Generic Medicine Manufacturers Research Programme 2023

ANALYTICAL FRAMEWORK

access to medicine FOUNDATION

ACKNOWLEDGEMENTS

The Access to Medicine Foundation would like to thank all the representatives of the many different stakeholders who contributed their views to the development of this framework.

FUNDERS

This report was created with support from:
UK Foreign, Commonwealth, and Development Office
Leona M. and Harry B. Helmsley Charitable Trust
AXA Investment Managers

EXPERT COMMITTEE

Hans Hogerzeil (Chair)
Alex Bernhardt
Esteban Burrone
Sudarshan Jain
Suzette Kox
Nazeem Mohammed
Bart van Osch
Mariana Roldão Santos
Fatima Suleman
Mariatou Tala Jallow
Prashant Yadav

AUTHORS

Claudia Martínez
Danielle Barnum
Camille Romero
Natalia Sánchez Villalobos
Pandora Zilstorff

EDITORIAL TEAM

Eleanor Bley Griffiths
Tessa Wiles

This acknowledgement is not intended to imply that the individuals and institutions referred to above endorse the framework for the Generic Medicine Manufacturers Research Programme, analyses or results. Decisions regarding inclusion of all feedback were ultimately made by the Access to Medicine Foundation.

ACCESS TO MEDICINE FOUNDATION

The Access to Medicine Foundation is an independent non-profit organisation that seeks to transform the healthcare ecosystem by motivating and mobilising companies to expand access to their essential healthcare products in low- and middle-income countries.

Naritaweg 227-A
1043 CB, Amsterdam
The Netherlands

For more information about this publication, please contact
Claudia Martínez, Research Programme Manager
cmartinez@accesstomedicinefoundation.org
+31 (0) 20 215 35 35
www.accesstomedicinefoundation.org

Table of contents

INTRODUCTION

Bringing generic and biosimilar medicines within reach

Generic medicines account for the vast majority of the global supply of pharmaceuticals.[1] Yet, even though generic medicines are generally priced more affordably than patented originator medicines, there are still huge global access gaps. Many people living in low- and middle-income countries (LMICs) simply do not have access to an affordable, reliable supply of the medicines they need.[2]

As at-scale suppliers of essential medicines, the impact and global footprint of generic medicine manufacturers is immense. Among the medicines included on the World Health Organization (WHO)'s Model List of Essential Medicines (EML) – meaning that they ought to be available in every country's health system – only 10% are on-patent, i.e. covered by a patent that excludes other companies from making or marketing the drug unless permissions are explicitly granted.[3,4] This indicates the central role of off-patent medicines, i.e. generics or biosimilars, as essential treatments across the world. Consequently, if generic and biosimilar medicine manufacturers step up their efforts to expand access to their products to more people living in LMICs, they can move the dial on access to medicine. Greater action by these companies, alongside other global health stakeholders such as national governments, is vital to achieving universal health coverage (UHC) and the Sustainable Development Goals (SDGs), specifically Goal 3.

In recognition of the critical role generic and biosimilar medicine manufacturers can play in tackling global health inequities by ensuring and expanding access to much-needed medicines in LMICs, the Access to Medicine Foundation has launched the Generic Medicine Manufacturers Research Programme. The programme's first analytical framework, outlined in this report, will form the basis of a per-company assessment of the actions and strategies of some of the world's leading generic medicine manufacturers.

Generic medicine manufacturers have shown their potential to scale up

Past actions from the generics industry show that when efforts are concentrated and focused, global scale-up of supply is possible. For example, the industry has been instrumental in scaling global access to quality-assured and low-cost antiretroviral medicines for the treatment of HIV/AIDS. Manufacturers have also created lower-priced generic versions of sofosbuvir, an essential treatment for hepatitis C, by engaging in licensing agreements.[5–7]

During the outbreak of the COVID-19 pandemic, manufacturers leveraged their at-scale manufacturing capacity to rapidly respond to the crisis. They ensured that many existing medicines remained available, despite global supply chain disruptions, and stepped in to manufacture health products for the treatment of COVID-19, such as dexamethasone.[8] Generic medicine manufacturers also helped manufacture and supply products for COVID-19 through their engagement in non-exclusive voluntary licences. For instance, several generic medicine manufacturers signed agreements with the Medicines Patent Pool (MPP) to manufacture and distribute certain antivirals in LMICs, including molnupiravir, remdesivir, and nirmatrelvir.[9–11]

Challenges and opportunities

There are still many challenges to tackle, and opportunities to seize, in expanding access to generic and biosimilar medicines. While standout examples are highlighted above, they are few and far between. For many people in LMICs, and

WHAT ARE GENERIC AND BIOSIMILAR MEDICINES?

