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Achieving Equitable Access to Healthcare Interventions

What are the challenges and what will Wellcome do?

February 2020

Executive Summary

A huge number of people lack access to the healthcare interventions they need. While exact figures are hard to measure, the WHO has estimated that nearly 2 billion people are affected. Those living in the world's poorest communities are hit hardest, with the least opportunity to access good-quality diagnostics, vaccines, medicines and other healthcare interventions, when they need them and at a price and quantity that are affordable and sustainable.

The reasons for this lack of access are many and varied, including:

- a lack of R&D in areas of unmet need
- varied mechanisms for intellectual property management and pricing
- diverse regulatory approaches

These access challenges are further exacerbated by weak health systems and inadequate healthcare financing.

While various initiatives have had some success in overcoming these challenges, progress has been uneven, and the current system is still not delivering enough for the people most in need.

Wellcome's role in access

As a funder of health R&D, Wellcome has an important role to play in addressing inequities in access. Our mission is to improve health for all, and we can only make progress towards this if the interventions we fund reach people regardless of where they live or how much money they have, and if these interventions address areas of unmet need. We currently support access in various ways through what we fund and how we fund it, and several examples are given throughout this report and the supporting case studies (Annex I). However, there is much more that we could do, and we are committed to taking further action.

We know that improving access isn't something that we will achieve overnight or on our own; we are one piece of a much larger puzzle in the context of global R&D. We are therefore prepared to work with many partners over a number of years to achieve the change needed, and we see our current work as just the start.

Our plans for improving access

In March 2018, we published a statement on our approach to access to healthcare interventions.[1] We will now build on this by taking actions to address two specific challenges:

1. A lack of transparency makes it hard for funding agencies to implement best practice on access.
2. A fragmented approach by funders makes the system more complicated and provides incentives that may work against access.

To tackle these challenges, we are committing to:

- **challenge ourselves on transparency** – being more open on the steps we are taking towards supporting access, continuing to report back through regular access reports, and developing a clearer vision of what success looks like for us as a funder and how we can measure our progress
- **support the development of an online repository of contractual provisions** for access that brings together the different approaches to access taken by institutions in global health agreements
- **develop and promote Global Good Access Practices**, co-creating a common set of guidelines that funders and others can use to embed good access practice at each stage of the R&D process
- **build upon Wellcome's own principles on access**, adding detail to our existing principles so it is clearer how they will be used in practice throughout our work
- **support the establishment of an Annual Global Forum**, which would bring together funders, regulators and others in the global community to accelerate the late-stage pipeline of critical medical and health products.

Why access matters

As many as 2 billion people worldwide do not have access to healthcare interventions that could transform their lives, according to WHO estimates.[2] Lack of access is an issue in every country, as governments in middle- and high-income countries are paying increasing attention to the cost-effectiveness of new interventions. Although substantial progress has been made in providing access to treatments for HIV, or to maternal and infant care, for example, much of the progress in health over the past 20 years has been uneven, and it is often the poorest communities globally that are hit hardest.

Improving equitable access is central to achieving wider global goals for health: it is a foundation stone for universal health coverage, enabling people to access the health services they need, where and when they need them; and it is key to achieving Sustainable Development Goal 3 (SDG3) – healthy lives and wellbeing for all at all ages.

Why are people unable to access the healthcare interventions they need?

There are many reasons people cannot access the healthcare interventions they need. Several of the key challenges are described below, together with a few examples of initiatives that aim to tackle these barriers (by no means the only initiatives that have been introduced to improve access). Underpinning all of these challenges is the need for healthcare interventions of assured quality; substandard and falsified medicines undermine attempts to improve access.

1. A lack of R&D in areas of unmet need

The current R&D system often fails to produce interventions for diseases that predominantly affect people in low- and middle-income (LMIC) countries, and for products such as new antibiotics, which are not expected to be sold in large volumes. Studies of new chemical entities (NCEs) of recent decades show that only 1% of NCEs were to treat neglected diseases that represent 12% of the global disease burden.[3,4] Companies (and their shareholders) can be reluctant to invest in these areas because of the lack of expected profit, although some companies are prepared to engage on a cost-neutral or not-for-profit basis. All funders of R&D – private, public and philanthropic – have a role in finding ways to ensure that research priorities better reflect unmet need. In recent years, several non-profit product development partnerships have been established to stimulate development in some of these areas. Such initiatives draw on knowledge, expertise and financing from the public, philanthropic, academic and private sectors.

