CO LAB
INTERNATIONAL
We facilitate co-creation, innovation, learning and change

Towards a reformed research and development ecosystem for infectious disease

The Global Conversation: an independent record of the proceedings
June 2023 to September 2023

ABOUT COLAB INTERNATIONAL

The nine Global Conversation workshops were designed and facilitated by CoLab, who also authored and produced this report.

CoLab is an experienced participatory process design and facilitation consultancy with a global reach. CoLab specialises in the inclusive engagement of diverse stakeholders to address multifaceted and complex problems.

ABOUT WELLCOME TRUST

The Global Conversation project was commissioned by Wellcome.

Wellcome is one of the world's largest charitable foundations, and has committed to spend £16bn over a ten year period to support curiosity-driven research and take on three of the biggest health challenges facing humanity – climate change, infectious disease and mental health.

Wellcome and **CoLab** would like to thank all the participants who took part in the Global Conversation events for the considerable time and energy they invested in sharing their ideas for a reformed R&D ecosystem. We hope you recognise your contribution to this important conversation when you read this report.

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Foreword

Wellcome would like to thank everyone who took part in this Global Conversation on how to transform the infectious disease research & development (R&D) ecosystem to make it more sustainable, equitable and effective.

Wellcome commissioned this document so that the wider global infectious disease community can also benefit from the rich and diverse range of perspectives that were shared. The content here compiles the totality of the themes discussed across the nine workshops and is not, therefore, a representation of Wellcome's own policy priorities in this area.

We would like to thank our facilitation partners, CoLab, who produced this independent record of proceedings from all the discussions that were held as part of the Global Conversation.

Wellcome is but one stakeholder in the ever-growing ecosystem of infectious disease R&D. This Global Conversation recognised the need to increase the diversity of voices in this space and support the inclusion of those most affected by infectious diseases.

This Global Conversation has been a key input into the development of Wellcome's own vision for the infection disease R&D ecosystem. This vision will be published in early 2024 and we look forward to sharing this with you.

Beck Smith
Associate Director for Policy, Wellcome Trust

Introduction

This document provides a detailed account of the Global Conversation - a multi-event online listening exercise, convened by the Wellcome Trust (Wellcome), which took place between June and September 2023. The objective of the Global Conversation was to bring together a broad range of global health experts, policy professionals, and research and development (R&D) stakeholders from all sectors of the infectious disease research and development ecosystem, with the aim of reforming it to better serve the needs of the world's populations regardless of their geographic location or economic circumstances.

The purpose of the document is to provide a full and honest account of the discussions that took place across the Global Conversation. It is not reflective of Wellcome's final vision for a reformed R&D ecosystem for infectious disease.

In this document, the infectious disease R&D ecosystem (the ecosystem) is defined as the broad system of connected endeavours that are involved in the research and development of the medical products (diagnostics, therapeutics and vaccines - DTVs) that are required to detect, treat and prevent infectious disease.

This ecosystem spans:

- Research priority-setting
- R&D itself (i.e., basic research, discovery research, and translational research)
- Clinical trials
- Regulatory compliance
- Manufacturing
- Product pricing and procurement
- Other processes that support the brokering of sustainable access to these products by the individuals and institutions that require them[1]

The term infectious disease encompasses "diseases [that] are caused by infectious agents (bacteria, viruses, parasites, and fungi and their toxic products)"[2] and includes endemic, epidemic and pandemic diseases, as well as emerging and re-emerging infectious disease, drug resistant infections, and neglected infectious tropical diseases.

This document serves as a comprehensive and independent record of the discussions that took place, including details of ideas for reform that were shared during the Global Conversation events. The purpose is to provide for the record an account that represents the breadth and depth of the whole discussion, regardless of whether it aligned with Wellcome's vision for the ecosystem.

[1] https://cms.wellcome.org/sites/default/files/2023-05/Policy-towards-reformed-research-and-development-ecosystem-for-infectious-disease.pdf

[2] https://www.aihw.gov.au/reports/australias-health/infectious-and-communicable-diseases

1

Background to the Global Conversation

1 Background to the Global Conversation

In May 2023, Wellcome published a **discussion paper** that outlined its early thinking around the vision for a reformed research and development ecosystem for infectious disease[3]. Despite significant progress made to tackle infectious diseases in recent decades, the current ecosystem does not support everyone that depends on it. Fragmented markets and imbalances of power result in significant inequalities, especially for low- and middle-income countries (LMIC), where the burden of disease is greatest. An individual's ability to access life-saving products often depends more on economic and geographic circumstances than on actual need.

The factors involved in promoting inequality are complex and it can be difficult to pinpoint the root cause. However, the paper outlines some recurring failures across the system, such as:

- Empty pipelines or stalled research into products addressing major infectious disease threats, particularly those affecting LMICs.
- Barriers during clinical development and registration can result in slow product approval or products that are never approved in some locations.
- Limited supply, logistical issues or high prices can make products that are available in some parts of the world inaccessible to affected communities.

In order to realise Wellcome's vision for an ecosystem that more equitably and effectively serves the needs of the global population, the paper proposes that reform is needed in Four Key Areas:

1. Equitable and comprehensive priority setting in research and development

2. The streamlining of clinical trial and regulatory approaches

3. Strategic scale-up of geographically diverse and sustainable manufacturing capacity

4. The centring of access and affordability while incentivising innovation

The Global Conversation was conceived in order to hear the voices of global, regional and local players in the ecosystem, and to collect a diverse range of perspectives that could help strengthen the vision for reform, and help shape the content of the final paper, to be published in early 2024.

As a global organisation based in London, UK, Wellcome recognises that it has only one perspective, reflecting its position in a high income country (HIC) in the global North. Wellcome does not have all the answers, and in order to truly understand the challenges faced by communities most affected by infectious diseases - who are overwhelmingly situated in LMICs in the global South - it needed to actively listen to a broad and diverse range of stakeholders across the ecosystem.

Wellcome is keen for its discussion paper to be a jumping off point that will stimulate productive dialogues with all stakeholders in the ecosystem, regardless of where they are based and of their affiliations. To this end, Wellcome commissioned CoLab International Ltd (CoLab) to design and deliver the Global Conversation aimed at gathering feedback from the global infectious disease R&D stakeholder community on the paper's ambitious vision for reform.

An overview of the participative process used can be found in **Appendix. 2**

[3]https://cms.wellcome.org/sites/default/files/2023-05/Policy-towards-reformed-research-and-development-ecosystem-for-infectious-disease.pdf

2

Event Proceedings

2 Event Proceedings

The Global Conversation comprised nine separate events, grouped into three distinct phases - convening (launch), exploring the four themed areas (four themed events) and finally global and regional deep dives (two global and two regional events). This section reviews the content of each event in turn. For a list of participating organisations and countries across all nine events see **Appendix 1.**

Supporting and additional material from all nine events can be found in appendices 3-7.

2.1 Phase One: Convening the Conversation

The Launch Event : Defining the challenge, the questions and the people

Phase one consisted of a **launch event** that aimed to

- Collectively define the scope of the challenge
- Propose the questions the system needs to address
- Encourage inclusive participation of people from across the global ecosystem to make this listening exercise as equitable as possible.

The launch event took place on 13th June 2023 over three hours, and was attended by more than 100 stakeholders representing organisations drawn from across all areas of the ecosystem. There was a notable mix of global, regional, and country level representation, with participants logging into the event from over twenty countries in total.

Defining the scope of the challenge

During the event participants acknowledged that, although similar conversations were happening in other forums regarding discrete elements of infectious disease R&D (e.g., manufacturing, clinical trials, regulation etc.), this Global Conversation which conceives the ecosystem as an interconnected whole was a dialogue that "is so overdue and sorely needed"[4] .

At the same time, there was concern about how to ensure the Global Conversation does not simply duplicate these parallel conversations but adds to and learns from them to foster tangible change. With respect to other global health conversations that might be taking place in other fora, participants were also keen "to learn from similar sectors and what they are getting right in the non-infectious disease R&D ecosystem"[5].

Proposing questions to be addressed

In terms of defining the questions for the Global Conversation, the overarching

[4]Plenary comment from a Global Health R&D Advocacy & Philanthropy professional.
[5]Plenary comment from a biotech company representative

theme was one of who is responsible, is able to, and is willing to drive this reform. The following two questions were raised repeatedly by different participants:

'Who sets the priorities? An important high-level question, because when funding stops or switches to a different disease this creates gaps in the R&D continuum'

'With respect to priority setting, how do we choose what to focus R&D on if we are trying to be equitable?'

During several breakout room discussions the participants worked in small groups to consider the four key areas for change addressed in Wellcome's discussion paper. Their considerable range of responses, issues identified, and questions raised were captured live on the interactive Miroboard. See **Appendix 3** for these collated participant contributions.

Perhaps reflecting the scientific background of the majority of the participants, precise definitions and measurement mechanisms were thought to be crucial to successful reform of the ecosystem. The following three participant statements are representative of that analytical approach to defining the scope of the challenge and the way forward for reform.

"Getting super-clear about what we're solving for, I think would help the dialogue because that gets us closer to the impact that we want to see"

"Equity vs impact – they are not the same and are sometimes in conflict"

"How do you measure what has been successful, and who determines success?"

Who should be included in the conversation

Moving on to the third objective of the launch event – exploring who should be included in the Global Conversation if not already present – it is important to note that although many participants represented organisations with a LMIC focused remit, these organisations were headquartered in high income countries.

Of the participants that declared their geographic location, only three LMIC countries[6] were represented (Brazil, Eswatini, and Nigeria). Due to the Matthew effect[7], this was not an unexpected occurrence and was precisely why part of the launch event was dedicated to ensuring that organisations and individuals who do not typically attend international events such as this are included in the subsequent phases of the Global Conversation.

Participants put forward 23 names of individuals and organisations who were not currently on Wellcome's invitee lists. After this launch event invitations to the subsequent two phases of the Global Conversation were forwarded to these people. Several participants with extensive LMIC networks committed to assisting Wellcome and CoLab to publicise the Global Conversation among their colleagues.

One participant questioned how it might be possible to support stakeholders with limited resources to attend the Global Conversation events. In response to this Wellcome, upon CoLab's advice, subsequently offered honoraria to individuals with limited resources to facilitate their attendance.

Many participants thanked Wellcome for beginning this reform initiative. Although the conversation was only just beginning, there was a feeling that the launch event had been an important and beneficial opportunity to exchange views with a broad range of infectious disease R&D stakeholders. Many expressed their desire to take part in the subsequent events to forge solutions and move towards the reform that is urgently needed.

"I appreciate the opportunity to get involved, and I hope this model for engagement will continue to be improved upon and replicated by other health-driven organisations"[8]

[6] https://wellcome.org/grant-funding/guidance/low-and-middle-income-countries

[7] Also known as the Pareto Principle, refers to the socio-economic phenomenon where those present at one table will be called to subsequent tables (see https://thereformedconservative.org/the-matthew-principle-and-inequality/)

[8] Launch Event participant comment from the post-event feedback survey

2.2 Phase Two

Exploring the Four Key Areas for Change: Identifying priorities, complex issues, and potential solutions

Phase Two of the Global Conversation consisted of four separate events, one for each of the discussion paper's key change areas. In these events, participants were asked to bring their unique perspectives, knowledge, and expertise to focused exploration of these four change areas. The aim of these events was to move from questions and problems to forging potential solutions. Nonetheless, it was also expected that some issues may be too complex to solve, and the objective was to identify such complex, controversial, or knotty issues as potential candidates to be discussed in the deep dive events that would occur in Phase Three of the Global Conversation.

2.2.1 Themed Event One: Equitable and comprehensive priority setting on research and development

The event took place on 27th June 2023 over three hours and was attended by over 60 stakeholders. There was a significant mix of global, regional, and country level representation, with participants logging into the event from more than 25 countries in total. This was an increase in regional representation from the Launch Event; with additional countries in attendance including, India, Japan, Cameroon and Uganda. Africa was particularly well represented at this event (seven countries).

All the Themed Events were designed to encourage active participation from the stakeholders. Participation began prior to the event with a pre-event survey. In this survey, respondents reported that they perceived there to be significant existing challenges and barriers that hinder equitable and comprehensive priority setting in the ecosystem (see appendix 4). Respondents were also asked to identify existing regional and global coordinating mechanisms with the potential to be emulated or built on. One example suggested was the antibiotic subscription model for incentivising R&D, currently being piloted in the UK.[9] Key opinions expressed in small group breakout discussions are summarised below:

- **The R&D system suffers from a lack of equity and inclusivity.** This includes misaligned economic incentives that are not guided by health needs, limited input from LMICs and other key constituencies, and the dominance of funders and experts from the Global North.
- **Participants highlighted that there is a lack of good data on R&D investments and R&D activity.** It was felt that the collection of relevant data is limited, and access to the data that is collected is often restricted. As one consequence of this, participants mentioned that it is difficult for academia and small and medium size enterprises (SMEs), particularly in LMICs, to have an overview of how much funding is available in which disease area, and what the eligibility criteria are for this funding.
- **While recognising a number of high-quality prioritisation exercises undertaken within a specific disease area**, participants pointed toward difficult questions around prioritising across disease areas. For example, it was stated that World Health Organisation (WHO) priority setting occurs only within a single disease area and does not set priorities across disease areas. As one example of a point of tension, one comment raised the question

[9] https://pharmaphorum.com/news/uk-launches-its-netflix-style-payment-model-for-antibiotics

of how priorities should be balanced between infectious versus non-communicable disease. In another example, some comments raised the question of whether priorities should be set relative to disease burden or relative to level of neglect.