▶ **Generic medicines** are pharmaceutical products developed and manufactured to be identical to the originator medicine already authorised and offer the same therapeutic and clinical benefits containing the same active pharmaceutical ingredients (APIs), dose, strength, and route of administration. They comply with the same stringent rules and regulations regarding quality, safety and efficacy as the originator product, which has already been marketed.[19] Generic medicines can be classified as either branded generics (generic medicines with a specific trade name) or unbranded generics (which use the International Non-proprietary Name (INN)).

▶ **Biosimilar medicines** are biological products that are highly similar to an already authorised biological medicine (the reference product), which has received approval for use and market authorisation.[20] A biosimilar medicine is not referred to as a generic of a biologic medicine, because of the natural variability as well as the greater complexity in the development and manufacturing processes which prevents biosimilar medicines from being replicated exactly.[20,21] Biosimilar medicines offer the same therapeutic efficacy, clinical benefits and safety profile as the original biological medicine.[21,22]

The Generic Medicine Manufacturers Research Programme focuses solely on generic and biosimilar medicines that are quality-assured – i.e., those that are required to comply with stringent rules and regulations regarding quality, safety and efficacy.

particularly for those living in the poorest countries and/or those from vulnerable populations, including women and children, many generic and biosimilar medicines are unavailable or unaffordable.

The following pages of this report explore key concerns, including weak supply chains; quality assurance; variations in pricing and affordability; security of supply; and difficulties in demand-planning and healthcare systems. For people living in LMICs, one additional difficulty can be that products are not adapted to their needs; there are challenges and opportunities here, too, in adaptive R&D. For example, companies can create heat-stable versions of medicines for use in areas without reliable refrigeration, or can develop practical combinations for certain populations, such as for treating malaria in children and babies.

How biosimilar medicines fit into the picture

In recent years, technological advances, combined with the expiration of patents for some significant biologic drugs, have ushered in the development of biosimilar medicines (see box, previous page). The introduction of these products can increase competition in the market, offering the potential for lower prices.[12,13] While biosimilars are increasingly used for the treatment of a range of diseases, including several cancers and autoimmune diseases, these medicines currently have a high price-point, limiting their reach in LMICs.[1,14]

However, the biosimilars market is now growing, especially as a number of patents have expired (or are soon set to expire) on blockbuster biologics, including many essential medicines. More generic and biosimilar companies are engaging in licensing activities enabling them to develop biosimilars and launch these products in LMICs, leveraging their commercial capabilities to tap into the growth of the biosimilars market and expand their portfolios to include biosimilar medicines.[15–18]

Looking ahead

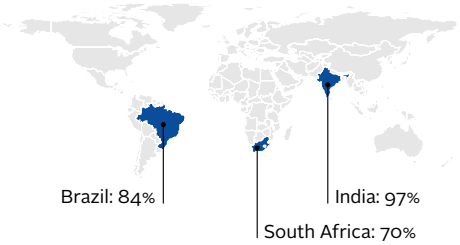
Many people living in LMICs do not have access to quality-assured generic and biosimilar medicines, whether that be because they cannot afford them, or because the products are simply not available. Without sustained effort and collaboration, inequalities in healthcare will continue to widen.

Generic and biosimilar medicine manufacturers have huge potential to change this situation. By design, generic and biosimilar versions of medicines are intended to be more affordable and accessible than the originator product, but there is now an opportunity for companies to go further by leveraging their capacity and expertise to ensure their products reach the people who need them. This framework will set out some of the positive ways generic and biosimilar medicine manufacturers can improve access to medicine in LMICs, ahead of an analysis of what some of the leading companies are currently doing in each of these areas.