Developing urgently needed antibiotics

The world urgently needs new antibiotics – but it is important that when they are made available that appropriate access is balanced with responsible stewardship. Wellcome is a key funder of CARB-X (Combating Antibiotic Resistance Bacteria Biopharmaceutical Accelerator), a $500 million non-profit partnership providing the world's largest early-development pipeline of new antibiotics, vaccines and rapid diagnostics.

CARB-X awardees are contractually obliged to produce and publish a Stewardship and Access Plan (SAP), which must outline the steps that developers will take to ensure appropriate stewardship and access in the territories where they do not intend to seek commercialisation. Commercial prospects for new products are precarious, so stewardship and access commitments need to be balanced against commercial interests. Wellcome is working with CARB-X and its other funders, product developers and stakeholders to develop a SAP template, which will provide guidance for awardees as they develop and implement plans. This is a ground-breaking commitment placed upon developers and should help to ensure that new products are made available where they are needed most – as well as helping to galvanise new norms for stewardship and access in the antibiotics R&D sector. See Annex I for further details.

HIV self-testing

Wellcome supported work led by Professor Liz Corbett, with colleagues at the Malawi-Wellcome-Liverpool Programme and beyond, which has helped transform HIV self-testing (HIVST) in Africa. The team designed and piloted a new approach to community-based HIVST, which was perceived as risky at the time, given sensitivities around HIV research in vulnerable populations. The trial resulted in a significant increase in initiation of antiretroviral treatment. This research provided the world's first evidence of the high accuracy, safety, feasibility, cost-effectiveness and preference over other approaches for HIVST, including among hard-to-reach groups. The project proved to be highly influential, informing WHO guidelines and technical advice. Building on this success, Corbett and colleagues established an implementation research consortium and secured funding from UNITAID for the HIV Self Testing Africa (STAR) initiative. STAR has now been implemented in six countries across southern Africa and has distributed 4.8 million self-test kits to date.

2. Intellectual property and pricing

The development of new interventions relies on the use of patents, which provide innovators with a period of exclusivity during which they can prevent others from exploiting the invention – for example, by preventing the launch of generic versions of a medicine. Under the right circumstances this creates an incentive for R&D investment, allowing innovators to recoup costs, provide returns for shareholders, and stimulate future innovation. Such a model has led to many breakthrough innovations, but it also has its challenges. During periods of exclusivity, products may be unaffordable to some people that need them. Companies highlight the high underlying costs of bringing new interventions to market as a key reason for pricing strategies. Prices of health interventions can also be too low, leading to shortages or drugs disappearing from the market because they are no longer economically viable for companies to produce. Various mechanisms have been introduced to improve affordability, including the use of TRIPS flexibilities,[5] tiered pricing strategies,[6] advance market commitments,[7] and licensing of patents to the Medicines Patent Pool.[8] Since 2008, the Access to Medicines Index has been helping to drive transparency and accountability in the pharmaceutical industry by tracking progress on access to medicines.

3. Diverse regulatory approaches

Regulation is there to provide vital efficacy and safety checks on products entering the market. However, challenges with the current system mean that, in some circumstances, regulation can also be a barrier to access. One key issue is that countries often have different regulatory requirements that must be met before a new intervention can be made available. Diverse regulatory pathways can increase the time and cost required to bring products to market in all countries that need them. A lack of national regulatory capacity can add to the challenge, further slowing and potentially discouraging the registration of novel products. Another challenge is that companies may decide not to register certain medicines in markets that are not considered to be commercially viable. The WHO Prequalification Programme[9] was set up to address regulatory gaps and has helped to accelerate access to certain quality assured generics produced in LMICs.[10]

4. Weak health systems

Countries with weak health systems fail to provide secure access to healthcare interventions and often lack a robust national medicines policy. Such a policy is essential for selecting the right products, for regulating safety, quality and efficacy, for procuring wisely, and for encouraging rational use of medicines. In some instances, programmes financed by global donors have been established to fill gaps and provide access to treatments in countries with weak health systems, particularly in areas such as HIV, malaria and TB. While such programmes have been successful in increasing access to medicines for certain diseases, people living with other health conditions remain underserved. For example, a child with type I diabetes in sub-Saharan Africa has a life expectancy of less than a year due to lack of insulin access.[11]