- **A number of comments suggested a feeling of an overall lack of investment by donors in neglected diseases research.** Relatedly, participants commented that the COVID-19 pandemic saw funding diverted from neglected diseases to pandemic preparedness.
- **From the perspective of economic incentives for R&D, participants highlighted that the relative funding of different disease treatment programmes also indirectly affects R&D prioritisation.** It was noted that R&D prioritisation takes place not only through deciding what proportion of grant funding will go to which disease area, but also by decisions regarding which diseases to fund, for example, decisions by the Global Alliance for Vaccines and Immunisation (GAVI) or the Global Fund. It was argued that if 'there is money in HIV', more HIV-relevant products will be developed. On the other hand, if neglected diseases (ND) treatment programmes get more funding, this could indirectly stimulate R&D for ND products.
- **There was significant support among participants for the idea of funding regional R&D hubs.** Establishing regional hubs (or 'centres of excellence') for R&D and/or manufacturing generally received support. Well-known examples of existing hubs that were making a difference were cited.
- **Participants reiterated the need to include access-related provisions in R&D agreements.** This point was discussed further during Themed Event four.
- **The concept of 'access and benefit sharing' (ABS)[10] was raised but not discussed in detail.**
- **Participants emphasised that funders should significantly increase the inclusion of LMIC voices in R&D priority setting, while recognising that it is difficult to create a truly democratic, bottom-up system for priority setting in R&D.** Participants did not reach a clear proposal for a framework for 'democratic' or 'bottom-up' priority setting, but were generally highly supportive of events such as the Global Conversation that make efforts to include LMIC participants, although it was noted that participation from some regions remained low.
- **Participants stated that funding that ringfenced or highly 'earmarked' funding limits the ability of low- and middle-income countries (LMICs) to set their own priorities.**
- **Participants criticised the channelling of LMIC research funds through intermediary organisations.** Participants mentioned that this can create inefficiencies and the feeling of a tiered system. However, specific examples of such 'middlemen' and difficulties encountered in dealing with them were not provided.
- **Participants argued that improved research capacity in LMICs (discussed further during Themed Event three) would also enable more equitable and democratised R&D prioritisation, if accompanied by long-term and 'horizontal' funding.**
- **Some participants argued that funding for LMIC-based research is too focussed on later-stage research.** The impact being that sometimes funding only becomes accessible once a proof-of-concept exists.
- **Some comments mentioned that research funders' priorities are not transparent.** However, specific examples of this lack of transparency

[10] Author note. ABS is a concept that has been most clearly crystallised in the Pandemic Influenza Preparedness (PIP) framework and the Nagoya Protocol. The principle is that if a useful genetic material is identified in a certain country, that country should share this information/material ('access') in exchange for certain benefits. As many valuable genetic materials are identified in LMICs ('biodiversity-rich countries'), certain country groups have lobbied for legal instruments that would protect their right to benefit from these.

were not provided by the participants who raised this issue.

- **Numerous comments suggested that more accountability is needed for funders of research.** For example, the establishment of an 'independent tracker and watchdog' was suggested, which would track what happens after priorities are set – for example, whether funds distributed according to stated priorities are producing viable results.
- **Participants called for funders to have a greater appetite for risk and to offer more 'patient' or 'sustainable' funding.** It was stated that a greater appetite for risk among funders could mean, for example, funding R&D for which no proof-of-concept exists, which uses a new mechanism of action or a new platform technology. With regard to innovative business models, a greater appetite for risk would enable investment in innovative financing modalities that have seen limited implementation to date, such as the suggestion of establishing prize or market entry reward mechanisms.

During the final plenary activity, which consisted of a fishbowl panel (see **Appendix 2**), participants built on these explorations of definitional inclusivity to introduce a potentially important imperative within the R&D ecosystem. Namely, that the current state of inequity across the ecosystem is a symptom of the effects of historical colonialism, and thus there is significant work to be done to decolonise it.

Several suggestions of what decolonisation might mean in the context of reforming the ecosystem were put forward. For example, one participant put forward the suggestion of de-centering research away from the current colonial mindset by establishing R&D hubs in Africa. Many participants felt it would be constructive to frame the concept of decolonisation as a question that research funders could reflect on. One participant articulated that question in the following form: How can the concept of decolonisation be operationalised in R&D funding prioritisation?

2.2.2 Themed Event Two: Streamlined clinical trials and regulatory approaches

Themed Event Two took place on 29th June 2023. The event was attended by over 70 stakeholders, representing organisations, pharmaceutical companies and individuals drawn from across the full extent of the ecosystem. The mix of global, regional, and country level representation was similar to previous events, with participants logging in from more than 25 countries in total. Participants worked on two sub-themes: streamlined clinical trials and regulatory approaches.

The key points from the two sub-themes are discussed below:

Sub-theme A: Strong and streamlined clinical trial infrastructure developed globally

Several breakout groups reported that there is an opportunity to retain and repurpose any in-country clinical trial capability and expertise that may have been established during trials of products for one disease, and redirect this capacity to trials in other disease areas. This was proposed in response to participants sharing experiences of instances where trial infrastructure and training capacity was built up for one project and left redundant after the project ended. The participants suggested therefore that funders should move away from project-based funding and shift towards the funding of clinical trial infrastructure for the long term. A proposal to move away from de novo clinical trial set-ups by moving toward the use of existing collective infrastructure through connecting regional networks echoed this idea.

"In the example of COVID, a lot of investment was made. Then as COVID reduced, this infrastructure was packed away and forgotten about" – Research Lead, East Africa Region

"Yes, in our group, clinical trials are thought of as very much project based, focused on one product – but what are the constants in CTs and what does that mean for health system infrastructure investments?" – Public Health Subject Expert.

"As a funders membership association we have been doing this very effectively with clinical trials networks. There are many, but these networks are not equally distributed, there are big holes around the globe where these should exist" – Scientific & Advocacy Director.

Sub-theme B: Streamlined regulatory processes underpinned by mature national and regional bodies

In these breakout groups, there was a clear consensus that contract research organisations (CRO) were key to facilitating the navigation of regulatory processes, because CROs are familiar with the logistical considerations and the ethical requirements that are local to clinical trial sites.

Collaboration between regulatory agencies in different countries, in the form of networks, was also seen to play a key role in streamlining regulatory processes, with the African Vaccine Regulatory Forum (AVAREF) and the African Medicines Regulatory Harmonization (AMRH) Partnership Platform cited as examples of regional networks of regulators that have been pivotal in speeding up clinical trial approvals in the Africa region. Stronger networks were also seen as key vehicles for knowledge exchange and the transparent and timely sharing of data, with it being suggested that smaller or less mature regulatory authorities can learn from the more established organisations.

Participants also underscored the importance of clarity in regulatory requirements and good communication with regulators. Points where clarity was stated to be especially important include key trial endpoints, key decision 'gates' for progression through development phases, and well-defined and standardised diagnostic tests.

"CROs are absolutely critical, they play a central role particularly if you have multicentre clinical trials" – South Africa based Senior Scientist, Private Sector.

"Education needed on innovative or adaptive clinical trials approaches. Bridging the Global North-Global South divide - how can Glocal North learn from Global South or support South-South learning?" – Sub-theme B breakout group finding.

"Timely regulatory approval may be hindered by opposition from the community, due to mistrust of the clinical trials process, a perception that it is 'western experimentation', and a lack of education around the benefits of clinical trials for the communities themselves" – Early Career Scientist, Africa.

"Yes, to get these benefits known, I'm thinking we should be educating at the level of the community healthcare worker, as these are the ones that educate and convince the local communities" – Clinical Operations Director, Europe.

Bringing the two sub-themes together

Following a plenary sharing of findings from the two sub-themes, participants broke out into mixed interest breakout groups. In these groups they were tasked with identifying practical actions that might contribute to the streamlining suggestions raised in the first part of this event.

The key themes raised were:

- Funder accountability to speed up the pace of reform, possibly via a 'watchdog'
- Harmonisation, starting at a regional level, building on limited examples in good clinical practice, checklists, and

guidance to create more uniform structures

- Bringing the ecosystem's stakeholders together to accelerate and drive forward the pace of reform
- External bodies getting the right people at the table
- More collaboration between regulators.

Emerging issues for consideration in the Deep Dive Events

Despite a significant level of consensus around the direction needed to drive reform of clinical trials and regulatory approaches, some potential areas of disagreement emerged from the participants. These included disagreements about the benefits of conducting trials among the populations with the greatest burden of infectious disease.

One breakout group emphasised that this is important because genetic variations among product target populations can have clinical implications. Another group questioned the benefits of conducting trials in regions with less mature infrastructure, suggesting that *"this is a thorny issue - why do we even need this? It creates problems like big delays, and costly and complex logistics"*.

There was consensus on the value of training and sharing inter-organisational learning to promote R&D capacity building, but several participants cautioned that this is far too often assumed to be a geographically top-down process (i.e. global North to global South), and that the value of South-South sharing and learning should receive more attention.

In summary, participants suggested that harmonisation and streamlining are ongoing processes involving many dispersed and diverse actors within the ecosystem. They felt strongly that reform of the ecosystem can be brought about by bringing these actors together to harness the collective power of networks.

2.2.3 Themed Event Three: Strategic scale-up of geographically diverse and sustainable manufacturing capacity

Themed Event Three took place on 5th July 2023. The event was attended by 35 stakeholders, representing organisations and individuals drawn from across the infectious disease R&D ecosystem. The mix of global, regional, and country level representation was similar to the previous events, with participants logging in from more than 15 countries in total.

Pre-event Survey

Prior to the first breakout activity CoLab shared the results of the pre-event survey with participants (see table 1). The purpose of presenting this survey was to collectively acknowledge the barriers that prevent products being manufactured at scale in the regions and countries where they are most needed. This enabled the focus of the event's collaborative activities to be directed towards finding solutions to these barriers.

What major barriers to a strategic scale-up of geographically diverse and sustainable manufacturing capacity need to be considered?

- **Market dynamics - manufacturing capacity concentration** (lack of geographic diversity in supply chains)
- **Strong established producers - barriers to new entrants to market**
- **Lack of coordination of manufacturing initiatives**
- **Funding for expanding manufacturing capacity**
- **Lack of data** - we don't know how much capacity we need and don't have good insight into what capacity we have.
- **The tendency toward more complex, proprietary technologies is a key barrier.**
- **Intellectual Property practices**
- **National and regional legal frameworks**

Table 1. Barriers to scale-up of geographically diverse and sustainable manufacturing capacity

There were then two rounds of small group discussions:

Small Group Discussion One

In the first round of small group breakout room discussions participants addressed the following three questions.

Question one: Are there any existing examples of scale-up of sustainable and geographically diverse manufacturing capacity?

Examples shared included:

- Drugs for Neglected Diseases Initiatives' (DNDi) partnership with Pharco in Egypt to produce ravidasvir;
- The mRNA hub at Afrigen in South Africa;
- Initiatives to expand manufacturing capacity being established in Uganda and Zimbabwe for the manufacture of HIV-related products

Question two: What types of additional manufacturing capacity, in terms of products and regions, should be prioritised?

Key points:

- Capacity building should not be limited to manufacturing technologies but also apply to the workforce in terms of training and education
- Local manufacture of active pharmaceutical ingredients and not just finished products should be prioritised regionally
- Manufacturing capacity priorities should be informed by the analysis of blockages in supply chains although

this would be significantly more complex and would likely require a higher level of investment

- Gaps in fill-and-finish capacity could be identified if the analysis starts at the patient access end of the supply chain rather than the early parts of the chain.

Question three: How do we balance the desire for self-sufficiency with economic viability and utility outside of global crises such as pandemics?

Small Group Discussion Two

It was recognised that this event's key change area is a complex and multifaceted one. Therefore, in an attempt to harvest tangible outputs that might inform revisions to Wellcome's discussion paper, participants were split into three sub-theme working groups. Each working group was tasked with answering two guiding questions related to their sub-theme, as follows:

Sub-theme A: Coordination of a global approach to manufacturing scale-up

- What different forums or conversations are needed to effectively coordinate a global approach to manufacturing?
- Which stakeholders need to be involved to ensure coordination is achieved in an inclusive way?

Sub-theme B: Sustainable financing for expanded manufacturing capacity

- How should sustainable financing for capacity-building be raised and coordinated?
- What role can major purchasers (e.g., national governments or global health agencies) play in driving a shift to expanded, regionalised manufacturing capacity using their procurement approaches?

Sub-theme C: The role of intellectual property

- To what extent are current approaches to intellectual property (IP) governance a major barrier to scaling up manufacturing?
- How can a more open approach to IP governance be achieved without damaging the commercial viability for product developers, and what practical measures are needed to enable better technology transfer?

The outcomes from the discussions held across the five working groups are broadly summarised as follows:

- To drive real change, there needs to be use of both voluntary mechanisms (the 'carrot') and mandatory mechanisms (the 'stick'). This point came up in numerous contexts during this event (and later in Themed Event four), including in points on IP sharing, technology transfer, and the use of taxes or levies as policy levers to influence private sector behaviour. Brazil's technology transfer policies[11] were mentioned as an example of a successful implementation of a mandatory measure.
- Participants recognised the tension between the need to provide products at affordable prices, and the aim of strengthening local/regional industries, which may require a degree of protectionism. It was argued that a nascent local industry will not be able to match the economies of scale and other efficiencies that established manufacturers have developed. Locally (or regionally) manufactured products will therefore most likely need to be priced higher than the lowest prices available on global competitive markets. LMIC governments are not always willing/able to pay a higher price for locally manufactured products. For example, the South African government chose to procure pneumococcal vaccines from an Indian generic supplier, rather than the domestically-based company Biovac. This demonstrates the fact that just having domestic capacity does not mean products will be procured locally, and that policy-makers need to act differently to stop this conflict between their vaccine

[11] The effect of Brazil's technology transfer policies has been particularly notable for strengthening local biologic manufacturing capacity (cf. Pimenta MV, Monteiro G. The production of biopharmaceuticals in Brazil: current issues. Brazilian Journal of Pharmaceutical Sciences 2019; 55. DOI:10.1590/s2175-97902019000217823.)

policy and their public procurement policies[12].