A fragmented market, with a few key players

The global market for generic and biosimilar medicines is heterogeneous and highly fragmented with numerous manufacturers supplying at the global, regional, and local level. This includes large multinational companies with global footprints in contrast to the regional and local players who operate at a comparatively smaller scale within regional and domestic markets.[23] People across the world, and particularly those living in LMICs, rely heavily on the supply of generic medicines. The market share of generic medicines is estimated at 97% for India, 84% for Brazil and 70% for South Africa (see Figure 1).[24] Similarly, many of the essential medicines procured internationally through international pooled procurement schemes are generic medicines, with generic medicines accounting for an estimated 87% of the medicine volume procured in the Caribbean region.[25] A significant portion of this global supply is manufactured in LMICs, with estimates suggesting that 20% of the global volume is manufactured in India and subsequently exported to upwards of 200 countries.[26]

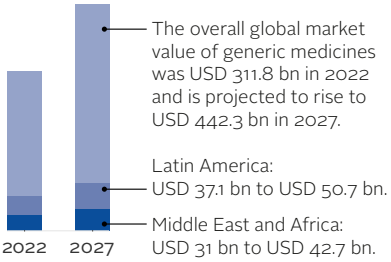
FIGURE 1 **Examples of market share of generic medicines, by volume**



Market growth trends of generic and biosimilar medicines

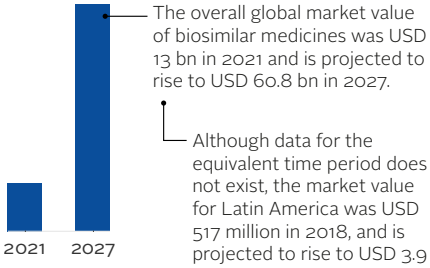
The global market for generic medicines has grown substantially over the last years and is projected to reach USD 442.3 billion by 2027 (up from USD 311.8 billion in 2022), growing at a compound annual growth rate (CAGR) of 7.24% (see Figure 2).[27–29] This is in part fuelled by the rise in chronic diseases, patent expiries of originator products and efforts by governments to contain healthcare costs.[30]

FIGURE 2 **The global market value of generic medicines is growing**



The global biosimilars market will reach USD 60.8 billion by 2027 (up from USD 13 billion in 2021), growing at a CAGR of 26.1% during 2022-2027 (see Figure 3).[31–33] In recent years the biosimilar market has been growing at a rapid rate. This is, in part, due to key blockbuster biologics coming off-patent, which enables biosimilar manufacturers to launch competing products. In particular, the expiry of patents on key products for non-communicable diseases such as cancer and diabetes has created an opportunity for the launch of more affordable biosimilar versions.[33–35] For example, on-patent cancer medicine pembrolizumab will lose its market exclusivity in various countries in 2028; this medicine is listed on the WHO EML, and is used in cancer immunotherapy to treat melanoma, lung cancer, head and neck cancer, hodgkin lymphoma, stomach cancer, cervical cancer, and certain types of breast cancer.[36,37]

FIGURE 3 **The global market value of biosimilar medicines is smaller, but rising rapidly**



Understanding access-to-medicine barriers

The expiry of patents and other exclusivity rights means generic and biosimilar medicine manufacturers can introduce generic or biosimilar versions to compete with higher-priced originator brands. However, there are still many barriers impacting the expansion of access to cost-effective and quality-assured generic and biosimilar medicines in low- and middle-income countries (LMICs).

Despite their comparatively cheaper prices, generic and biosimilar medicines remain unaffordable for many

Stark inequalities in the price of medicines, and particularly those medicines classed as essential according to the World Health Organization (WHO)'s Model List of Essential Medicines (EML), mean that many people are unable to access the treatments they need. While generic medicines are generally priced lower than originator products, they can still be unaffordable for many people living in LMICs. In some LMICs, and most notably in Least Developed Countries, essential generic medicines can cost 20 to 30 times more than a minimum international reference price – a method for benchmarking and comparing prices of pharmaceutical products amongst countries.[38]

Affordability concerns are particularly prevalent for products targeting non-communicable diseases (NCDs). For example, in India and South Africa, an essential treatment for breast cancer can cost around 10 years of average annual wages.[37,39] Even older and off-patent essential cancer medicines are associated with catastrophic out-of-pocket expenditures for people living in LMICs.[37,39] Many NCDs require chronic, long-term treatment and care, resulting in high medical costs across a person's lifespan, for example diabetes mellitus, which is treated with insulin. Yet, while the availability of several insulin biosimilar versions has led to lower prices than for originator brands in some LMICs, in some countries the introduction of biosimilars has not been matched by significant price reductions.[40,41] There are many factors that limit the affordability of biosimilar and generic medicines for NCDs in LMICs, and it is important for companies and other global health stakeholders to address these access barriers.