5. Inadequate healthcare financing

Medicines are one important part of the wider health system, which must also include public health infrastructure and universal health coverage. A quarter of health expenditure globally is for medicines, yet most LMICs underspend in this area. The Lancet Commission on Essential Medicines Policies[12] calculated that between $13 and $25 per capita is required to finance a basic package of 201 essential medicines in all LMICs. Yet in 2010, the majority of low-income countries and 13 out of 47 middle-income countries spent less than $13 per capita on pharmaceuticals. These figures indicate that many people worldwide do not have access to even the most basic package of pharmaceutical care. By contrast the per capita spending on pharmaceuticals in the UK is $469.[13] Because of the lack of universal health coverage, 50 to 90% of expenditure on medicines in LMICs is out of pocket – individuals paying healthcare providers directly at the time of service.[14]

Promoting access and rational use of antibiotics for children

Despite the low cost and wide availability of off-patent antibiotics, millions of people in LMICs still lack access to these lifesaving drugs. UNICEF and Wellcome are partnering on a project to advance global understanding of how to broaden access to antibiotics in LMICs, particularly for children, while promoting their appropriate use and stewardship in community healthcare. This two-year project will explore barriers to access in five LMICs. Once context-specific barriers have been identified, a research protocol will be developed and a call for proposals issued in each country for local researchers to apply for grants to develop solutions to increase access to antibiotics.

Maximising the use of limited cholera vaccines

Cholera affects up to 4 million people every year around the world, often in environments with significant health challenges. An oral vaccine can help provide protection during an acute outbreak or help provide breathing space in endemic areas to enable the implementation of long-term interventions. However, manufacturing capacity is often unable to match demand for the vaccine. Last year, for example, over 36 million vaccine doses were requested but only 16 million were received. The Global Task Force on Cholera Control is working with partners in the affected countries and globally, including Wellcome, to find the most impactful strategies for cholera prevention and control. Wellcome is investing in cholera research to support this. With research improving programmatic efficiencies and decision-makers equipped with a clearer picture of cholera in their country, the objective is to maximise access to and impact of this limited resource until supply challenges are alleviated.

Wellcome's plan of action

Wellcome and other funders of health R&D have an important role to play in addressing inequities in access. Our mission is to improve health for all, and we can only make progress towards this if the interventions we fund reach people regardless of where they live or how much money they have, and if these interventions address areas of unmet need. We know that there is no single, straightforward solution on access, and that improving access isn't something that we will achieve overnight or on our own. We are therefore prepared to work with many partners over a number of years to achieve the level of change needed to make progress.

In March 2018, we published a statement on our approach to access to healthcare interventions. Our action plan for 2020 builds on this, focusing on two specific challenges that we think must be addressed in order to make progress towards an R&D ecosystem that supports access and better serves the global public interest.

Challenge 1: A lack of transparency makes it hard for funding agencies to implement best practice on access

There is a lack of transparency across several aspects of the R&D system, including among funders of R&D. For example, we do not have a clear picture of the different approaches funders take to support access through their work. Sharing this information has not been a priority, particularly given the difficulties posed by the confidentiality of some agreements. Therefore, when trying to establish a new funding agreement with an innovator, it is not easy to know what kinds of terms and conditions have previously been successful – or not – in improving access. The inclusion of access terms and conditions in an agreement is, of course, not enough in itself to improve access; these terms must also be enforced and respected. However, greater transparency on funders' actions that have and have not worked, including access-related clauses in agreements, would improve their ability to compare, improve and act on previous practice.

We will:

- **Challenge ourselves on transparency** – We want to be more open about the steps that we are taking to support access. We will continue to report back and will start developing a clearer vision of what success looks like for us as a funder and how we might measure our progress, so that we and others can monitor how we are doing. Over the next year we will scope how we can be more open to encourage access, including through our funding agreement templates, and to be more open about what access provisions we actually agree with partners in future negotiations.