Some participants argued that, when the COVID-19 pandemic was considered a national security issue, this made it possible to pay higher prices for locally manufactured products. Also highlighted was the need for the higher prices required to support the development of local industry to be budgeted into health system and treatment programme plans, at least for the first few years.

Relatedly, participants pointed to the challenge that procurement by international global health agencies can create subsidised or highly managed markets that in turn lower prices on international markets to such an extent that it is hard or impossible for local competitors to enter the market.

- Participants cautioned that, for local manufacture, considerations for fill-and-finish plants differ from those for API production plants. For fill-and-finish facilities, active pharmaceutical ingredient (API) is imported and then formulated into a tablet or vial. It was stated that it would be difficult or impossible to entirely avoid a globalised supply chain as most APIs come from India or China, and most 'raw materials' (i.e. those used to synthesise APIs) come from China. For biologics (e.g. insulin, monoclonal antibodies, or vaccines), discussions around local or regional production mostly concerned local or regional manufacture of (biologic) APIs – posing a very different set of challenges to fill-and-finish facilities, because it involves a far higher level of complexity and investment.
- Numerous comments supported moving away from discussing plans for expanded manufacturing capacity in terms of commercial viability. This was an interesting perspective, as arguably, global health policy discussions often treat DTV products as inherently commercial. When considering other health system aspects, policy discussions rarely see the same insistence on commercial viability. To illustrate this point, it is notable that questions such as "What business model can we create to make breast cancer surgery commercially viable?" are rarely heard.
- Several participants mentioned a need for greater transparency in the economics of pharmaceutical developers and manufacturers. It was argued that better information on cost of production (which is normally kept as commercially confidential) would help evaluate which projects could work for local/regional manufacture.
- Participants noted the high potential impact of technology transfer for platform technologies. One well-known example of a platform technology is mRNA vaccine technology, which can (in theory) be applied to a great range of different pathogens. Other platform technologies would include, for example, a 'cell platform' in which different monoclonal antibodies can be expressed.

Following this breakout activity, participants were brought back to the main room and shared their findings in a final plenary. There was strong consensus around a statement that suggested "the underlying problem was that the current market doesn't work" and that in response to that there "are more questions than answers". Having said that, there was a suggestion that the answers to scaling-up manufacturing at the local and regional level might come from reframing the need for this as a global public good, and it maybe that, by considering the question in this way, solutions to sustainably financing such an endeavour may be found at the global level.

[12] https://healthpolicy-watch.news/despite-hosting-mrna-hub-south-africa-buys-vaccines-from-india-highlighting-tension-between-price-and-local-production/

During the final plenary activity, which consisted of a fishbowl panel (see Appendix 2), participants built on these explorations of definitional inclusivity to introduce a potentially important imperative within the R&D ecosystem. Namely, that the current state of inequity across the ecosystem is a symptom of the effects of historical colonialism, and thus there is significant work to be done to decolonise it.

Several suggestions of what decolonisation might mean in the context of reforming the ecosystem were put forward. For example, one participant put forward the suggestion of de-centering research away from the current colonial mindset by establishing R&D hubs in Africa. Many participants felt it would be constructive to frame the concept of decolonisation as a question that research funders could reflect on. One participant articulated that question in the following form: How can the concept of decolonisation be operationalised in R&D funding prioritisation?

2.2.4 Themed Event Four: Centering access and affordability while incentivising innovation

Themed Event Four took place on 6th July 2023. The event was attended by 40 stakeholders, representing organisations and individuals drawn from across the infectious disease R&D ecosystem. Although the majority of these participants were affiliated to 'Global North' entities, several of these were organisations that are particularly focused on improving access to DTVs in LMIC countries (for example FIND, GSD Bio, Global Health Innovation Alliance Accelerator).

Initial collaborative task

To facilitate collaboration between participants during breakout room activities and promote the exchange of verbal contributions during the subsequent plenary sharing, participants worked in small groups to brainstorm the prompt 'What does centering access mean to you?' Initial responses to this question included:

- Amplifying the role of diagnostics in universal health coverage
- The importance of involving all stakeholders in access
- The notion that affordability is a key aspect of access that should be designed-in early in the pipeline rather than only considering this later on in the R&D process
- Access also means timing, i.e. reducing the time between availability in HIC and LMIC settings

The development of these initial thoughts around what access might mean in a reformed ecosystem also resonated well with the synthesised findings of the pre-event survey that participants completed prior to joining the event (see tables 2 and 3 below).

Participants' inputs: What other major barriers to maximising access to new products in affected communities in low-resource settings need to be considered?

- Sustained, flexible funding for R&D and innovative products ✓✓✓✓✓✓
- Tying R&D prioritization to national/ regional demand.
- Information and experience sharing on developing, implementing and measuring success of an access plan
- Political stability at community to national levels
- How to truly consult with most affected communities.
- Thinking about genuine and equitable community engagement (most affected communities). Shifting power.
- STEM (science-technology-engineering-mathematics) workforce development in LMICs.

Table 2. Participant responses to pre-event survey part A (ticks ✓indicate this point was mentioned by lots of people)

Participants' inputs: What could innovative business models or commercial partners look like that would enable access to new products while incentivising innovation?

- Create a "Global Health Inc" mega-PDP (product development partnership) with contributing companies getting bronze, silver or gold ESG (environmental and social governance) status for priority review
- Advanced purchasing mechanisms that guarantee return on investment for manufacturers serving LMICs, favoring regional producers.
- Partnerships with funders and NGOs to expand access to new products. Early access plan is critical.

Table 3. Participant responses to pre-event survey part B

Taking the input from the pre-event survey and the brainstorm two rounds of small group discussions took place around two sub-themes:

Small Group Discussion One: Innovative business models and commercial partnerships

'What novel business models or commercial partnerships for controlling and treating escalating infectious diseases might be possible?'

There was broad support for implementing innovative new or early-adopter R&D financing mechanisms. In a range of different comments, participants support the creation of 'pull' incentives, moving away from the predominance of grants or loans as financing instruments, such as:

- Prize (market entry reward) or subscription models
- A system that offers financial rewards proportional to health impacts
- Cash prize for eradicating or near-eradicating a disease

The merits of providing retrospective funding via an impact award scheme were contrasted with both NICE's subscription-based model for procuring antibiotics (often described as the 'Netflix' model) and the 'Swedish Market Model'.

Other ideas discussed included:

- Shareholder and investor buy-in for the development of a 'mega-PDP' could be achieved through the leveraging of environmental, social and governance (ESG) requirements.
- Investment models that involve governments having a financial stake in the R&D of neglected tropical diseases (NDT) may be a way to fund the development of products to combat these diseases
- investment could come from multiple stakeholders, including investment from the communities that might benefit from the resultant products. In this model it was suggested that incentives could be linked to health impact, perhaps via a similar mechanism to the impact award suggestion
- More broadly, the approach to R&D should move away from the current paradigm, in which it is assumed that a commercial sponsor is an absolute necessity for product development.
- Greater exploration of mandatory mechanisms should be made instead of relying on voluntary initiatives.
- Increased transparency in R&D costs, as per the 2019 World Health Assembly resolution calling for the same.[13]

Small Group Discussion Two: Investigating the different roles various stakeholder types have in driving innovation, access and affordability

Participants explored the potential compromises between funders and

[13] https://cdn.who.int/media/docs/default-source/essential-medicines/intellectual-property/gspa/a72_r8-en.pdf?sfvrsn=8ecefe84_3&download=true

governments and the private sector that could have the biggest impact on reforming the current market dynamics:

- Greater transparency around profits might lead to companies self-regulating their profit expectations
- The above could be combined with a mandated percentage of their R&D to be spent on access initiatives, and/or this could be incentivised by governments in the form of tax rebates or other reimbursement mechanisms
- Access to high income markets being conditional on subsidised provision of product to LMIC regions
- Delinkage of profit from products, moving away from product = profit to product=health=profit. Example: infectious disease R&D is a "global endeavour" and in that respect is similar to CERN or the International Space Station neither of which draw on commercially viable business models to fund their scientific contributions to society

A representative from Access to Medicines Foundation left a closing remark acknowledging that reform is a continuous process and collective endeavour:

"Things are moving in the right direction, pharmaceutical companies used to tell us access plans are not possible, it is too much of a burden. But last year we saw that six companies now have 100 access plans for their latest products[14]. If we all, public and private sector, push in the same direction more of this type of progress can be made."

2.3 Global and Regional Deeper Dives

The final phase of the Global Conversation consisted of four "deep dive" events. The aim of these events was to generate a deeper global and regional analysis of the key challenges, controversial issues, priorities, and solutions with the greatest potential to make the global R&D ecosystem more equitable and innovative. With the aim of encouraging participation of often neglected LMIC voices the deep dive phase began with two regionally-focused events.

2.3.1 Regional Deep Dive One: Focus on Asia

The first regional deep dive event took place on 1st August 2023.The event was attended by 40 participants representing the voices of seven Asian countries (India, Indonesia, Japan, Myanmar, Singapore, Thailand and Vietnam). In addition to being joined by wider members of Wellcome's team, two representatives of Global North based organisations, with a special interest in Asia, also attended (Life Arc, UK; and Veterans Affairs, USA).

To ensure that both regional deep dives reflected the priorities of the participants from this region, this event diverged from the facilitation approach used in the previous Global Conversation events. In the previous events the agenda was set by Wellcome with each themed event focusing on a particular aspect of the discussion paper. In contrast, this first regionally focused deep dive event used Open Space Technology[1] to put the agenda setting firmly in the hands of the participants.

The use of Open Space Technology provides participants with the opportunity to propose and contribute to conversations aimed at defining the key changes and strategic actions that they believe are required to reform the R&D ecosystem in

[14] https://accesstomedicinefoundation.org/news/2022-access-to-medicine-inde-more-companies-move-to-address-access-to-medicine-will-they-now-go-further

[1] https://colabinternational.co.uk/open-space-technology

their region. Open Space Technology works as follows:

- Any participant can propose a conversation around a relevant topic they are interested in
- Other participants then join the conversation that they are most interested in or feels most relevant to them
- Participants are free to enter and leave discussions at will. This means they can stay in one room for the whole discussion or jump between breakout rooms to cross-pollinate their ideas.

Using this approach, 12 participant-centred conversations took place over two rounds:

Summary of Round One Conversations

Conversation one: *"Research funding and training opportunities for early career researchers in Asia"*

Proposer: Professor of Tropical Medicine based in Thailand

Participants: nine (in addition to proposer)

The participants of this discussion began by stating that the foundations of a twenty-year vision need to be laid now. This means thinking about the Asian researchers coming through the pipeline and considering how their professional development can be supported.

Discussion points/ideas

- Provide funding to increase training provision
- Mentorships (using local senior researchers, perhaps using the DELTAS Africa programme as a template)
- Revive the Wellcome Masters Fellowship (which had shown promising results)
- Modify the Discovery Science scheme so that it also focuses on translational research in LMICs
- Specific support for grant application processes and proposal writing, in particular for overseas funders
- Include local universities and regional organisations in the support structure as their smaller grants are easier to access and manage

Conversation two: *"How to strengthen surveillance data collection and use it to set priorities?"*

Proposer: epidemiology research lead based in Thailand

Participants: five (in addition to proposer)

Discussion points/ideas

- Closer regional collaboration and closer working with WHO and global funders
- More systematic process for collecting disease burden data
- Improve the process for accessing data
- Standardise data format

Conversation three: *"Capacity development for infectious diseases research"*

Proposer: Vice Dean of Global Health & Infectious Diseases, Singapore

Participants: seven (in addition to proposer)

The proposer of this conversation felt that direct investment in research capability in Asian countries themselves was the most efficient means of ensuring regional priorities can be addressed.

Ideas

- Direct regional investment in research capability to ensure local priorities can be addressed
- Funding for the more junior and admin roles within a research team - dedicated funding and broadening grants to include this lower-end capacity and enable better pay is crucial

- More collaboration and knowledge sharing between countries, including improved sharing of genetic sequence data (GSD)
- Creation of a "regional roadmap for capacity building" to steer efforts in a structured way

Conversation four: *"How to enhance R&D as a catalytic accelerator for regional self-sufficiency in novel diagnostics, therapeutics and vaccines?"*

Proposer: a representative of the Centre for Outbreak Preparedness, Singapore.

Participants: five (in addition to proposer)

Discussion points/ideas

- Post-COVID pandemic, significant manufacturing potential has emerged within the region. However, a reluctance to share data and a lack of pooled procurement mechanisms hamper the realisation of this potential
- Regional self-sufficiency conversations need to broaden beyond just Central and SE Asia
- Need for new business models that incentivise Big Pharma to invest more heavily in the region's infectious diseases R&D pipeline

Conversation five: *"Creating a regional network for harmonised regulation based on the needs of LMICs"*

Proposer: research associate at the Japan Centre for International Exchange

Participants: three (in addition to proposer)

Discussion points/ideas

- Releasing medical countermeasures to the Asian market as quickly as possible hinged on regulatory harmonisation and that this needed to be discussed more widely in the region.
- This requires funding and training in regulatory harmonisation to increase manpower
- Creating a network would require the commitment of multiple stakeholders including national regulators (e.g., Product Development and Management Association in Japan), national centres for infectious disease, government ministries, and international bodies (e.g., International Coalition of Medicines Regulatory Authorities)
- Sufficient political will to champion regional harmonisation.