A market comprised of multiple generic manufacturers is needed for each product, in order to ensure sufficient competition and foster downward pressure on prices. In the US market for generic medicines, a 39% drop in price is seen after one entrant; 54% with two; 74% with four; and up to 95% with six or more competitors entering the same market.[42] Conversely, too few players can result in market concentration and monopolies, ultimately jeopardising the supply of affordable essential medicines.[43] This is especially concerning for smaller LMICs, where competition is generally more limited.[38]

The availability of quality-assured essential medicines remains limited in LMICs

People in LMICs face many challenges in accessing generic medicines, with one of the core challenges being unavailability. Despite the WHO's voluntary target of 80% availability of affordable essential medicines, research from one study showed that across the 37 LMICs analysed, the median availability of selected generic medicines was only 57% in the public sector and 65% in the private sector.[44] In particular, within the public sector of many LMICs, there is often a lack of quality-assured generic medicines for chronic conditions including cardiovascular diseases, diabetes and asthma.[45]

Generic and biosimilar medicine manufacturers can facilitate the availability of essential medicines by bringing products to market soon after patents have expired, by rapidly filing the product for registration in a range of LMICs and/or applying for

WHO prequalification for eligible products. However, manufacturers may be cautious about entering LMIC markets. For example, when the originator product has not yet been introduced in LMICs, there can be uncertainty around launching the generic version – as the drug is yet to be integrated into the continuum of care, and demand can be harder to predict. While the regulatory framework for the licensing of generic medicines is well established in most countries, obtaining market authorisation can still be a costly and lengthy process, particularly in countries without strong national regulatory authorities.[46,47]

Registration of biosimilar medicines presents a different set of challenges, due to their complex manufacturing processes and the fact that they are non-identical to the originator medicine. Manufacturers must demonstrate similarity to the reference biological medicine through analytical comparability, pre-clinical in-vitro and in-vivo comparability and clinical bioequivalence studies, which requires investment by companies, as well as expertise, capacity and resources within national regulatory agencies to ensure that products meet acceptable levels of quality, safety and efficacy.[35,48]

Additionally, if the reference product for the biosimilar medicine has not yet been filed, registering and introducing the biosimilar medicine in the respective country becomes more complex and challenging. Efforts from governments to streamline regulatory guidelines, as well as the expansion of WHO's prequalification programme to biosimilar medicines, are important steps to facilitate and speed up regulatory uptake of quality-assured biosimilar medicines in LMICs.[49] In recent years, several key biosimilar products have attained WHO prequalification, including human insulins and the cancer medicines rituximab and trastuzumab.[50,51]

In addition to registration, many LMICs face chronic challenges in ensuring a sustainable supply of quality-assured medicines due to stock-outs and a lack of healthcare infrastructure. The supply chain can also be severely impacted when there is an over-reliance on only a few manufacturers of finished products or raw materials, such as APIs.[52] For example, in Zambia one company is responsible for the supply of 98.7% of contraceptives, and in Senegal there is one company overseeing 72.4% of medicines for diabetes.[38] In 2020, stock-outs, exacerbated by the COVID-19 pandemic, made it virtually impossible to fill prescriptions for psychiatric drugs and oral contraceptives in South Africa.[53] To prevent stock-outs companies can take specific steps, including ensuring sufficient or committed capacity to meet demand, transferring knowledge and expertise to local parties to build local manufacturing capacity or by leveraging their geographical footprint to rapidly respond to demand coming from different regions.

Good manufacturing practices are also essential to ensure that medicines are manufactured at a scale and quality that ensures safe and reliable access. The use of substandard or incorrect APIs, raw materials and packaging components, poor environmental conditions throughout the manufacturing process, and failure to indicate the necessary storage conditions on the product's packaging can all impact and severely jeopardise the quality of products.[54] Generic and biosimilar medicine manufacturers can implement strategies for continually monitoring their manufacturing processes and ensuring that their own facilities and those of third-party manufacturers comply with internationally recognised quality standards. To ensure products meet stringent quality standards for international procurement, companies with eligible products can engage in WHO prequalification or seek regulatory approval through WHO Listed Authorities (WLAs). To help safeguard the quality of products, efforts can also be made to both improve supply chain management capabilities and implement strong systems for ensuring drug quality and safety. This is particularly important for medicines that require continuous cold-chain storage, such as oxytocin, which if not stored at 2-8°C will degrade and lose its potency.[54–56]