- **Support the development of an online repository of contractual provisions** – We will support the Master Alliance Provisions Guide (MAP Guide), developed by the Global Health Innovator Alliance Accelerator, which will provide an easily accessible list of different approaches that have been taken by public, corporate, philanthropic and multilateral institutions to address key access issues in global health agreements. The online guide will illustrate the policy language and legal terms used in agreements between parties. This should lead to discussions that are more productive and have the potential to accelerate the negotiation of future agreements by providing a point of reference for all funders and developers of new healthcare interventions.

Challenge 2: A fragmented approach by funders makes the system more complicated and provides incentives that may work against access

Across the variety of funders working in the R&D ecosystem, there is a lack of coordination and alignment on approaches to ensuring access. Funders typically follow their own principles or guidelines, which means there is a lot of variation in practices and in minimum requirements. Variation in funders' conditions makes it harder for innovators to understand what is expected of them and increases the complexity of the system they have to navigate. Funders could provide greater consistency for innovators and make faster progress towards improving access by taking a shared, cohesive, principles-based approach. Better coordination would also enable funders to identify and prioritise more effectively specific areas for collective action.

We will:

- **Develop and promote Global Good Access Practices** – We want to encourage a more coordinated approach across funders of health R&D. The Global Action Plan for Healthy Lives and Wellbeing for All calls for affordable access to be the core driving principle at each stage of the R&D process, with the ultimate aim to embed good access practice across the whole pipeline. We are committed to supporting these efforts and will work with interested stakeholders to do this, raising standards higher than the current practice. We will begin this process working with other funders of health R&D to consider what we can do together at an early stage in the process, to help develop and encourage commitment to a set of common guidelines and to provide more coherence across our different policies. The aim is for funders of health R&D to, where possible, align their policies and grant agreements with these practices.

- **Build upon Wellcome's own principles on access** – Linked to this important work at the global level, Wellcome has a set of principles that outline how we will achieve our access aims: support sustainable access and innovation; foster collaboration and partnership; be flexible and pragmatic; promote transparency to support innovation and access to products. Alongside the Global Good Access Practices, we want to go a step further and put more detail into our own principles, so it is clearer how they will be used in practice. By sharing our detailed principles we hope to increase transparency and do our part in addressing access early.

- **Support the establishment of an Annual Global Forum** – The Global Action Plan, which aims to drive progress towards Sustainable Development Goal 3, has recommended the development of an Annual Global Forum to accelerate the late-stage pipeline of critical medical and health products. This initiative would allow funders, regulators, financing institutions and the global community to get behind interventions that are nearing licensure or have recently been licensed but are facing late-stage access challenges. Agreeing what should be prioritised will be a particular challenge and one we all commonly face in global health, but if successful this action could make a significant contribution to getting a few major interventions to people who need them quicker. We want to help turn this idea into a reality and will support the signatories of the Global Action Plan and interested stakeholders to scope how the forum might work in practice.

What's next?

The steps we are taking now will begin to have impact, but this is just the start of the journey. We are therefore committed to working with like-minded partners over the long term, towards a more equitable healthcare innovation system, underpinned by shared principles, where research discoveries and innovations result in quality interventions that are accessible and affordable to all those who need them.

Annex I: Wellcome case studies

These case studies set out a few examples of some of the access work that Wellcome is already doing. They give a flavour of what we fund and how we think about access when making decisions.

New grants policy to encourage translation

Wellcome supports a breadth of work to improve health for everyone. As a charitable foundation we must ensure that the results of the research we fund are applied for public good. Most of the work we fund best supports our mission by being freely disseminated through scholarly journals, in accordance with our open access policy. However, sometimes the work we fund best supports our mission through some form of commercialisation of the IP it generates (e.g. patent or copyright).

Last year, we made changes to our Policy on Consent and Revenue and Equity Sharing. As a result, not-for-profit universities and research institutions now have a waiver on the requirement to get our prior consent before commercialisation, to simplify the process and encourage translation. We will instead review details of the transactions of Wellcome-funded IP by such institutions on an annual basis, when reviewing their consolidated IP and commercialisation reports. Provided these transactions are reported fully to us and comply with our policy on IP, the waiver on prior consent will remain in place.