Conversation six: *"Knowledge transfer through exchange programmes aimed at graduate students and Postdocs"*

Proposer: representative of the Indian Council for Medical Research

Participants: two (in addition to proposer)

Discussion points/ideas

- The motivation for setting up the exchange programmes discussed in this conversation echoed some of the ideas discussed in Conversation 1 above.
- Mutually and equally beneficial exchanges vital
- Ideal length: six months to one year
- Mentoring that occurs during the exchange can continue beyond the placement when the researchers return to their home institution.
- These types of exchange can foster deeper collaborative relationships between the institutions involved, thus setting the groundwork for further collaboration projects.

Conversation seven: *"Developing an equitable local innovation/IP capture system"*

Proposer: representative of Veteran Affairs, USA

Participants: two (in addition to proposer)

Discussion points/ideas

- When research was funded by a major pharmaceutical company or international partner the IP generated would often go to the contributor of the funds

- Mechanism needed to reward local researchers for their contribution to IP - local IP capture system

Means to achieving this:

- Researchers receive training in IP law and to give them opportunities to work on start-up environments to gain direct experience of IP management and capture
- Technology transfer initiatives to support translation of university or hospital research into products

Summary of Round Two Conversations

Conversation one: *"Sustainable, inclusive clinical trial networks for infectious diseases - how do we make them happen?"*

Proposer: representative of Advance ID, Singapore

Participants: nine (in addition to proposer)

Discussion points/ideas

- The current "one trial at a time" approach was deemed to be cumbersome, inefficient, and costly
- Set up trials networks in the region where infrastructure, knowhow and manpower can be retained and used to continue to perform trials after the initial project has finished.
- Stimulate the creation of these networks by disseminating case studies of successful local trials
- Priorities and new research ideas should come from "the bottom up" (i.e. researchers teams on the ground)
- Disease specific or disease agnostic?
- Need for a common data sharing platform

Conversation two: *"How to move away from a market driven approach"*

Proposer: Professor of tropical medicine, Shoklo Malaria Research Unit, Thailand

Participants: four (in addition to proposer)

Discussion points/ideas

- Market driven approach (ie no profit perspective) is an obstacle for innovation
- "lost profit" (the costs of illness, lost workdays etc.) could be used as a metric to incentivise governments to fund innovation when industry won't, and that making this argument to ministries of finance (or equivalents) could help mobilise new funds.
- Could global funders be incentivised to fund these empty pipelines?
- One way to encourage global investment in developing DTVs for locally prevalent infectious diseases was to emphasise their importance for business and tourist travellers travelling to and through the region
- Gather robust surveillance data to motivate alternative funders and donors to contribute to infectious disease R&D in the region
- Wealthier Asian-Pacific countries should contribute financially to novel global 'pull' incentives

Conversation three: *"Local lists of priority diseases"*

Proposer: researcher at Oxford University Clinical Research Unit, Vietnam

Participants: six (in addition to proposer)

Discussion points/ideas

- How are priority diseases (e.g., TB and Dengue in India, Enterovirus A71 in Japan, and SFTS virus) decided on?
- Evidence-based approach to priority setting, through promoting basic research, systematic reviews, mapping and setting frequencies for updating this data and in turn updating the priorities
- Local or regional lists of priority diseases could be linked to a regional joint approach on research and procurement for priority diseases

Conversation four: *"Strengthen existing R&D infrastructure and extend the capacity not only at the central level but to district level too"*

Proposer: representative of the National Centre for Global Health and Medicine, Tokyo

Participants: four (in addition to proposer)

Discussion points/ideas

- Strengthening infrastructure in the major cities can have a knock-on effect that can be used to extend that capacity out into the districts
- Lack of expertise and infrastructure in the districts could be addressed by setting up small, localised teams with streamlined approaches and technologies
- These teams could then recruit and train the local researchers to build their capacity gradually
- Governments were best placed to fund this sort of activity basic infrastructure improvements were often needed before meaningful research is possible (e.g., transport links, stable electricity distribution grids, and reliable internet connections for data sharing)

Conversation five: "Changing grant review/selection system to match with the new policy on equity for LMICs"

Proposer: microbiologist from MORU, Thailand

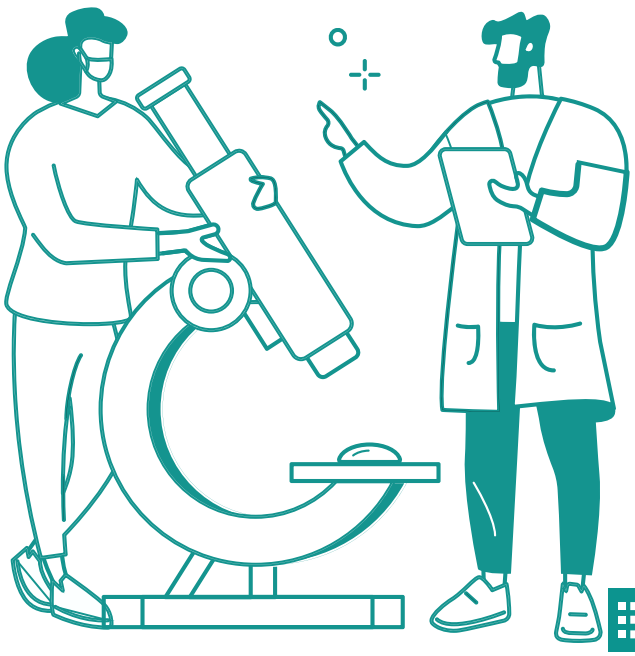
Participants: two (in addition to proposer)

Discussion points/ideas

- Grant review or scoring system is the cornerstone to bringing about equity.
- What does 'equity mean: "Is it equitable impact of research or is it equitable contribution to research?"
- 'positive discrimination' of LMIC researchers, for example, through prioritising grants to LMIC researchers in grant application reviews
- If equitable priority setting is the goal, then there is a need to define the metrics for assessing equity in grant applications. The funders of the grants themselves clearly had a role to play in this
- Contribution of LMIC scholars researching neglected tropical diseases needed to be measured in some way (bearing in mind that they often don't have the research publication histories that HIC scholars working on global diseases have)
- Making resources available for researchers from LMICs so that they know how to clearly navigate the grant application process would also help to even the playing field
- This could also be supported through 'grants for grants': small grants to support work in developing a larger grant application.
- How can non-English speaking researchers participate in an English dominated research world?

Participants valued the opportunity to have the Asia regional voice centre-stage. This sentiment was captured in the following quote from the post-event evaluation survey.

"It was inspiring to hear similar thoughts and concerns about the research environment and ways people were trying to make it better. For me, the actions I want to take would be starting from myself. I learned from the session what actions I take to co-create a better research environment and work toward more sustainable outcomes."



2.3.2 Regional Deep Dive Two: Focus on Africa

The second regional deep dive event took place on 3rd August 2023. The event was attended by 41 participants representing the voices of nine African countries (Namibia, Malawi, Uganda, Kenya, Nigeria, Zimbabwe, Ethiopia, Ghana and South Africa), with representatives of a number of Global North based organisations, with a special interest in Africa, also in attendance (FIND,

Switzerland; Life Arc, UK; GloPID-R, Germany; and MDGH, Australia).

The 14 conversations proposed reflected the priorities of the region from the participants' perspective, in particular some of the systematic and structural challenges facing the region and having a generally less developed R&D ecosystem compared to the mature ecosystems in high-income countries outside of Africa.

Conversation one: *"How can we bring our universities onboard to actively participate in R&D. Especially, in rare and AMR diseases where incentives for manufacturers are lacking."*

Proposer: representative of PANTHER Health, Kenya

Participants: two (in addition to proposer)

Discussion points/ideas

- Potential of African universities and research institutions versus lack of funding to translate research into products
- Collaboration key to changing this
- Develop partnerships with global north research institutions
- Bring product developers into these African universities to create an effective interface between regional research and the development of products in the region for the region
- Africa CDC was mentioned as a key enabler of the formation of such partnerships
- Much of the funding for research in Africa is awarded to later-stage R&D projects, and increasing funding for early or 'discovery' research would have a knock-on effect of strengthening ability to attract funds for later stage research

Conversation two: *"Developing a common understanding of an equitable collaborative partnership"*

Proposer: representative of Science for Africa Foundation

Participants: four (in addition to proposer)

Discussion points/ideas

- Need to develop more equitable funding partnerships, as it was felt the funder often drives the agendas of the beneficiaries and this is not the best foundation for an equitable relationship
- Dialogue between funders and beneficiaries needs to begin much earlier so that African voices can have a greater role in setting funding priorities
- To develop the long term relationships needed for the above start with selected African universities networking with regional and global funders
- Introduce more forums such as this Global Conversation where such networks can be developed

Conversation three: *"Building human capacity for AMR genomic surveillance in Africa"*

Proposer: Nigerian Postdoctoral researcher

Participants: two (in addition to proposer)

Discussion points/ideas

- Africa lacks access to antibiotics for resistant micro-organisms and suffers a high prevalence of multidrug-resistant bacteria strains
- Education around antibiotics directed and healthcare professionals and the lay public is key to addressing this challenge

- Collaboration (e.g., in the form of public/private partnerships, and more developed countries helping to train Africa life scientists from less developed sister countries), and sufficient funding are key
- Increased whole-genome sequencing (WGS) capacity, and international sharing of bacterial genomic data, was highlighted. The Africa CDC Genomic Pathogen Institute -AMR Focus group was cited as an organisation that is working effectively in this area but more needs to be done.

Conversation four: *"Strengthening research institutions"*

Proposer: representative of Oromia Agricultural Research Institute, Ethiopia

Participants: one (in addition to proposer)

Discussion points/ideas

- Africa is a reservoir of pathogens and consequently provides an abundance of infectious disease R&D opportunities that might also benefit other countries
- The region lacks sufficiently developed and advanced research infrastructure (i.e., labs, facilities, equipment and supplies).
- Multi-sectorial response needed to address this - donor organisations, African governments and regional organisations, intergovernmental organisations, global health agencies, and the private sector all had a role to play in developing African research infrastructure

Conversation five: *"How do we move manufacturing to Africa - nexus between industry and regulators"*

Proposer: representative of Science for Africa Foundation, Kenya

Participants: four (in addition to proposer)

Discussion points/ideas

- Establishing a manufacturing base in Africa was an important and ambitious goal
- Progress towards this goal is hampered by a lack of funding and regionally harmonised quality standards.
- Significant funding commitments needed to be in place to attract industry to the region. The funding should be directed to growing regulatory and technical capacity, and infrastructure.
- Funding from global partners needs to be augmented by funding from domestic governments and regional inter-governmental organisations in order for "Africa to spearhead its own priorities".
- EU felt to be a good model for intra-regional harmonisation and jointly funded development initiatives. The African Medicines Agency Treaty Alliance was cited as an example of work that is beginning in this area.

Conversation six: *"Equitable research participation between the local and global*

researchers"

Proposer: representative of the Ghana Health Service

Participants: six (in addition to proposer)

Discussion points/ideas

- When research is coordinated at the international level, local expertise is only tapped into in terms of data collection and this creates a knowledge gap
- To tackle this funders need to make it a grant condition that local researchers are equitably involved in the wider research process beyond data collection including analysis, publication, follow-up and implementation
- For this to be practical, capacity building in African institutions and research staff may be needed so that "it's not just the few well-developed institutions that [are able to] apply for and get funding"

- Principles for equitable partnerships' to be designed by African stakeholders and partnerships to be led by co-creation
- Fully involve Africans in international research by establishing international research networks and forums that are accessible to African researchers. African partners should be included in the design of grant calls and grant management

Conversation seven: *"Strengthen research laboratories in Africa"*

Proposer: microbiologist based in Ethiopia

Participants: two (in addition to proposer)

Discussion points/ideas

- Capacity building and the development of African laboratory infrastructure were key to developing the R&D ecosystem in the region.
- The Crick Africa Network was cited as an initiative that was working towards capacity building in the region
- Domestic governments have a role to play in securing the funding needed to invest in laboratory infrastructure
- Laboratory limitations pose practical barriers to strengthening African research institutions' ability to undertake drug development, for example, due to limited capacity in toxicology, laboratory analysis, and running PK/PD or Phase one (safety) trials
- Need for developing African reference intervals for human biochemical parameters, as reference intervals based on populations in the Global North may lead to inaccurate research conclusions.[15]

Summary of Round Two Conversations

Seven conversations were proposed for round two's co-created agenda. Two of the proposed conversations received little participation (one regarding advocacy to enable an African-centric R&D ecosystem, and another regarding the active participation of African women in R&D) and the proposers of these questions subsequently joined the conversations proposed by their peers.

Conversation one: *"Funding linked to regional research priorities"*

Proposer: representative of GloPID-R, Germany

Participants: four (in addition to proposer)

Discussion points/ideas

- Infectious disease R&D capacity in the region can be built by targeting funding at regionally identified priorities
- For this to happen the funders needed to be aware of these priorities
- Key to this lies in establishing effective collaborative networks that map the needs of the region and then communicate that to the global funders
- Some initiatives and organisations are attempting to set regional priorities in this way -African Academy of Sciences, Africa CDC
- Moving away from 'earmarking' of funds by funders, enabling flexibility by local/regional grant-receiving institutions, would empower local/regional priority setting

Conversation two: "How to effectively strengthen health coordinating organisations in Africa at the regional, sub-regional and national level?"

