription models and milestone prizes.

## 4. Conclusion

Access and stewardship of antibiotics is becoming one of today's major global public health challenges. Fostering the responsible use of antimicrobials is a key priority of the global strategy to tackle antimicrobial resistance whilst not compromising access to treatments for all those who need them. Shaping future access and stewardship interventions was the objective of this two-day workshop by bringing experts together from across the antibiotic R&D value chain. Making tangible, collaborative and multisectoral recommendations, communicating the need for action to politicians, and involving civil society, governments and the private sector is an essential step forward.

There was a clear consensus that new ways of thinking and partnerships are needed to address AMR. Participants recognised the urgent need for the AMR global community to work with renewed commitment, collaboration and perseverance to bring new antibiotics to market – as no single actor or group can deliver a solution alone.

**Participants agreed that some constructive interventions had been proposed. These include:**

- Orienting R&D towards the development of new treatments by generating evidence for treatment guidelines and to support sustainable access of antibiotics in development, and establishing a framework to facilitate access and stewardship.
- Improving the availability of treatments by harmonising regulatory requirements and enabling parallel regulation processes and common dossiers with a regular update of treatment guidelines while improving the communication around existing harmonized regulatory requirements and their flexibilities.

- Supporting manufacturers of antibiotics and public health organizations on access strategies by developing practical guidance on responsible manufacturing, environmental standards, best practices for marketing, and data sharing (surveillance). The importance of a pooled procurement mechanism for antibiotics and of working on new pricing models were also suggested.

- Exploring activities to increase patient access and stewardship by developing a checklist of best practices for access and stewardship of antibiotics and the inclusion of these criteria as a requirement for public funding and for registration of a new antibiotics.

In terms of sustainable financing, novel financing approaches are needed to make the production / distribution of existing antibiotics and the development of new antimicrobials financially sustainable. Broad-based, multilateral funding is required to support access and stewardship activities that both public and private entities can benefit from, and which could support countries in implementing parts of national action plans or developing other AMR measures. Governments and other funders should engage in and contribute to funding innovation, access and stewardship for antibiotics in parallel with measures to encourage investment by the private sector. There is an urgent need for pull mechanisms to be piloted, exploring a range of approaches including subscription models and milestone prizes.

Donor fatigue was mentioned as an important issue, particularly in the context of trying to set standards on access and stewardship where there are currently none. It is challenging to get people to engage or fund initiatives while there are no concrete actions showing the way forward. It was suggested that any pilots carried forward from the workshop should be guided by a clear common action plan, with timely, visible and measurable results.