Another change to our policy created a new incentive for our award holders to engage in translation or improve access. We have an obligation under charity law to ensure that private benefit arising from our funding, such as wealth creation, is within acceptable bounds. To meet this obligation, we typically take a share of any revenue and equity our award holders generate from commercialising Wellcome-funded IP and use this income to support our work. To strike a balance between incentivising translation and meeting our charitable obligations, we have chosen our default revenue and equity share to be 25%. Each funded organisation can apply to retain some or all of this aggregate amount payable to Wellcome from the previous year. We will consider applications where the retained sums will be used to advance our mission by supporting new translational activity or improving equitable access to healthcare interventions – particularly in low- and middle-income countries. Wellcome-funded IP must not be used solely to block further R&D by others, either actively or passively. We expect registered IP to be abandoned if there is no credible plan to commercialise it and if it presents a barrier to other researchers.

Principles and practices for funders

Several challenges limit the early adoption and scale-up of innovations. Among these is the need to ensure that each stage of the biomedical R&D process plays a role in delivering access of new healthcare products to those who need them. There are already best practices and proven interventions that could be scaled up and promoted through collaboration but there is a lack of consistency across funders in terms of addressing access barriers that hinder products being introduced and scaled.

As a prominent funder in the biomedical R&D space, Wellcome recognises the urgency of providing more commonality of funders' policies on access provisions to achieve end-to-end R&D for global health priorities, in the public interest. In July 2018, we co-hosted a workshop on principles and practices for biomedical R&D in the public interest with the Drugs for Neglected Diseases Initiative (DNDi) and the Graduate Institute's Global Health Centre. The meeting explored what role funders do and could play, as well as how to move from shared principles to practical implementation in different thematic areas.

The conclusions of the workshop supported our thinking in 2019, when we co-led work on the R&D, Innovation and Access accelerator with the World Health Organization to inform the Global Action Plan for Healthy Lives and Wellbeing for All (GAP). The GAP called for the development of Global Good Access Practices for innovation in health, including principles such as impact, affordability, effectiveness, efficiency, and equity, and we remain committed to supporting this effort, building from the outcomes of the 2018 workshop and stablishing common ground among funders for health R&D.

One of the key challenges we faced during these activities, which could hinder further improvement, is the limited appetite to address this problem in a transparent and holistic way. Moreover, finding a consensus on such a polarised issue will not be easy, given the different interests at stake and the plethora of actors involved in the discussion, including private sector, civil society, philanthropic funders and regulators. The GAP is an opportunity to generate some momentum behind this challenge, encourage stakeholders to find areas of agreement and forge common ground to address access challenges.

Principles-based approach to working with partners

Treating malaria is a global challenge. With increasing resistance against artemisinin-based combination therapies, there is an urgent need for new and efficient antimalarials. To help tackle this challenge, Wellcome entered into a partnership with Novartis to co-fund drug discovery and development of potential new compounds to treat malaria. At the early stages of funding, the project was still in preclinical development. A key challenge with this type of project is that investing early in drug discovery does not guarantee an approved drug, yet the investment is needed to drive future access. Another challenge was that the entities involved have different drivers. Novartis, as a publicly traded company, needs to generate returns while following through with its commitment to global health. Wellcome, as a charitable foundation, needs to ensure that the philanthropic funding it provides does not yield a disproportionate private benefit. This challenge was addressed in a partnership agreement that ensures collaboration to address unmet needs of patients.

We took a principles-based approach through the contract:

- We agreed a TPP (target product profile) with the company, agreeing what factors should be considered for the development of the antimalarial drugs to ensure their best chance of end use (such as appropriate formulations, dosing regimen and cost of goods), and therefore access to patients.
- We agreed a not-for-profit, not-for-loss model. We do not want to fund companies in such a way that they are obliged to support loss-making products. This is not a healthy or sustainable way to engage with companies who have shareholders. We also do not want to provide significant funding only to find that the benefit of Wellcome de-risking the project is purely to increase shareholder value, not to deliver public benefit. We therefore agreed that, if successful, products would be made available to those who need them, in sufficient quantities to meet demand, and at prices which are affordable. Priority would be given to malaria-endemic developing countries to maximise access. As part of its Access Principles, Novartis commits to systemically integrating access strategies into how it researches, develops and delivers new medicines. Tiered pricing was also allowed under the contract.
- In the context of these negotiation, we discussed the way in which the company might facilitate product access in hard-to-reach settings and support efforts to strengthen health systems in order to maximise impact. Wellcome and Novartis recognised that other parties would need to be brought along as the product moves towards commercialisation.