Proposer: Postdoctoral Research Fellow from Queens University, Belfast

Participants: two (in addition to proposer)

Discussion points/ideas

- The organisations at these three levels were not yielding results. There is a strong will in the region, but lack of funding and the starting point of a less developed African

[15] See for example: Fiseha T, Alemayehu E, Mohammed Adem O, Eshetu B, Gebreweld A. Reference intervals for common clinical chemistry parameters in healthy adults of Northeast Ethiopia. PLoS One 2022; 17: e0276825.

R&D ecosystem presented significant barriers to progress

- How at the three levels (national governments; sub-regional organisations e.g., Economic Community of West Africa States, WOHA; and regional organisations e.g., Africa CDC) could work better together on harmonisation, capacity building and data sharing. Participants were in agreement that more collaboration was clearly needed, but how that might be achieved was difficult for them to define.

Conversation three: *"Building translational research capacity in Africa to bridge the gap between research and commercial development"*

Proposer: representative of LifeArc, UK

Participants: three (in addition to proposer)

Discussion points/ideas

- The gap refers to the lack of development of the later stages of the R & D pipeline in the region.
- Establishing this sort of capacity was a long-term endeavour that would require the support and collaboration of Africa CDC, research institutes, national governments and ministries of health, and the private sector.
- How can national governments and regional organisations more effectively pull the necessary funding into the region.[16]
- There needed to be better understanding of the barriers that exist within the ecosystem, and participants wondered if there were any case studies available that might suggest how these barriers could be overcome

Conversation four: "Regulatory harmonisation. How will it be achieved and when?"

Proposer: representative of Medicines Development for Global Health, Australia

Participants: five (in addition to proposer)

Discussion points/ideas

- The benefits of regional harmonisation is not being adequately sold to national governments
- The precise benefits of harmonisation (security and sovereignty) are seen as risks, and that governments need to be convinced that by being involved in harmonisation discussions they actually improved their security and maintained their sovereignty
- Greater standardisation of regulatory requirements and research protocols needed, including through templates
- Practical steps towards greater harmonisation and digital innovation are seen as key to sharing data between regulatory agencies located in different countries. Tanzania and Ghana were noted to be the only countries in the region that had reached Maturity Level 3 on WHO's Global Benchmarking Tool, and these countries could be used as role models and pathfinders to help bring the rest of the region up to this level

Conversation five: *"Africa has great scientists in universities, but these scientists do not have the financial muscle to support and sustain innovations. Africa relies entirely on the North for funding which is not adequate. Increasing funding to Africa would greatly see the flourishing of science in Africa."*

Proposer: researcher at the University of Malawi

Participants: five (in addition to proposer)

Discussion points/ideas

- The region's potential being hamstrung by a lack of adequate funding
- Need to train Africa researchers in

[16] For an explanation of the terminology of 'push' and 'pull' mechanisms for funding R&D, see for example: Page 29, Report of the United Nations Secretary-General's High-Level Panel on Access To Medicines. 2016. available at: https://static1.squarespace.com/static/562094dee4b0d00c1a3ef761/t/57d9c6ebf5e231b2f02cd3d4/1473890031320/UNSG+HLP+Report+FINAL+12+Sept+2016.pdf

sourcing their own funding opportunities and grants, and then to train them in grant application writing skills

- Systemic inequalities relating to how research is funded globally. One place where African scholars learn to navigate the research funding landscape is through international placements. This is good for Africa if the researcher returns home, however, often international placements lead to international opportunities and they may not return to practise in their home country (exacerbating brain drain which is common in STEM fields)
- A returning scholars fund might incentivise researchers to return home and thus alleviate brain drain
- It is often the researcher that secures funding rather than the institution in which they work. Therefore, participants wanted to find a mechanism to fund the research institutions, which are static, rather than the researcher who may end up working outside of Africa.

Concluding Remarks

In summary, although several distinct conversations were held during this event, there were many commonalities among the concerns of the participants. The conversations were heavily focused on the research end of the pipeline, rather than product delivery after development. This perhaps reflected not only the participant list (which was heavily skewed towards research institutions and academia) but also the limited development of the implementation and manufacturing ends of the supply chain in the region.

Funding the development of this part of the ecosystem was a common concern among participants. The participants were also in agreement that partnerships, collaboration, and networks are key to ensuring that any funding that can be secured targets and drives the changes they hope to see in their region.

2.3.3 Global Deep Dive One: Focus on equitable and comprehensive priority setting

The first global deep dive event took place on 5th September 2023. The event was attended by 16 stakeholders and four additional members of the wider Wellcome Team. The participating stakeholders represented a good mix of research, manufacturing, advocacy, and funding organisations. Although these entities were predominantly based in the 'global north', several of the participants were representatives of entities based in India, Kenya, and Singapore.

Exploring Potential Mechanisms for Change

The previous Global Conversation events produced a significant number of findings related to Change Area One of the discussion paper (equitable and comprehensive R&D priority setting). Based on these, the Wellcome infectious diseases policy team drew up eight potential mechanisms for change that warranted further interrogation.

In the spirit of co-created agendas and to derive maximum benefit from the participants' unique perspectives and areas of expertise within the ecosystem, participants were asked to express their preferences for up to three mechanisms. The overall top four mechanisms were selected and then discussed in three rounds of small group breakout discussions (see figure 1).

Participants were asked to consider their chosen mechanism and discuss their answers to the questions set out in a guiding framework (see figure 2).

Figure 1: Eight mechanisms for change - 2,4,6 and 8 selected for discussion

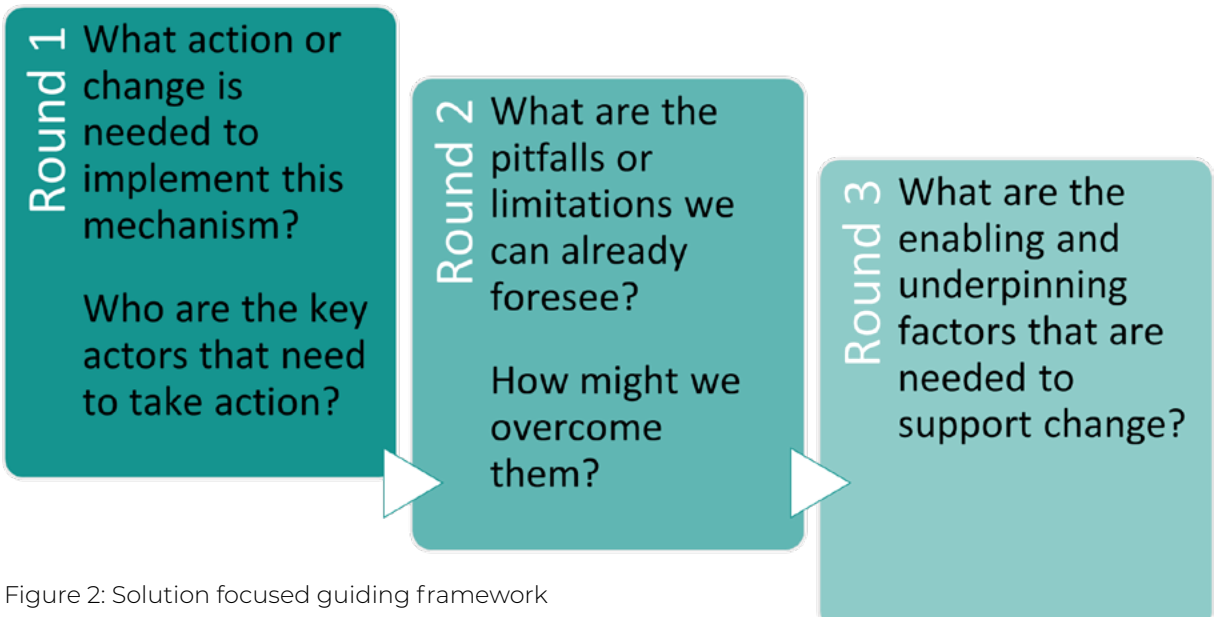


Figure 2: Solution focused guiding framework

A summary of these discussions for each mechanism for change is set out below.

Mechanism Two: The strengthening of existing mechanisms that encourage coordination between major funders of infectious disease R&D

Gaps/challenges	Change needed
Pathogen specific (e.g., NTDs) Stage specific (e.g., early surveillance was cited as not being "sexy" to funders) Region or country specific Lack of coordination across research funders, e.g. for diagnostics The diversity that exists among funders. Funders eligibility rules are different, their geographical remit is different, their scope is different (e.g., some fund clinical trials, others don't etc.); also, the way they work internally can be very different, for example the speed at which they release funding via their selection processes and peer review varies. This diversity also applies to the recipients of funding. The group asked, "are they constituted to receive funds, have they been vetted to receive certain levels of funding, can they manage the funds appropriately?"	Comprehensive, pragmatic and accessible coordination and information/ knowledge sharing across funders and grantees

Solutions

One international organisation should take on the role of being a leader or 'champion' that spearheads work on increased coordination.

The underpinning structure of a global convening platform was suggested as a means of supporting the patchwork of coordination activity that is already happening to bring it together and plug the gaps. It was suggested that WHO and its regional centres could provide that function

A map of existing funding and funders of infectious disease to enable organisations to more easily navigate the infectious disease funding landscape and thus find suitable organisations to partner with more efficiently

Such a tool would reveal the existence of gaps, and a clearly identified gap could attract funders to an otherwise "unsexy" underfunded area. Although the COVID-19 funding commitment tracker was cited as a useful pathogen specific example of mapping at the access to tools end of the ecosystem, it was reiterated that the ideal of a comprehensive ecosystem-wide map was the group's aspiration

Fostering more communication between funders. A recent meeting of a funders forum in South Africa was cited as an example of a space where funders came together to talk about the key areas that each funds and discuss larger areas of R&D that could be co-funded. There was much evidence at this forum of useful

Solutions

cooperation between funders in terms of sharing strategy and planning of funding programmes

Ways for funders to manage those questions by having prefabricated structures that can be used to pre-vet an applicant organisation and assist them to be grant ready.

Funders need to look to themselves to ensure they are looking out and are open to a radical change of culture. A change that would take them away from a colonial model of philanthropy that often leads to "empire building" among the big established funders.

Examples of good practice

GLOPID-R, whose attempts to bring funding together around one call are based on a model established by the Global Alliance for Chronic Diseases

in the field of AMR that has an established ecosystem with **coordinated funding** from basic research through to product development

Mechanism four: Expansion of regional priority setting mechanisms, centring the needs of affected communities and demonstrating demand for products in the region, using this to advocate for greater focus and investment.

Gaps/challenges	Change needed
Many of the issues that negatively impact regional priority setting are not simply a result of inadequate funding but are a consequence of attitudinal or cultural problems among the many actors involved in the existing priority setting practices. Culture change needed.	The actors or organisations (not only the global donor side but also the scientists on the ground in the regions and countries affected) that occupy this space need to develop a much more collaborative and open culture There needs to be not only a willingness but also an ability to engage on all sides of priority setting

Solutions

To strengthen and encourage these "bottom-up" regional actor by working at the level of empowerment of the individual eg offering scientific leadership fellowships

Also necessary to similarly empower newer or less well-developed organisations (e.g The Association of African Universities) with the skillset and confidence required to engage with high-level funders so that they can more forcefully assert their funding priorities

HOWEVER the burden to create a cultural shift from top-down to bottom-up priority setting should not lie only with the individuals and organisations at the bottom - the high-level global organisations and funders need to be empowered to look beyond their "usual suspects" of disease, product, geographic, or recipient specific priorities. It was acknowledged that this might be a significant shift for many top-level entities, and that an engagement toolkit or benchmark of some kind could play a role in assisting them to make this shift. **The UKCDR's guidance on equitable partnerships** was cited as one example of such a tool.

Deploy 'task forces' that interview 100+ individuals in a given region or setting regarding their views on R&D priorities, with this approach potentially giving regional stakeholders confidence that nothing is being overlooked or missed

Bring in regional or domestic funding to complement donor funding. This would help to create "buy-in" on the side of regional actors and promote them taking responsibility for ensuring that their needs are matched by the funding available

Endow a convening or coordinating organisation to take the lead on bringing to international funders attention the fields where needs and priorities in certain regions are not being met (e.g., diagnostics, endemic diseases). Within this coordinating role there might be a data mapping exercise that compares the funding allocated or available to the actual needs of the communities where this funding is directed. They stated that such data tracking tools already exist (e.g., **G-Finder**,) but there needed to be a coordinating organisation whose remit is to use these tools to identify unmet priorities.

Mechanism Six: Independent assessment of R&D funding activity to understand current coverage of funding and drive greater accountability from R&D funders (public & private).

Gaps/challenges	Change needed
G-Finder - the principal existing tool for measuring R&D spend. Its analysis is skewed towards the research end of the ecosystem and that much more data on development spend is needed (note: G-Finder continues to be developed iteratively)	A radical reframing of what is tracked is needed - this would mean defining success metrics far beyond ROI (money in, money out)

Solutions

Aspirations for what these iterations of G-Finder or the components a new tool might include:

The need to look further down the chain to the delivery of the products produced (including where they are accessed)

The efficiency of the development process (e.g., the length of time for a product to progress through clinical trial phases)

More "humanistic" impact measures such as tracking, for example, reductions in rates of mortality and morbidity, or the reduction of instances of disease as a result of a particular product being available, or the wider economic benefit of a particular development

Obtaining this type of outcomes data is significantly more challenging than collecting the data on the funding input - who might fund a new tracking and accountability of spend tool. Gates Foundation currently funds the G-Finder tool, but the radically expanded scope of a new or existing tool may require a coalition of funders to fund it

As this new tool would be used as an accountability measure, perhaps it was more appropriate to identify and solicit a new funder who doesn't fund R&D to step into funding of the development of this new tool (a participant shared that they had attempted to convince a number of such funders and a for-profit pharmaceutical data analytics provide to self-fund this, but both approaches had been unsuccessful)

How will the results of the data influence funder actions? This points to the need for a predetermined policy on how funding decisions will change in response to findings of such analyses.