Not all products are suited to the needs of people living in LMICs

Health products are only beneficial when they meet the priority healthcare needs of the population and can be deployed effectively in a particular setting. Medicines developed for deployment in high-income settings may therefore not always be appropriate for dispensing in LMICs. As such, when introducing medicines into LMICs, certain adaptations may be necessary to help overcome context-specific access issues. Adaptions may include heat-stable variations, paediatric formulations, fixed-dose combinations or long-acting injectables, and should consider local needs, gaps in local health-care infrastructure, and environmental conditions in LMICs.[57,58]

For example, studies have shown that over half (59%) of healthcare facilities across certain LMICs lack the reliable electricity supply needed to power cold chain storage equipment, and similarly, throughout sub-Saharan Africa, only 28% of healthcare facilities have access to reliable electricity.[59,60] Such challenges can be overcome by developing heat-stable formulations for products that currently require cold chain storage, thereby enabling access for people living in LMICs.

Some products also need to be adapted for different demographic groups, particularly for babies and children, for whom there are a lack of available and appropriate treatments.[57,61] Manufacturers can create palatable flavours and develop differing dosages or fixed-dose combinations for paediatric use, which may improve ease of administration, dose flexibility, and therefore, advance treatment adherence.[61,62] Such examples underscore the importance of adapting formulations for essential medicines and bridging critical gaps in treatment. Manufacturers can carry out adaptive projects either in-house or through partnerships with other organisations, such as product development partnerships (PDPs).

Vulnerable and underserved populations face particular access-to-medicine challenges

Many of the world's most vulnerable people struggle to access the life-saving medicines that they need. The situation is heightened for those in Least Developed Countries, as they are often overlooked by manufacturers due to a combination of several or all the barriers highlighted above. Additionally, certain vulnerable groups, such as women and children (especially girls), members of the LGBTQIA+ community, people from indigenous and minority communities, those living with disabilities and/or mental health conditions and populations at the lower tiers of the income pyramid, may face further barriers to access due to stigma and economic constraints. For instance, while many essential mental health treatments are currently available in generic form, between 76% and 85% of people in LMICs with severe mental disorders do not receive the treatment they need.[63] Many of these barriers also extend to people living in conflict zones or informal settlements, who may lack access to the traditional health system and rely on donations in order to access the medicines they need.

To maximise the availability of their products to the most vulnerable people, generic and biosimilar medicine manufacturers can leverage their at-scale manufacturing expertise to increase supply or design systems of intra country differential pricing to reach the lowest economic tiers, either independently or in partnership with other organisations. They can also engage in donations, which are particularly relevant in the event of natural disasters, humanitarian crises and other circumstances when needs are high.

The first-ever framework to track and guide manufacturers' actions in access

To date, there has been no publicly available tool for mapping the efforts of generic and biosimilar medicine manufacturers to make their products more available, accessible, and affordable in LMICs. The goal of the Access to Medicine Foundation's Generic Medicine Manufacturers Research Programme is to guide and incentivise companies to deepen their efforts to expand access to essential medicines in LMICs. Generic and biosimilar medicine manufacturers have critical roles to play as we track progress towards achieving the Sustainable Development Goals (SDGs) by 2030 and attaining universal health coverage (UHC).

The framework will map the actions of a group of companies that are well positioned to make essential medicines available and accessible to patients living in LMICs, assessed against the consensus view of the companies' core roles and responsibilities in global health, highlighting where greater engagement is urgently needed and what good practice looks like. Companies will be assessed in three areas: their capability to expand access to essential products; their capability to ensure a continuous supply of quality-assured generic and biosimilar medicines; and, when applicable, their capability to adapt products to meet the needs of people living in LMICs.

Bringing best practices and opportunities to the fore

The framework will guide an analysis of the access-to-medicine efforts of generic and biosimilar medicine manufacturers. By examining where and how these manufacturers are already taking action, the Generic Medicine Manufacturers Research Programme will bring best practices to wider public attention and facilitate greater information-sharing between companies and other stakeholders. It will build awareness of issues and best practices by transparently documenting activities of manufacturers linked to access to medicine, as well as highlight specific opportunities for these companies to focus their efforts and break down access barriers in LMICs.