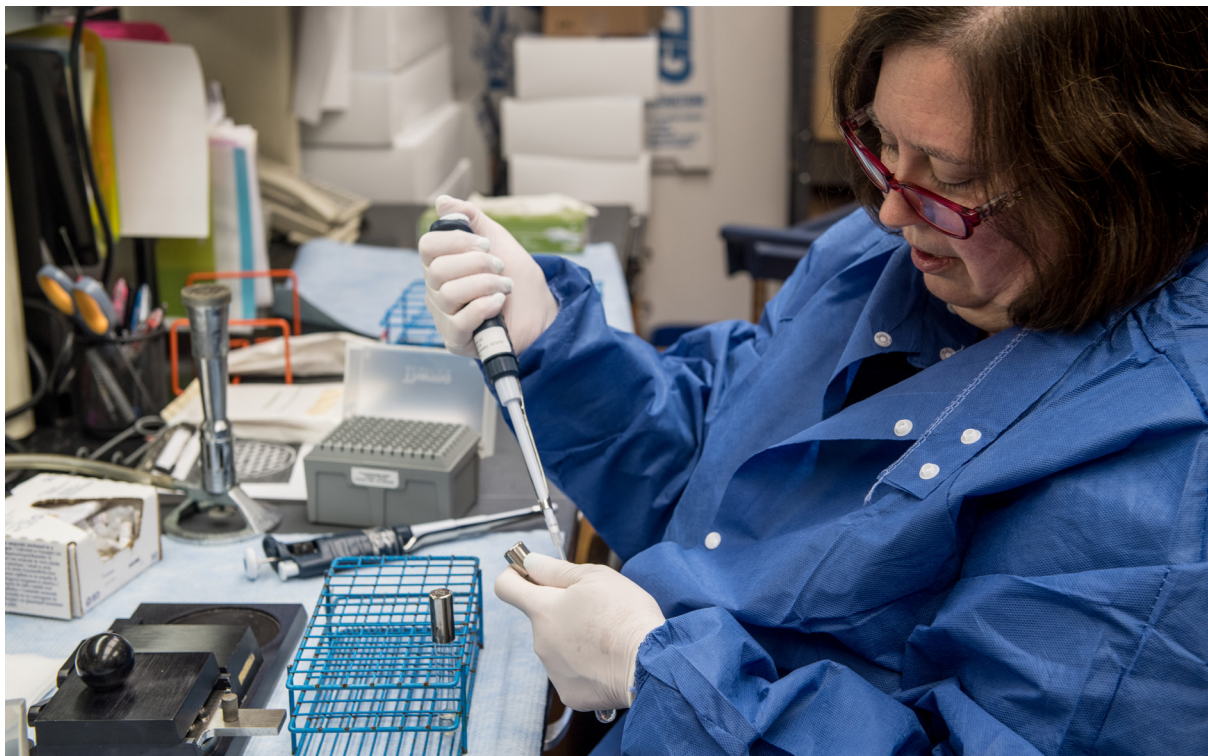
## 5. Next steps

Building on the outcomes of this technical workshop, GARDP is hosting a high-level panel discussion during the World Health Summit in October 2019 to explore how to take the practical solutions recommended forward.

Measures proposed require piloting concepts as there is a lack of evidence on what works and how best to implement measures on access and stewardship, including in resource-stretched settings. These pilots will require leadership and support from appropriate international bodies in global health.

Governments need to be engaged and take responsibility for implementation, and national action plans are essential to make progress. Momentum for

AMR needs to be driven at the highest level and kept on the national and international health agenda, with all actors with a role in antibiotic R&D and access working together. Action is needed at all levels, from communities, local hospitals, sub-national, national to the global level.



# Appendix 1: Workshop agenda

## Summary

- Objectives:**
- Define a roadmap of activities pre and post registration of a new antibiotic that promotes both access and stewardship
  - Identify practical ways to implement the roadmap, including the key steps, potential funding mechanisms and critical success factors
- Participants:** Key stakeholders with an interest in the promotion, access and appropriate use of new antibiotics, including:
- Technical experts
  - Public health organizations / non-governmental organizations / industry / government representatives from low and middle-income countries and high incomes countries
- Venue:** Domaine de Penthes, Geneva, Switzerland  
18, chemin de l'Impératrice, CH – 1292 Pregny-Chambésy  
<http://www.penthes.ch/>
- Date:** 1 and 2 July 2019

**The workshop is organized by GARDP in partnership with the Medicines Patent Pool and the World Health Organization**

## Workshop objectives

The objective of the workshop is to consider and shape future access and stewardship interventions, and understand how to make them successful.

This document outlines the agenda for a two-day interactive workshop that will convene a multi-disciplinary group of experts and stakeholders to achieve this goal.

**Chair of the workshop:** Ramanan Laxminarayan, CDDEP

# AGENDA DAY 1

(Monday 1 July 2019)

**Breakfast & registration** 09:00-09:30

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**Welcome & workshop overview** (Ramanan Laxminarayan, CDDEP) 09:30-09:40

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## Session 1: Plenary introduction

**The complexity of sustainable access** (Ramanan Laxminarayan, CDDEP) 09:40-10:05  
*Setting the scene regarding the challenges and complexity of securing sustainable access globally*

**A vision of sustainable access** (Manica Balasegaram, GARDP) 10:05-10:30  
*Laying out GARDP's vision and aims for sustainable access through their new business strategy*

**R&D, access and stewardship** (Peter Beyer, WHO) 10:30-10:55  
*Presenting the WHO perspective on how to enable development of affordable new treatments and use them appropriately*

**Licensing standards for manufacturing and supply** (Chan Park, MPP) 10:55-11:20  
*Understanding key areas of importance in the licensing, manufacturing and commercialization of new antibiotics that are relevant to good stewardship and equitable access, and how the MPP's experience could translate such considerations into better licensing practices*

**Q&A and next steps** 11:20-12:00

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**Lunch & networking** 12:00-13:30

# Appendix 1: Workshop agenda

## Session 2: Break out parallel working sessions

13:30-15.30

**All participants will be assigned to one of four working sessions. The objective of these working sessions is, for each thematic area, to:**

- develop a list of activities/measures that can facilitate access and stewardship
- define the different actors linked to these activities/measures, and the role each could play for a new antibiotic
- consider how to measure the impact of such activities/measures including potential economic impact

**Each session includes discussion questions as thought-starters, but the goal of the moderator will be to expand on these.**

### Parallel working session 1: Research and development

(Moderator: Kevin Outterson, CARB-X | Rapporteur: tbc)

*This session is focused on activities/measures that will accelerate R&D for key public health priorities while incorporating actions to facilitate access and stewardship*

- How can partnerships between innovators and organizations like CARB-X and GARDP accelerate R&D for key public health priorities?
- What actions can help to facilitate access and stewardship while the candidate is under development, including clinical trial design and location, expanded indications, regulator engagement, and WHO's AWaRe categorization?
- What assistance can be offered to SMEs to help them build in provisions for access and stewardship?