Mechanism Eight: Amplify existing research centres and establish new research hubs in the countries and regions most affected by infectious diseases, and focusing research in these hubs on local priorities

Gaps/challenges	Change needed
Complexity of system change in this area Knowing where the focus is - research or development. If the latter, there are a number of challenges due to the scale of funding required to develop this complex area of the ecosystem at the local or regional level, particularly when it comes to establishing new centres or hubs.	Funding for amplification and creation of hubs needs to be sustainable with long-term commitments expressed

Solutions

Start by robustly mapping the research landscape to identify what already exists, and building on that to further identify existing connections and collaborations between these research centres and hubs that could be leveraged.

As well as revealing gaps where potential sites for new research centres and hubs should be located, this mapping exercise would highlight where better coordination between less well-connected hubs or centres is needed. It may also identify where individual hubs or centres, or collaboration between these might best benefit from additional funding.

Funding needs to be targeted at research infrastructure investment and capacity building (skills and training). Capacity building of individuals could be funded through schemes such as the WHO TDR fellowships, and further funding should be used to develop mechanisms that attract back or retain research talent in their home region (for example, the H3D Foundation in Africa)

The amplification needed to consider building end-to-end processes. This was stated as particularly important in low resource settings where it might contribute to strengthening the "last mile of delivery" which is often a significant barrier to equitable access.

What other factors would facilitate the development?

- is there scope for regulators to be more flexible around management of local trials while the lowest resourced centres are supported to bring their standards up to international levels.

- crucial to increase the involvement of the governments of the countries where the centres and hubs are located, including mobilising local/regional investment in these initiatives, so that they have a sense of "buy-in". This may be achieved by partnership working with the regional associations of universities, prestigious universities from the global north, and using the support of product specific global facilitators such as CEPI, FIND and DNDi

Concluding Remarks Although several mechanisms were discussed during this event there was a strong three-stranded thread running through the four groups' findings:

- a clear need to map several aspects of the ecosystem more effectively
- a call for a convening body/bodies to take responsibility for bringing the different actors within the ecosystem together to ensure that bottom-up voices are heard
- if all voices are to be truly listened to, a radical cultural shift in the global and regional institutions was called for.

Both the mapping and convening that the participants called for requires significant and long-term commitments to funding to bring about an ecosystem that is driven by more equitable and comprehensive priority setting.

2.3.4 Global Deep Dive Two: Centering access and affordability while incentivising innovation

The second global deep dive event took place on 7th September 2023. The event was attended by 27 stakeholders and several members of the wider Wellcome team. In addition to representatives of pharmaceutical companies, the participating stakeholders represented a good mix of non-profits, research, manufacturing, advocacy, and funding organisations. Although these entities were predominantly based in high income countries, several of the participants represented organisations based in Brazil, Botswana, Kenya, and Singapore.

Small-group discussion round one: Product Development Partnerships (PDPs)[17]

Prior to being divided into five small breakout groups, participants were given a brief overview of the nature of PDPs and provided with a non-exhaustive list of these partnerships that are currently operating in the infectious disease R&D space (see Appendix 6).

In this first round of conversation, the groups were tasked with looking at three aspects of the PDP landscape and were presented with several questions to guide their discussions:

1. What is currently working well that should be strengthened or scaled up?
2. What new PDPs are needed and what might these look like?
3. What enabling and underpinning factors are needed to improve existing models and mechanisms or implement new ones?

The valuable mix of participants in each breakout room comprised representatives of PDPs, funders, pharmaceutical companies, NGOs, and advocacy and civil society organisations. This reflected the wider ecosystem with which PDPs routinely interact and led to productive discussions. A summary of these discussions is set out below.

What is currently working well that should be strengthened or scaled up?	What new PDPs are needed and what might these look like?	What is needed to improve existing PDPs and/or establish new ones?
Example given of positive and fruitful collaboration between PDPs and large multinational - funding, understanding the end user, access to clinical collaboration, advocacy role to shape new drug launches 'Systems integrators' to bring together different stakeholders in partnership for joint health technology development, mechanism for risk sharing Many PDP staff bring expertise from large pharma companies to global health arena. African PDPs help attract qualified staff back from professional roles abroad Not so driven by commercial pressure and can transparently	Flip the question, rather focusing on creating new PDPs, there should be a bigger focus on creating an enabling environment PDPs are working well so no wheel reinvention required	Scope to extend the remit of PDPs to include taking on a more active role in production, commercialisation and delivery, enabling PDPs to fully develop a technology without an industry partner. Strengthen existing PDPs by expanding the range of their drug portfolios, to go beyond focusing on one disease area/one product Strengthen each other through sharing expertise and experiences, helping avoid duplication and identify gaps Develop the way PDPs collect and share data, to help demonstrate the impact of investment in PDPs and raise confidence among donors and procurers in the efficacy of the PDP model.

[17] Advancing Innovation and Access to Medicines: The achievements and under realised potential of the product development partnership model https://repository.graduateinstitute.ch/record/300282?ln=en

What is currently working well that should be strengthened or scaled up?	What new PDPs are needed and what might these look like?	What is needed to improve existing PDPs and/or establish new ones?
set health-driven priorities Global perspective of huge value to industry partners Focus on end result at the heart of their success Depth of access plans very comprehensive due to partnerships with access organisations		Create more sustainable, long-term, less risk averse, less 'staccato' funding was the establishment of a large global health fund for infectious disease R&D modelled on national sovereign wealth funds (eg Australia's Medical Research Future Fund) Educate or encourage donors and procurers to get together to understand the needs of PDPs in order that the funding they provide sustains continued innovation, rather than stopping once a product is delivered. A need to understand the reasons behind a drop in funding for PDPs' NTD projects Regionally based entity (rather than the globally controlled GAVI and Global Fund) would be a beneficial evolution that could better match product development to the needs of individual countries.

Small-group discussion round two:

Focus on alternative business models and market-shaping mechanisms

In the second part of the event, participants explored the potential of alternative business models and market-shaping mechanisms to improve equity of access and drive sustained innovation. This began with a short presentation that described several existing examples of such models and mechanisms **(see Appendix 7)**. Once again, the participants were divided into five small breakout groups and provided with a guiding framework of questions to discuss:

- What models and mechanisms are currently working well, and how might they be strengthened or scaled up?
- What alternative models and mechanisms are needed, and what might these look like?
- What enabling and underpinning factors are needed to improve existing models and mechanisms or implement new ones?

What is working well and could be strengthened/ scaled up?	What alternative models and mechanisms are needed, and what might these look like?	What is needed to improve existing models and/or implement new ones?
No examples	The funding needed to create significant change in the R&D ecosystem is on the scale of billions Requires greater government involvement either through direct funding or collaborating to form new funding frameworks Role of donors such as Wellcome to convene government-led solutions for ID R&D financing Develop more donor-independent models as gaps created by donor shortfall is a root cause of current system failure Need to get policy makers, govts and society to value ID R&D more highly by demonstrating the impact better - generate high quality data on need and outcomes Frame investments in domestic or regional R&D financing initiatives as good industrial policy: These initiatives can be linked to technology transfer and other policies that can launch or strengthen a domestic biotechnology industry.	Repetition of supporting mechanisms from round 1: Global wealth fund Creation of devolved versions of GAVI/GFATM Development of mechanism to tap into buying/market shaping power of middle-income countries with high endemic disease occurrence Civica Rx example (see appendix 2). The effectiveness of this model, that could be replicated by other ventures, was partly due to the economies of scale it achieves. This enables it to make generic medicines accessible and affordable. And it was questioned whether a similar model might be successfully applied to the upstream end of the ecosystem and contribute to development of novel rather generic products.

Final Plenary Comments

In a concluding plenary and via the chat participants shared their final thoughts regarding this event. A clear call to comprehensively map the ecosystem was reiterated.

"We talk about the ecosystem but we have no map of what that is. This makes it hard to speak to policy makers with little background in global health or R&D. We mapped the ecosystem about 15 years ago but it has exploded since then" – Retired infectious disease R&D philanthropy professional

It was stated that such a map would not only facilitate the identification of the specific gaps the ecosystem needs to address, but would also be a tool to convince policy makers and leverage the political will that many participants state was crucial for realising the reform required of the ecosystem.

"My key takeaway, no matter what business model, it will need government/ political will to lead to policy and provide the appropriate financing." – Senior third sector government relations officer

The notion of a "convener" or coordinator to bring the ecosystem together was also raised again by several participants:

"New business models need somebody to provide cohesion. Neutral partners and funders could assist with this." – Scientific director, medical research funding organisation

Concluding Remarks

In demonstrating the need and appetite for this convening role that Wellcome took on to bring the many and varied actors from across the diverse and complex ecosystem together during this Global Conversation, a number of participants mentioned suggested themes for future events, perhaps assuming that this much needed forum would continue beyond the life of this current listening exercise. Indeed there was much value to be seen in the way participants were split among breakout groups with biotech representatives sitting in the same room as representatives of PDPs, and a representative of the organisation responsible for G-Finder sitting in on an ecosystem-wide discussion of new and improved tools to track funding spend.

3

Summary Remarks & Recommendations

3.0 Summary Remarks and Recommendations

Through the course of the nine events, it became increasingly clear that the findings of Wellcome's discussion paper and its overall vision for reform were well-received and supported by the participants of the Global Conversation. Representatives from the broad range of invited stakeholder organisations[18] underlined in their shared experiences and recommendations a broad agreement with Wellcome's priority areas for reform. In addition, participants also largely agreed with the proposals for change that the discussion paper put forward. There was also much evidence heard that a number of the new mechanisms, models, and ways of working referred to in the discussion paper are beginning to have a positive effect in the nascent reform of the ecosystem.

Beyond the numerous points outlined above, four recurring and cross-cutting themes emerged during the course of the Global Conversation:

Decolonisation

Many participants were of the opinion that the current state of inequity across the ecosystem is a symptom of the effects of historical colonialism, and thus there is significant work to be done by all stakeholders to dismantle this and build a more equitable and decolonised R&D ecosystem. This requires a radical culture shift that ensures reform is driven from the bottom up, by communities and countries that are most affected by infectious diseases, rather than dictated by large NGOs, donors and intergovernmental bodies in the Global North.

Ideas for how decolonisation might be dismantled in the context of reforming the ecosystem were put forward:

- The decentering of R&D activity away from the current global north hegemony by establishing R&D hubs in regions of the global south.
- Funders of R&D should embed the concept of decolonisation into grant criteria.
- Stronger LMIC-centred priority-setting and agenda shaping mechanisms, driven by more LMIC voices were inclued in the priority-setting discussions of the global funders, multilaterals, and the larger regional organisations.

Transparency

There was a strong sense across all the events of a need for greater transparency across the ecosystem, in order to support greater inclusion, equitable access to information, and enable more informed and targeted decision making. This would involve stakeholders in all aspects of the ecosystem sharing data and information more readily, and being more open about how decisions are taken and the true costs of conducting R&D. This is as much about a change of mindset towards greater collaboration and inclusion, so that transparency becomes a norm within the ecosystem, as it is about taking specific actions. Examples of areas in which greater transparency would be beneficial are:

- Priority-setting processes
- Access to research data
- How funding is allocated
- The costs of R&D
- Product pricing

Mapping

Closely related to transparency was the theme of mapping. The ecosystem has evolved into an increasingly complex system over recent decades (hence the benefit of Wellcome's ecosystem- wide view), and therefore to fully understand the extent of the gaps, successes, and

[18] See Appendix 1 for a detailed list of participating organisations

existing partnerships, participants felt a comprehensive mapping exercise was long overdue. Such a map would enable funders and policy makers to navigate the system and more easily advocate and evidence the need for reform.

During the Global Conversation it became clear that:

1. There was a considerable degree of asymmetrical knowledge of the ecosystem among participants, who despite considerable expert knowledge and perspectives, generally did not bring the broad system-wide perspective contained in the discussion paper.
2. Many of the potentially scalable ideas discussed were already being trialled somewhere in the ecosystem and producing promising results, which suggests that the much-needed reform is happening in specific ecosystem settings.

A mapping exercise could favourably impact both of these fragmentations in the knowledge and understanding of the ecosystem.

Coordinating bodies

The two examples of fragmented knowledge cited above underline the calls from participants for a body or consortium of organisations to take responsibility for marshalling the different actors within the ecosystem to accelerate the pace of reform. Any such initiative would of course need to address the inherent tension between coordinating everything to maximise efficiencies and reduce duplication, and too much coordination becoming bureaucratic and stifling to innovation.

Although not in itself coordination, participants acknowledged that the Global Conversation has proved a valuable forum for facilitating discussion and engagement between different stakeholders in the ecosystem. Participating individuals and their organisations benefited from the opportunity to connect, strengthen existing alliances and forge new ones, and gain a deeper understanding of what is needed from the ecosystem as a whole to work together towards a more equitable infectious disease R&D ecosystem. It may be that Wellcome does have a role to play as convenor of more global conversations, thus providing a process for coordination to take place organically.

In closing this proceedings document, the authors would like to thank all those who took part in the Global Conversation and hope that this report and its recommendations will contribute to their collective endeavours to accelerate the much needed reform of the R&D ecosystem for infectious disease.