Building the framework

The analytical framework for the Generic Medicine Manufacturers Research Programme outlines the core roles and responsibilities of generic and biosimilar medicine manufacturers in access to medicine and sets out ambitious but achievable expectations for action. To develop the analytical framework, the Foundation undertook a process of examining existing sources and resources coupled with external engagement with key stakeholders and subject matter experts.

Internal review and insight into generic medicine manufacturers

From December 2021 to February 2022, the Foundation established the broad parameters for the analytical framework through a feasibility study and review of relevant literature, comprising of academic papers, peer-reviewed literature and policy reports from relevant organisations. The review sought to identify the key areas where action from companies is most needed.

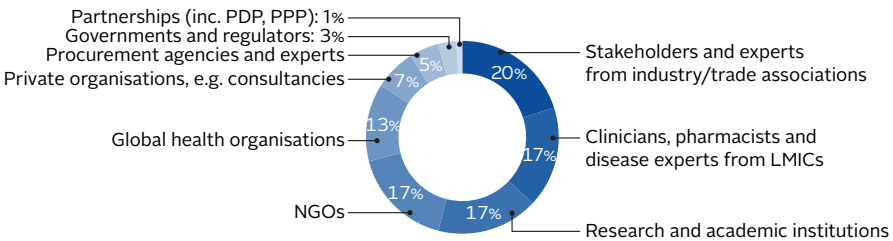
Initial stakeholder dialogue

In April 2022, the Foundation convened a workshop with experts working with and within generic and biosimilar medicine manufacturers and/or industry associations to discuss the core roles and responsibilities of manufacturers in improving access to medicine and to identify tangible strategies for future action.[64] The workshop highlighted concrete examples of how companies are currently working to improve access to medicine within LMICs and focused on opportunities to further leverage their capabilities to expand access to medicine beyond their conventional roles in manufacturing and supplying affordable generic medicines.

Targeted stakeholder engagement process

From April 2022 to July 2022, the Foundation undertook a targeted external stakeholder engagement process to refine the analytical framework and to ensure a diverse range of viewpoints and technical expertise were incorporated. Consultations were held with over 60 experts across the pharmaceutical and access-to-medicine ecosystem, including individuals working in industry and trade associations, non-governmental organisations (NGOs), global health organisations, research and academic institutions, private organisations, procurement agencies, and governments. This process sought to establish the core roles and responsibilities of generic and biosimilar medicine manufacturers in access to medicine and to ensure that the framework is a rigorous tool that can assess company action over time. The experts consulted provided critical and in-depth insights into specific questions and concerns, with a focus on company actions that can make a tangible difference. Core topics for discussion included the research areas, themes and assessment parameters for industry analysis.

FIGURE 4 **Overview of experts and stakeholders consulted**



Role of the Expert Committee

The framework proposals were reviewed by an Expert Committee (EC) comprised of 11 experts, including from industry associations, the private sector, research and academic institutions and international and non-governmental organisations. The EC discussed the areas where issues and uncertainty remained and provided strategic guidance to ensure the proposals were robust and relevant for company assessment and represented areas where industry analysis would be the most change-making.

Expert Committee members:	
Hans Hogerzeil, *chair*	University of Groningen and formerly World Health Organization (WHO)
Alex Bernhardt	BNP Paribas Asset Management
Esteban Burrone	Medicines Patent Pool (MPP)
Sudarshan Jain	Indian Pharmaceutical Alliance (IPA)
Suzette Kox	International Generic and Biosimilar Medicines Association (IGBA)
Nazeem Mohammed	Aga Khan Fund for Economic Development (AKFED)
Bart van Osch	IDA Foundation
Mariana Roldão Santos	World Health Organization (WHO)
Fatima Suleman	University of KwaZulu-Natal
Mariatou Tala Jallow	TalaConsult
Prashant Yadav	Center for Global Development (CGD)

What the framework measures

The framework for the Generic Medicine Manufacturers Research Programme assesses company action relating to a specific subset of diseases and products and within a specific geographic scope. The following pages set out the rationale for these scopes and how they have been defined.