### Parallel working session 2: Availability

(Moderator: tbc | Rapporteur: Michelle Childs, DNDi)

*This session is focused on activities/measures that can expedite in-country availability of new antibiotics, particularly focusing on regulatory measures*

- What are the different approaches to registration that can facilitate availability? For example, targeting key, harmonized markets? Harmonized support from regulators? WHO Prequalification?
- Are there alternative approaches to regulatory requirements that can hasten availability? For example, consider packaging and pharmacovigilance requirements (which are particularly difficult for small companies to fulfill)?
- Can appropriate diagnostics be identified, registered, and made available simultaneously?



### **Parallel working session 3: Manufacturing, distribution, supply and access**

(Moderator: Brenda Waning, Global Drug Facility | Rapporteur: tbc)

*This session is focused on activities/measures to support best practices in terms of manufacturing, distribution, procurement and pricing to ensure rapid availability in high burden countries - but also stipulations to support sustainable use*

- *What should be expected from manufacturers with respect to manufacturing, distribution and supply for Access, Watch and Reserve antibiotics?*
- *Can we encourage producers to license small volume antibiotics and build in stewardship provisions?*
- *Should there be a centralized procurement mechanism for new antibiotics (especially for developing markets)? Or large pooled procurement initiatives? What would be the knock-on effects? Advantages and disadvantages?*
- *What is the right approach to reaching an appropriate (affordable and sustainable) price for a new antibiotic?*

### **Parallel working session 4: Access and stewardship**

(Moderator: Marc Mendelson, Univ. of Cape Town | Rapporteur: tbc)

*This session is focused on innovator-initiated (e.g. GARDP) activities to increase patient access and stewardship, and manage the dynamics between these two aims*

- *What assistance can be provided to groups developing national clinical guidelines to ensure that a new antibiotic is appropriately positioned in guidelines? What type of training can support this positioning? Can surveillance validate appropriate use and if so, how?*
- *What type of information or package design would be useful to ensure that a new antibiotic is used appropriately?*
- *What measures within healthcare settings and the community can be supported to ensure an appropriate balance between access and stewardship?*

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<b>Break</b>	<b>15.30-16:00</b>
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<b>Session 3: Reporting back of parallel working sessions (4 x 20 mins)</b>	<b>16:00-17:20</b>
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<b>Wrap-up of the day</b> (Manica Balasegaram, GARDP)	<b>17:20-17:30</b>
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<b>Drinks/light food and networking event</b>	<b>18.00-20:00</b>
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La Vie des Champs, 15 Chemin de la Vie des Champs 1202, Geneva, Switzerland <https://laviedeschamps.ch/>

# Appendix 1: Workshop agenda

## AGENDA DAY 2

(Tuesday 2 July 2019)

**Breakfast**

**08:00-08:30**

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### **Session 4: Role-play session**

**08:30-10:30**

**All participants will be assigned to one of four teams and given a role (e.g., intellectual property holder, generic producer, regulator, national civil society representative, national public health official etc.). Each team will have a moderator and a rapporteur, and will receive a scenario with the following information**

1. a product summary describing the antibiotic [hospital-based CRE drug and community-based drug], indications, formulations, IP holder, ...
2. a surveillance map of the unmet public health need for the antibiotic including forecast of need
3. access and stewardship objectives

**The objective of the role-play is to brainstorm on bottlenecks for each scenario and find solutions to ensure that the patient receives the appropriate antibiotic at the right time.**

**Each group will be required to provide:**

- a list of perceived bottlenecks
- a list of solutions, activities and/or measures to facilitate access and stewardship
- a high-level access and stewardship strategy and plan

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**Break**

**10:30-11:00**

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<b>Session 5: Reporting back of parallel sessions (4 x 20 mins)</b>	<b>11:00-12:30</b>
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<b>Lunch &amp; networking</b>	<b>12:30-14:00</b>
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**Session 6: Sustainable access and financing**

**The objective of this plenary session is to identify possible mechanisms to implement / facilitate such activities/measures, and define the critical success factors. The discussion should begin with a “big picture” perspective, and then get into the details based on the two antibiotic case studies.**

<b>Panel and plenary discussions</b>	<b>14.00-16.30</b>
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Moderator: Marc Gitzinger, BEAM Alliance

Panel Members: Anna Zorzet, ReACT | Jeremy Knox, Wellcome Trust | Louise Norton-Smith, UK Dpt. of Health & Social Care | Martha Gyansa-Lutterodt, Ghana Ministry of Health | Nina Grundmann, AMR Industry Alliance | Ramanan Laxminarayan, CDDEP