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4

Appendix

Appendix 1

List of participating organisations and countries

Organisations

Access to Medicine Foundation, Netherlands

ADVANCE-ID, Singapore

Africa Centres for Disease Control and Prevention

Africa Health Research Institute

African Medicines Agency

AMR Solutions

Amref Health Africa

Aids Vaccine Advocacy Coalition (AVAC)

BEAM Alliance (Biotech companies for Europe in Anti-Microbial resistance research)

Bill & Melinda Gates Foundation

Biovac

BioVersys

Canadian Antimicrobial Innovation Coalition

Combatting Antibiotic Resistance Bacteria (CARB-X)

Centre for Drug Design and Discovery (CD3), Leuven, Belgium

CellNua

Centauri Therapeutics

Centre for Science and Environment, India

Coalition for Epidemic Preparedness Initiatives (CEPI)

Changescape - Public health consulting

Chemical Biology Ventures Ltd

Center for Infectious Disease Research and Policy (CIDRAP)

Civica Inc.

Christian Medical College Vellore, India

Drugs for Neglected Diseases Initiative (DNDi)

Deutsche Stiftung Weltbevölkerung (DSW).

Duke-NUS Centre for Outbreak Preparedness, Singapore

EH!WOZA (South Africa)

F2G Limited

Foundation for Innovative New Diagnostics (FIND)

Fiocruz

Global Antibiotic Research and Development Partnership (GARDP)

GCC Medical Products & Technologies Grand Challenges Canada

Global Health Innovative Access Alliance (GHIAA)

Global Health Technologies Coalition (GHTC)

Gilead Sciences

Global AMR (antimicrobial resistance) R&D Hub, Germany

Global Health Center in Geneva

Graduate Institute Geneva

Global Health Security Consortium

Global Healthcare Innovation Accelerator

Global Research Collaboration for Infectious Disease Preparedness (GloPID-R)

Greater San Diego Biological Solutions, USA

GSK (GlaxoSmithKline)

Hilleman Labs, Singapore

Hokkaido University, Japan

International AIDS Vaccine Initiative (IAVI)

Immunisation Clinical Advice and Response Service (ICARS)

International Federation of Pharmaceutical Manufacturers and Associations (IFPMA)

Incentives for Global Health

Innovate UK

Intrepid Alliance

International Pandemic Preparedness Secretariat (IPPS)

Johnson & Johnson

Kamuzu University, Malawi

LifeArc, UK

Liverpool School of Tropical Medicine

Market Access Africa

Medicines Development for Global Health (MDGH)

Medicines Patent Pool (MPP)

Microbion Pharma Corp

Ministry of Health, India

MMV Medicines for Malaria Venture

Mahidol Oxford Tropical Medicine Research Unit (MORU) Thailand

Medical Research Council

Merck Sharp & Dohme

Médecins Sans Frontières (MSF) Access Campaign

National Drug Authority, Uganda

National Institute for Research in Tuberculosis, India

National University of Singapore

NICD/Wits University, South Africa

NovaBiotics

Novartis

Oromia Agricultural Research Institute, Ethiopia

Oxford University Clinical Research Unit, Vietnam

Pandemic Action Network

PANTHER Health, Kenya

PATH (formerly Program for Appropriate Technology in Health)

Policy Cures Research, Australia

Protas, UK

Queens University Belfast

Royal College of Radiologists, Uganda

ReAct - Action on Antibiotic Resistance

South Africa Medical Research Council (SAMRC)

Saw Swee Hock School of Public Health, UK

Science for Africa Foundation (SFA)

Seeding Labs, USA

Synexa Life Sciences

Tony Blair Institute

United Nations Development Programme (UNDP)

United Nations Foundation

Univercells SA

University of Alabama, USA

University Medical Center Nijmegen, Netherlands

United States Department of Veterans Affairs, USA

Veterans Health Administration, USA

Yale University - Global Justice Program, USA

Youth and Women for Change in Eswatini

Countries

Australia, Belgium, Brazil, Botswana, Cameroon, Canada, Colombia, Eswatini, Ethiopia, Finland, France, Germany, Ghana, India, Indonesia, Ireland, Israel, Italy, Japan, Kenya, Malawi, Malaysia, Myanmar, Namibia, Nigeria, Norway, Singapore, South Africa, Spain, Sweden, Switzerland, The Netherlands, Thailand, Uganda, UK, USA, Vietnam, Zambia, Zimbabwe

Appendix 2

Participative process overview

Appendix 2 provides an outline of the processes used to reap maximum benefit from the Global Conversation.

CoLab's work in designing and facilitating comprehensive listening exercises in the fields of health and social policy is heavily informed by a facilitation approach known as The Art of Hosting & Harvesting Conversations That Matter https://artofhosting.org/. This is a proven approach that CoLab has successfully used to design stakeholder consultation exercises with notable clients such as the United Nations Development Program, The Colombian Ministry of Agriculture & Rural Development, Utrecht University, the NHS, and the New Economics Foundation.

Overview of Event Proceedings

Utilising The Art of Hosting Conversations that Matter approach CoLab worked closely with the Wellcome Trust to co-design a series of online listening events that consisted of three distinct phases:

Phase one: Convening the Conversation

Phase two: Exploring Four Key Areas for Change

Phase three: Global & Regional Deeper Dives.

These three distinct phases enabled the conversation to move from the general to the specific and cover issues at a global, regional, and local level.

More about Participative Process

The aim of participative process is to enable democratic and equalising conditions for participation to take place. Participative process is designed in a way to encourage participants to feel valued, safe and validated and able to speak and be heard. It does this by centering co-creation, generating conversation and sharing in small and larger groups, providing multiple opportunities for participants to contribute. At the same time, to ensure that content remains relevant, useful and insightful, powerful appreciative questioning is used to frame and guide conversations.

Typically creating the conditions described above cannot be done via conventional webinars but by designing highly participatory international online forums where professionals from across the global infectious disease R&D ecosystem come together with the aim of co-creating an equitable and sustainable vision for the future.

To facilitate participation of the widest possible cross-section of the global infectious disease stakeholder community, the events were conducted virtually using Zoom supported by and various interactive collaborative platforms such as Miro

The Zoom meeting chat was heavily utilised by participants throughout the events. Space was provided in the introductory check-in and soft-start that enabled participants to get to know each other. A number of participants used this as an opportunity to network via the chat and several exchanges between participants evidenced attempts to form potential new partnerships.

Each event was led by a three person 'host' team, supported by a tech host to ensure Zoom features ran smoothly, and a chat-box host to monitor and gather relevant content from the chat-box.

Extensive use was made of small group discussions via breakout rooms. Each breakout room had a dedicated Miro board to record its discussion, replicating an in-person meeting with flip chart/ white board/post-it notes.

A range of other recognised participative process tools were used as required during the nine workshops – world cafe, Open Space Technology and fish bowl.

The use of open space, for example, provided participants with the

opportunity to propose and contribute to conversations aimed at defining the key changes and strategic actions that they believe are required to reform the R&D ecosystem in their region. In this approach, participants that proposed conversations invited other participants to join them in breakout room discussions. Participants were free to enter and leave discussions at will. This means they had the option to stay in one room for the whole discussion or jump between rooms to cross-pollinate their ideas.

Interpreters were employed where needed, offering Spanish, Portuguese and French simultaneous translation. This supported the attendance of people without language being a barrier to participation. A team of notetakers were also employed to support the capture of information in breakout rooms and provide light-touch facilitation when required.

CoLab facilitators were constantly learning throughout the nine events what worked and what didn't and adjusted processes and content accordingly to maximise the participative experience. For example, in Themed Event Four an initial icebreaking task was introduced. This had a positive effect on the fostering of productive breakout room discussions and increased the willingness among participants to share their thoughts verbally in the plenary sessions. This icebreaking task was then included in the agendas of the subsequent events of the Global Conversation.

Getting the Right People in the Room

Encouraging wide participation began with the invitation process. Wellcome, in consultation with CoLab, drew up a list of possible attendees and these potential participants were directly approached to express their interest in taking part in one or more of the events from across the three phases of the Global Conversation. Additionally, the events were publicised across Wellcome's social media channels and website with a mechanism for participants to express their interest via an EventBrite webpage. Throughout the invite process participants were encouraged to nominate colleagues and other stakeholders that they felt may be instrumental to discussions. The Launch event was also used to generate further nominations for potentially absent invitees.

The resultant cohorts of participants that attended the events were drawn from policy making organisations, global and regional funders, product developers (e.g., the pharmaceutical sector), academia, civil society, advocates, regulators, and clinicians. These stakeholders represented both high-income countries and low- and middle-income countries.

In total, across all nine events, more than 250 individuals from 38 countries participated in the Global Conversation. Although many participants chose to attend specific events, a significant number of participants attended several of the events. Bearing in mind the events had a duration of up to three hours, this demonstrates that participants felt the events provided them with a valuable opportunity to exchange their views with one another.

Attendance numbers dropped slightly in later events and it's difficult to infer why numbers dropped, it could be related to several factors. These factors might include: fatigue among repeat participants, availability to attend (we couldn't avoid the holiday season in every region), interest in levels in the specific themes of events, very tight timeline for the advertising and invitation process.

Learning and Barriers to Participation

If Wellcome decides to step into the role of becoming the coordinator and convener that participants of the Global Conversation called for, a number of issues related to the **Matthew Effect** raised during the launch event should

be addressed if possible. While it was welcomed that there were dedicated regional deep dive events aimed at engaging participants from these regions, there were no similar events for Latin America and Caribbean and the LIMCs of the Western hemisphere.

The timing and duration of the Global Conversation events may have presented another barrier to participation. For example, Australia and New Zealand were not well served by the 1pm BST start time of the themed events, nor even in the earlier start time of the Focus on Asia event which began after business hours in Australia.

The three-hour duration required of the highly participative nature of the events, although effective in terms of harvesting conversations, may not have been accessible to representatives of smaller grass-roots stakeholders. An honorarium to facilitate participation from such organisations was offered in the latter events. However, it is not clear how facilitative of additional engagement these honoraria were as they were deliberately offered without the stigma of qualification criteria.

Although there were a wide range of stakeholder organisations present (see appendix one), many LIMC voices were represented by global organisations with a LMIC focus based in the Global North rather than through direct representation of LIMC based actors themselves. Therefore, it is recommended that part of a potential coordinating convener's remit would include fostering greater engagement with the voices that were absent from Global Conversation.

The difficulty of such a task should not be underestimated and should perhaps begin with a substantial analysis of the participants both present and absent from this conversation. Leveraging networks of networks was suggested as one means to bring neglected voices to the table. In a similar vein, it was noted that in discussions involving funding infectious disease R&D and developing new models for financial reimbursement of pharmaceutical product, development, manufacture and supply, economists and political philosophers were absent from the Global Conversation.

Appendix 3

Record of Launch Event Breakout Room Discussions

Due to the overlapping boundaries between the four change areas and the cross-cutting nature of some of the questions raised, the following themes and questions have been categorised according to their placement on the Miro board.

Theme: **Equitable & comprehensive R&D priority setting**

Questions:

How to incentivise governments to engage and invest for the long term?

How can we ensure that there are mechanisms to back up the existing priority lists with the necessary funding for procurement and necessary systems to reach patients?

How can high burden countries make commitments to pull through innovative products that address their needs?

How do countries see themselves as players in the global R&D network?

How do we choose which indications are most important to pursue development for with respect to priority setting if we are trying to be equitable?

How do we support systems where there is market failure?

What routes currently exist to enable LMIC governments and researchers to agree and set strategic aims reflecting their needs and ambitions and how well-known are these?

How can we strengthen R&D capabilities/ know-how across R&D? And how do we pool resources to support this and work across diseases?

Theme: **Strategic scale-up of geographically diverse & sustainable manufacturing capacity**

Questions:

Who is identifying the unmet need?

Scale is not the bottleneck, but rather raw materials availability, supply chain, expertise in GMP and local infrastructure and regulatory framework to support product registration.

How can we change the approach to tech-transfer to ensure sustainability of manufacturing sites?

How can we deliver the products where they are needed?

How can Wellcome and other funders support Global South manufacturing and R&D? Strengthening the life science sector?

Do we need manufacturing in every country? How to keep the focus on the key problem we are trying to solve - i.e., robust, resilient, and efficient supply chain that gets medicines to patients globally. Geographically diverse manufacturing may be part of the solution, but also policy changes.

How to create a proper link between registration and commercial availability?

Manufacturing is just one piece of the puzzle, how can we complement with support PV, regulatory, product innovation for neglected EIDs?

How do you get governments to want to own the solutions rather than corporate organisations?

We need to ensure voices of those most affected are heard, but we can't have every country doing everything from an innovation perspective - need to establish what makes most sense and is viable.

Who is best placed to fund development of regional capabilities in this space and how can/will funders outside a given region devolve delivery to the people of that region?

Theme: **Streamlined clinical trial and regulatory approaches**

? Questions:

Link (and enforce) trial participation of certain countries to access of medicine post-approval as a first step to making medicines widely available to all that need it from other parts of the world (where the developers are usually located)?

How can we understand where demand is accurately? e.g. covid experience

What steps should governments take to facilitate regulatory approval?

Is this a country plan issue or is it a global issue?

Theme: **Centring access & affordability while incentivising innovation**

? Questions:

How do we make sure LMIC countries are not only used for trials but also get the drugs?

How to get big pharma actors to be more involved?

Wouldn't it be beneficial to have funders involved in the process?

Can we think about separate systems for incentivising R&D of a product and for driving access? Both are big, complex problems and it may not be possible to solve them with one single elegant solution.

Important not to think about broad country categorisations, but more granular detail within countries. Needs of end-users must come first.

How to build in the downstream and pull-through investments needed earlier into the process?

How to get middle income countries to value and pay for innovation that meets their needs?

What is the ecosystem for absorbing non-pandemic / regional innovations once brought to the R&D finish line?

Incentives in this space are largely set by commercial markets in the global north - how can we influence the landscape to prioritise health impact at scale? Some work exists, to e.g. provide secure revenue streams for novel antimicrobials, but can similar schemes be realistically scaled up for wider impact?