Overall, partnerships must be built on a foundation of trust, and it is key that the involved parties have similar interests in addressing unmet medical needs for which commercial drivers are not sufficient to bring innovations to patients. It is important to have discussions about the impact of investment up front, because the Wellcome leverage in a negotiation is significantly diminished after grant funding has been paid. It is difficult to ascertain the full public benefit that can be achieved through a product given high levels of uncertainty in early-stage funding – and therefore contractually agreeing a principles-based structure seems to be the cleanest way forward. Investing early in new drug development contributes to a pipeline of potential medicines that could address unmet global health needs and ultimately improve the lives of individuals. It is important for both parties to agree up front on some post-approval access principles to ensure that the medicine will reach patients most in need on a sustainable basis.

CEPI – developing new vaccines

Historically, vaccine development has been a long, risky and costly endeavour. Planning for emerging infectious diseases today is especially challenging because the market potential for vaccines against these diseases is limited and testing such vaccines is difficult.

There are specific challenges around vaccines for epidemics, which means that traditional metrics of access (e.g. price and volume) may not be the most appropriate. Many of these vaccines will exist in globally maintained stockpiles and will only be used sporadically in small quantities. Other challenges may be more pertinent, for example the lack of manufacturing capacity available to make these vaccines.

The Coalition for Epidemic Preparedness Innovations (CEPI) finances and coordinates the development of new vaccines to prevent and contain infectious disease epidemics. The research is needs-based, with pathogens identified from World Health Organization priority lists. CEPI has secured over $750 million towards its $1 billion target, with support provided by Wellcome, the Bill and Melinda Gates Foundation, the European Commission, and the governments of Australia, Belgium, Canada, Germany, Japan, Norway and the UK, and with aligned support from the government of India and the European and Developing Country Clinical Trials partnership.

CEPI supports sustainable access and innovation by funding new interventions to address unmet needs and providing timely access to them. It directly funds vaccine development projects, and it is creating investigational stockpiles which allow the rapid deployment of these vaccines in outbreak settings.

Establishing an access position and policy has been a challenging process for CEPI, and for some this hasn't gone far enough. MSF Access has been particularly vocal about the responsibility to put people's health first – it has recommended changes to CEPI's access policy including, triggers for step-in rights and stronger measures on pricing, availability and affordability.

CEPI has responded to MSF's challenge by reasserting its commitment to achieving equitable access to products but acknowledging that ensuring access is complex and it won't be able to please everyone. Recent steps that CEPI has taken include: forming a Board-level Equitable Access Committee to increase focus and scrutiny on the implementation of CEPI's Equitable Access Policy; publication of a paper that explains how this policy is being implemented; and a commitment to include independent experts in the stage-gate reviews of CEPI-funded projects.

As a key investor in CEPI we welcome these actions and are committed to continually monitoring the implementation of the access policy and seeking improvements where necessary. CEPI's access position will ultimately be judged on whether promising candidates are able to be brought to market at a sustainably affordable price.

World Mosquito Programme

The World Mosquito Programme (WMP) is a not-for-profit initiative that works to protect the global community from mosquito-borne diseases such as Zika, dengue and chikungunya. Pioneered by Australian researchers, the WMP uses safe and natural bacteria called Wolbachia to reduce the ability of mosquitoes to transmit these viruses. The ambition is to protect 100 million people by 2023 and 1 billion by 2030.

Wellcome is a major funder alongside others to help WMP build an organisational structure that can meet anticipated demand. This involves providing training to others to support in-country expertise, and developing country-wide frameworks. We are also supporting the team to optimise the product and delivery tools to be able to deploy at high quality and at scale at a target cost.

There are a number of technical and ethical challenges that the programme has to overcome, including the need to find a sustainable business model to support long-term implementation of this approach in poorer communities. WMP also needs to have sufficient resources over time to monitor the long-term impact of this type of intervention.