*The discussion will be organized around 3 topics:*

- 1. How to generate political will and agreement amongst governments to a) finance a comprehensive response to AMR and b) ensure cooperation where it is needed on the end-to-end development of new antibiotics?*
  - 2. How such funding should be applied as it relates to the effective operation of an end-to-end model including a) the role of incentives, reimbursement and strengthening national health care systems and b) where cooperation is needed to ensure that an end to end model operates effectively?*
  - 3. How funding should be applied and where cooperation is needed (based upon the discussions from the previous sessions). This question will be discussed in the context of the two antibiotic case studies.*
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<b>Session 7: Wrap up (Ramanan Laxminarayan, CDDEP)</b>	<b>16:30-16:45</b>
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<b>Next steps (Manica Balasegaram, GARDP)</b>	<b>16:45-17:00</b>
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## Appendix 2: Workshop participants

**Anna Zorzet**, ReACT

**Bernhard Achleitner**, Ernst & Young

**Brenda Waning**, Global Drug Facility

**Bruce Altevogt**, Pfizer

**Céline Pulcini**, Ministry of Health

Coordinator of the French AMR NAP

**Chan Park**, MPP

**Chantal Loze**, GARDP

**Dagmar Reitenbach**, Federal Ministry of  
Health, Germany

**Damiano de Felice**, Access to Medicine  
Foundation

**Dominique Junod**, DNDi

**Edward Cox**, Food and Drug Administration,  
United States

**Els Torreele**, MSF Access Campaign

**Erica Westwood**, Department of Health and  
Social Care, England

**Esteban Burrone**, MPP

**Estelle Onyekachi Mbadiwe**, Ducit Blue  
Solutions

**Esther Bettiol**, GARDP

**Fernando Pascual**, MPP

**Francois Franceschi**, GARDP

**George Jagoe**, Medicines for Malaria Venture

**Giancarlo Francese**, Teva

**Greg Frank**, BIO

**James Anderson**, GSK

**Jean-Pierre Paccaud**, GARDP

**Jenny Hellman**, Public Health Agency,  
Sweden

**Jeremy Knox**, Wellcome Trust

**Katerina Galluzzo**, UNITAID

**Katrine Thor Andersen**, Gates Foundation

**Kevin Outtersen**, CARB-X

**Lauren Sweeney**, Fleming Fund

**Lynn Filpi**, Department of Health & Human  
Services, United States

**Magda Moutafts**, Global R&D AMR Hub

**Manica Balasegaram**, GARDP

**Manos Perros**, Entasis Therapeutics

**Manuel Martin**, MSF Access Campaign

**Marc Gitzinger**, BEAM Alliance

**Marc Mendelson**, University of Cape Town,  
South Africa

**Marco Cavaleri**, European Medicines Agency

**Marie Petit**, BEAM Alliance

**Martha Gyansa-Lutterodt**, Ministry of  
Health, Ghana

**Merana Mussa**, Ministry of Health,  
Mozambique

**Michelle Childs**, GARDP

**Nathan Ford**, WHO

**Nina Grundmann**, AMR Industry Alliance

**Nithima Sumpradit**, Food and Drug Admin-  
istration, Thailand

**Oliver Williams**, Wellcome Trust

**Pascale Boulet**, DNDi

**Paul Domanico**, Clinton Health Access  
Initiative

**Peter Beyer**, WHO

**Ramanan Laxminarayan**, CDDEP

**Renata Da Costa**, GARDP

**Rohit Malpani**, ReAct

**Sabiha Yusuf Essack**, University of  
KwaZulu-Natal, South Africa

**Sandra Nobre**, MPP

**Seamus O'Brien**, GARDP

**Silas Holland**, MSD

**Skhumbuzo Ngozwana**, Kiara Health

**Stefan Mühlebach**, Federal Office of the NES,  
Switzerland

**Sumathi Nambiar**, Food and Drug  
Administration, United States

**Theoklis Zaoutis**, Penta

**Tim Eckmanns**, Robert Koch Institute

**Tina Guina**, US, BARDA

**Tracie Muraya**, ReAct Africa

**Viviana Munoz**, South Centre

**Yann Ferrisse**, GARDP



# GARDP

Global Antibiotic Research  
& Development Partnership

A joint DNDi / WHO initiative

**Global Antibiotic R&D Partnership (GARDP)**

15 Chemin Louis-Dunant

1202 Geneva

Switzerland

t: +41 22 555 1990

e: [contact@gardp.org](mailto:contact@gardp.org)

w: [www.gardp.org](http://www.gardp.org)