If monetary pull incentives are not available for clinical stage products, what other incentives (i.e. government or regulatory driven) can be provided that will be attractive to both developer and investor?

Extended regulatory or patent exclusivity?

How can we make it easier to explore products under development to be studied in other indications? (that may be less attractive financially, but still is useful data)

Include APIs/raw materials suppliers in the value chain / product dev chain to secure product affordability and access.

Equity vs impact - not the same and are sometimes in conflict

Theme: **Other**

? Questions:

How to figure out the parts of the system that need to be fixed / integrated?

How to involve people who don't have time and resources to participate in events like this one?

What can be the alternatives to the current 'pull' of the US market?

How does Wellcome intend to take these Change Areas forward considering different urgency in each of the areas?

Who takes ownership and accountability for impact?

What are we trying to solve for? Impact? Equity? Both?

Alliances are going to be critical to create new products.

Transparency and measurements critical - what happens after funding is provided?

Governments need to be onboard/ready

to use of products - an end to end system.

How do you measure what has been successful, and who determines

success? How do you develop metrics over time?

How do we change demand signals so that they bring a greater mix of impact and equity - move away from donor/ money led demand signals?

Explore links between R&D ecosystem / innovation development and economic growth.

How to persuade LIMC Govs to contribute towards system development if the primary focus is on everyday needs and sustaining basic social/healthcare population needs?

Appendix 4

Themed Event One: Existing challenges perceived by respondents to the pre-event survey

Respondents identified five key aspects related to the existing challenges and barriers that hinder equitable and comprehensive priority setting in the infectious disease R&D ecosystem:

Lack of equity and inclusivity: This includes the absence of a public health approach, limited input from decision-makers, and the dominance of global north funders and experts, while patient voices and frontline healthcare workers are overlooked.

Resource allocation and funding: Challenges lie in linking priorities to funding and ensuring resources are directed appropriately. There is a need for sustained non-profit funding and inclusion of equitable access in R&D funding agreements.

Collaboration and coordination: Silos, poor coordination, and ineffective partnerships hinder comprehensive priority setting. There is a need for better communication, formation of effective partnerships, and coordination among stakeholders.

Profit - driven motivations: Counterproductive incentives for pharmaceutical firms, concerns about commercialization, and the inability to make money from treating infectious diseases (excluding pandemics) create barriers to equitable and comprehensive priority setting.

Capacity building and research influence: Challenges include inadequate surveillance, limited skills and capacity of researchers, and the importance of political commitment and actionable research evidence to influence local policymakers.

Raw pre-event survey responses grouped by key ideas

Key idea one: Lack of equity and inclusivity

Lack of a public health approach to priority setting when funding R&D for new interventions.

Initiatives led by the global north with experts from this region, missing patient voices, and frontline healthcare workers.

Lack of input from those making decisions to purchase and use the products.

Power is still held by global north funders, with academics outnumbering practitioners/policymakers in panels and priority exercises.

Inclusion of equitable access in R&D funding agreements.

Inadequate understanding of the true burden of disease in LMICs due to inadequate surveillance.

Limited ability of low- and middle-income countries (LMICs) to set their own priorities due to external funding sources.

Poor health systems to contain emerging infectious diseases due to climate change.

Does not set priority areas of focus and allocate funds in a way that supports a rich and balanced R&D environment.

Empty pipelines or stalled research, particularly for diseases that affect LMICs.

Priorities and resources are often set by only the most influential global stakeholders: those with political and financial power, often from the Global North.

Donors' priority setting mechanisms come with their own political and strategic agendas and do not always take into account wider perspectives –

particularly those of the most affected communities.

Key idea two: Resource allocation and funding

Setting priorities is not the challenge; linking priorities to funding/systems that will pull them through to patients.

Unwillingness of funders to direct resources appropriately.

Lack of sustained non-profit funding.

Funding and capacity development challenges.

The massive, complex, and tech-driven nature of the infectious disease R&D ecosystem, leading to resource dependencies that hinder equitable solution-driven priorities.

Challenge to balance investment across existing infectious disease burden and potential future emerging outbreaks.

Funding allocations can bring disproportionate results.

Donors can also lack the long-term thinking and commitment needed to see products all the way through development and distribution, leaving products continually fighting for support as they progress through the R&D ecosystem.

Key idea three: Collaboration and coordination

Silos and over-concern about commercialization of innovation in infection control, particularly vaccines and devices.

Lack of coordination, communication, and effective partnerships.

Key idea four: Profit-driven motivations

Market dynamics alone do not provide sufficient incentives across infectious disease R&D.

Counterproductive incentives for pharmaceutical firms driven by profit motives.

Inability to make money out of treating infectious diseases, except during pandemics.

Market dynamics alone do not provide sufficient incentives across infectious disease R&D.

Global pharmaceutical R&D is critically dependent on the private sector.

The biopharmaceutical industry holds a huge amount of control however, infectious disease is characterised by unprofitable and poorly functioning markets, driving commercially-led R&D efforts towards more profitable areas of innovation Key Idea 5: Capacity building and research influence

Political commitment and actionable research evidence.

Skills and capacity of researchers who can influence local policymakers.

Socio-economic challenges in prioritisation.

Private sector innovators must secure steady returns on investment if they are to stay commercially viable.

The dynamics of disease spread result in peaks and troughs leading to uncertainty around how reliable returns might be.

Key idea five: Capacity building and research influence

Political commitment and actionable research evidence.

Skills and capacity of researchers who can influence local policymakers.

Socio-economic challenges in prioritisation.

Appendix 5

Round up of ice-breaker activities in Deep Dive events

Regional Deep Dive Asia: Initial ice-breaking task.

Following presentations from Wellcome that framed the regional context and scope of the event, the participants got to know each other by taking part in a short ice-breaking task, where in small groups they shared a topic that they would like to discuss during the event. Topics participants hoped to discuss included:

- Issues of community access, and equity of IP ownership by countries where research is being conducted
- Pandemic preparedness, health infrastructure and universal access to key Interventions
- Capacity building and knowledge transfer R&D to act as a catalytic accelerator for regional vaccine self-sufficiency
- How to conduct research in lower income countries in Asia with a focus on achieving access to anti-infectives
- Long term commitment from Wellcome to support clinical research in Asia
- Contributions of local communities to the development of research agendas and funding priorities
- Access to DTVs ensuring these are low cost, affordable and available to those who need them is an important issue that needs discussion, particularly for LMICs
- Robust early warning systems in-built into the various surveillance systems and monitoring of outbreak responses
- How new innovations can be commercialised quickly and made available in the market for public use
- Global collaboration with clearly coordinated roles and responsibilities directed towards common goals
- New uses of existing products vs development of new products

Regional Deep Dive Africa: Initial Ice-breaking task

Following presentations from Wellcome and Professor Tom Kariuki (Science for Africa Foundation) to frame the regional context of the event, participants took part in a short ice-breaking task, where in small groups they shared a topic that they would like to discuss during the event. Topics relevant to the Africa region that participants hoped to discuss included:

- Seeking a sustainably funded regional R&D ecosystem through catalysing the increased mobilisation of domestic funding and strengthening of domestic Funding Agencies.
- A desire to hear more about innovations that support African priorities, in particular those that provide support beyond proof of concept and towards infrastructure and governance of the innovation marketplace.
- The need to strategically interrogate three areas of research systems at African institutions a) the context within which the research system operates, b) the components that constitute the system, and c) the dynamics of the system.
- Standardisation of the protocols and processes that occur in early-stage research.
- Increased domestic funding and capabilities to drive R&D on the continent.
- Focused funding for innovations in institutions and with scientists living and working in the region.
- Actions and support for strengthening regulatory systems to provide a

supportive environment for research and development.

Global Deep Dive one: Initial ice-breaking task

Following a brief opening presentation, which summarised Wellcome's key findings from the previous seven Global Conversation events, participants were asked to share in small breakout groups the key ideas that they had heard and taken away from their attendance at these previous events.

One group stated that while they welcomed and were impressed by the scale of Wellcome's ambitions for reform, they were unclear how such a vision would be realised as it necessitates significant cross-collaboration across the disparate sectors of the ecosystem to enact real change. This group added that they were also somewhat concerned that in setting out this vision there appeared to be some oversimplification of thinking about the infectious disease space, stating by way of example that HIV doesn't require the same actions as RSV. They also stated that it was important to acknowledge that infectious disease was a 'low return space' and that new approaches to funding (called for in the previous Global Conversation discussions) would be required to secure the level of investment this ambitious reform requires.

Another group stated that they recalled during their previous discussions on accountability that the changing priorities of funders in turn often led to abrupt changes in their strategies. This was thought to be a "double-edged sword" that could be beneficial for novel R&D activities but could also negatively impact ongoing progress in research or development of products for some disease areas. One group was struck by the effect the regulatory environment in different regions and countries has on cost/benefit decisions taken by entities undertaking infectious R&D.

Extending the theme of accountability, another group added that while funding spend is tracked, there is often a lack of a similar level of analysis in the outcomes of that funding further down the R&D pipeline and even less so its impact on eventual access, this prevents "us from having accountability of those who fund and those who implement". On this tracking of return-on-investment theme, it was stated that it is necessary to redefine what success looks like and in doing so to be clear what the impact or nature of reform we are trying to achieve is.

This point about defining what constitutes successful outcomes was echoed by another group that felt "different parts of the ecosystem may use the same language, but the meaning can be very different, and this makes working together [toward a common goal such as this reform] very difficult".

On the theme of equity, one group reiterated a cross-cutting need for "simply having more research investment and especially in building research capacity in LMICs" that came through in previous sessions. Equity for this group also included rebalancing how research is distributed geographically.

This group also stressed how stronger local research ecosystems are especially important for early warning and surveillance. They were in agreement that this work is often conducted in the research and academic sector, and this has important implications for detecting emerging infectious diseases and outbreaks, as strengthened local research ecosystems would positively impact early warning mechanisms.

Global Deep Dive Two: Initial ice-breaking task

The event began with an initial icebreaking task where participants were asked to share in small breakout groups the key ideas that they had heard and taken away from their attendance at the previous events of the Global Conversation.

Back in the main room the participants used the chat facility to report the key themes that had resonated with the members of their breakout rooms. These included a general desire to move towards implementation via the funding of the many and varied constructive ideas for reform that they'd heard discussed during previous events. Participants reaffirmed the need to keep the patient at the centre of the ecosystem by planning for access from early-stage product development onwards.

One participant stated that their icebreaking group had been very appreciative of the high-level discussions but highlighted a pragmatic need to get into the "nitty gritty details" of what actions can be taken to bring about reform. Other participants stated they had heard a clear need to focus on regulatory coordination and collaboration at the regional level, especially with regard to the licensing and approval of new products.

One group reported that they recalled an important focus on equity in LMIC contexts, but that this needed critical attention to progress beyond an aspiration. They stated there were three components to equity: determining investment priorities in funding and conducting research; improving LMIC access to finished products; and a need to focus on the strengthening and expansion of product development partnerships (PDPs).

Another group recalled the theme of decolonisation that had been raised several times and they were concerned that greater diversity among the participants of reform conversations was needed. A representative of a large biotechnology advocacy organisation reflected on the need to foster greater interaction between industry and LMICs to better understand the nature of the unmet needs in these regions and countries.

This, they stated, would include creating data sharing mechanisms to drive the design of appropriate target product profiles that can be matched to balancing scientific feasibility and accessible pricing. Another group emphasised that they had heard much about the need for the ecosystem to improve the way it shares and measures all types of data. As they felt this provided the necessary intelligence that was key to so many aspects of reform from planning to accountability.

As with the previous Global Deep Dive event, Wellcome launched the day's proceedings with a presentation that briefly summarised their key findings from the previous 8 events of the Global Conversation, before introducing the two topics to be discussed at this final event – Product Development Partnerships, and Alternative Business Models and Market Shaping Mechanisms.

Appendix 6

Non-exhaustive list of existing PDPs

Drugs for Neglected Disease initiative (DNDi)

Global Antibiotic Research and Development Partnership (GARDP)

Foundation for New Diagnostics (FIND)

The Global Alliance for TB Drug Development (TB Alliance)

Medicines for Malaria Venture (MMV)

PATH

International Vaccine Institute (IVI)

Innovative Vector Control Consortium (IVCC)

Malaria Vaccine Initiative (MVI)

Tuberculosis Vaccine Initiative (TBVI)

Medicines Development for Global Health (MDGH)

International Partnership for Microbicides (IPM)

European Vaccine Initiative (EVI)

Appendix 7

Examples of alternative business models and market shaping mechanisms

Hilleman Laboratories – A joint venture between Wellcome Trust and Merck & Co, Inc to provide end-to-end development and manufacture of safe, effective and affordable vaccines and biologics that address areas of unmet need in low resource settings. The programme is currently developing rotavirus, cholera and meningococcal vaccines

Civica – Set up by a coalition of healthcare providers, philanthropies and impact investors in response to high prices and frequent shortages of essential generic drugs in the US market. The model bypasses major drug makers by pooling demand for generics at member hospitals, taking on responsibility for manufacturing directly

AMR Action Fund – The world's largest public-private partnership making investments in small and mid-size biotech companies that are developing antimicrobial therapeutics for WHO and CDC priority pathogens

Advance Market Commitments (AMCs) – A legally binding contract between often government funders or multilateral funding agencies and product developers to guarantee a viable market for a product once it is successfully developed.

Innovative product reimbursement models – Approaches that delink volume of sales and profit for products in 'broken' markets, such as antibiotics. For example, the subscription-based model being piloted in the UK NHS currently

Further examples can be found in **this database of alternative R&D initiatives.**