Affordable monoclonals

Monoclonal antibodies (mAbs) are safe and effective treatments for many chronic diseases, including cancers and immune disorders, and have had a transformative impact on health and medical practice in the past two decades. Despite recent advancements in the production of mAbs and an increase in development and commercialisation, mAb prices remain high and access continues to be a challenge. Wellcome is funding a report by the International AIDS Vaccine Initiative to consider the challenges and opportunities for affordable global access to mAbs. The report will consider the development and commercialisation pathway to set out how targeted investments can catalyse innovation to overcome gaps and challenges. The report will allow us to consider ways of encouraging access to safe, effective products in new disease areas and contexts. We know that Wellcome cannot hope to address all the issues raised, but we will use the report findings to inform our own decision-making and to engage with other partners and drive action.

CARB-X – developing urgently needed antibiotics

The world urgently needs new treatments, as well as improved use and stewardship of existing antibiotics in humans and animals, to tackle the rising global threat of drug resistance. Antibiotic discovery is challenging due to the complexity of bacteria, which are easily able to genetically modify and become resistant to medicines, but also because of declining investment by larger companies. Without innovation we won't have the antimicrobials of the future, without stewardship these treatments will soon become ineffective, and without appropriate access these products will not have their maximum impact on human health.

CARB-X (Combating Antibiotic Resistance Bacteria Biopharmaceutical Accelerator) is a global non-profit partnership dedicated to accelerating antibacterial research to tackle the global rising threat of drug-resistant bacteria. With more than $500 million to invest, CARB-X funds the best science from around the world. The CARB-X portfolio is the world's largest early-development pipeline of new antibiotics, vaccines, rapid diagnostics and other products to prevent, diagnose and treat life-threatening bacterial infections. Wellcome has committed £125 million to the CARB-X portfolio, and also acts as an 'accelerator', providing scientific, technical and business support to CARB-X funded product developers.

CARB-X awardees are contractually obliged to produce and publish a Stewardship and Access Plan (SAP). This SAP must outline the steps that product developers will take to ensure appropriate stewardship and access in the territories where they do not intend to seek commercialisation (predominantly LMICs – although the decision is at the discretion of the product developer). The SAP will be published on the CARB-X website for transparency.

The requirement of CARB-X awardees to make their plans for ensuring appropriate stewardship and access publicly available for new products is a ground-breaking commitment placed on antibiotic, vaccine and diagnostics developers. It should help ensure that new products are made available where they are needed most, and will help galvanise new norms for stewardship and access in the antibiotics R&D sector.

Commercial prospects for a new product are precarious, as demonstrated by the recent case of the developer Achaogen filing for bankruptcy soon after launching a new antibiotic, so it is important that the obligation of product developers to ensure appropriate stewardship and access is balanced with the viability of the product in the market.

Most CARB-X awardees are small biopharmaceutical companies with little or no experience of developing or implementing such a plan. We are seeking to ensure that important stewardship and access commitments do not worsen the commercial challenges currently being faced by antibiotics developers. To help address this problem Wellcome is working with CARB-X, the partnership's other funders, product developers and other interested stakeholders to develop a SAP template, which can provide guidance for CARB-X awardees as they develop and implement plans for their products. This template will be made available to developers before the first CARB-X awardees bring their products to market.

Endnotes

1. https://wellcome.ac.uk/what-we-do/our-work/access-healthcare-interventions/wellcomes-approach-equitable-access-healthcare-interventions
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5. TRIPS flexibilities are provisions in patent law that allow the supply of generic medicines despite the existence of a patent.
6. In a tiered pricing strategy, the pricing of a product differs according to the market in which it is sold. This is usually based on an evaluation of ability to pay and means setting higher prices in high-income markets and lower prices in lower-income markets.
7. In an advance market commitment, donors commit money to guarantee the price of a product in advance of its development, providing incentive for commercial investment in areas that are not otherwise seen to have a viable market.
8. The Medicines Patent Pool is a UN-backed public health organisation that negotiates with patent holders for licences on medicines. These licences permit other pharmaceutical manufacturers to produce generic versions of patented medicines for low-income countries.
9. The WHO prequalification programme assesses the quality, safety and efficacy of products that address global public health priorities, guiding procurement decisions of purchasing agencies and of many low-income countries
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Wellcome exists to improve health by helping great ideas to thrive.

We support researchers, we take on big health challenges, we campaign for better science, and we help everyone get involved with science and health research.

We are a politically and financially independent foundation.

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