TABLE 1 **Scopes for the Generic Medicine Manufacturers Research Programme**

Company inclusion	An initial group of five generic and biosimilar medicine manufacturers selected based on a combination of global revenue, dominance in regional markets and relevance of product portfolios for low- and middle-income countries.
Disease scope	82 diseases, conditions and pathogens: • 22 communicable diseases; • 18 non-communicable diseases; • 20 neglected tropical diseases; • 10 maternal and neonatal health conditions; • 12 priority pathogens.
Geographic scope	108 low- and middle-income countries.
Product scope	102 off-patent essential health products listed on the 22nd World Health Organization Model List of Essential Medicines. The products included represent those with proven affordability and availability issues in low- and middle-income countries. For each company, up to five in-licensed products are also in scope.

Scopes and inclusion

Company inclusion

The Generic Medicine Manufacturers Research Programme assesses a core group of generic and biosimilar medicine manufacturers on their policies and practices in improving access to medicine for people living in low- and middle-income countries (LMICs). Considering their portfolios, resources, global reach or local presence, these companies have clear opportunities and responsibilities to increase access to medicine.

Companies are selected for inclusion based on a combination of criteria. These include whether they ranked in the top 10 by global revenue; hold dominant positions in key regional markets; possess a relevant product portfolio for people living in LMICs; possess a specific dominance in one or more disease areas; and/or are identified by external stakeholders or industry experts as priorities for inclusion. The selection of companies included within the programme's scope may evolve in future based on changing market dynamics, e.g., divestments, mergers and acquisitions.

For the first company analysis based on this Analytical Framework, the Foundation will focus on five generic and biosimilar medicine manufacturers, highlighted in blue in Table 2. Specifically, these companies are Cipla, Hikma, Sun Pharma, Teva, and Viatris.

For future analyses based on this Analytical Framework, and for subsequent assessments as part of the Generic Medicine Manufacturers Research Programme, the companies in scope may include, but are not limited to: Aché; Aspen; Aurobindo; Biocon; and EMS.

TABLE 2 **Generic and biosimilar medicine manufacturers in scope of the programme**

Name	Country	Stock exchange	Ticker	2021 revenue (Bn USD)
Cipla Ltd	IND	NSE, Mumbai	CIPLA	2.921
Hikma Pharmaceuticals plc	JOR/GRB	London	HIK	2.553
Sun Pharmaceutical Industries Ltd	IND	NSE, Mumbai	SUNPHARMA	5.188
Teva Pharmaceutical Industries Ltd	ISR	New York/Tel Aviv SE	TEVA	15.878
Viatris Inc.	USA	NASDAQ	VTRS	17.886
Aché Laboratorios Farmaceuticos	BRA	N/a	N/a	0.723
Aspen Pharmacare Holdings Ltd	ZAF	Johannesburg	APN	2.368
Aurobindo Pharma Ltd	IND	NSE, Mumbai	AUROPHARMA	3.148
Biocon Ltd	IND	NSE, Mumbai	BIOCON	0.988
EMS S.A	BRA	N/a	N/a	0.822

Disease scope

The disease scope of the Generic Medicine Manufacturers Research Programme is deliberately broad to ensure that all the policies and actions of the generic and biosimilar medicine manufacturers are considered and captured following the same inclusion criteria as set out in the methodology report for the 2022 Access to Medicine Index.[65] However, in contrast to the Index methodology, Disease X* is excluded and coronaviral diseases are only included for in-licensed products - as no products for these diseases are currently listed on the World Health Organization (WHO)'s Model List of Essential Medicines (EML). As such, the Generic Medicine Manufacturers Research Programme considers 82 diseases, pathogens and

*Disease X is defined by WHO as a pathogen currently unknown to cause human disease that could cause a serious international epidemic.

conditions. One of these diseases is cancer, which encompasses 19 different subtypes. A full list of the diseases (including cancer types), pathogens and conditions included within the scope of the programme can be found in appendix I.

Defining the disease scope of the programme

To define the disease scope and pinpoint those diseases, pathogens, and conditions for which greater access to medicine is the most urgent, the Foundation used data on disease burden and incidence rates, together with independent prioritisations. Data from the Institute for Health Metrics and Evaluation's 2019 Global Burden of Disease study was used to outline the Disability-Adjusted Life Years (DALYs). For cancer, data from the Global Cancer Observatory 2020 was used.[66,67]

Geographic scope

The Generic Medicine Manufacturers Research Programme measures the actions and practices of generic and biosimilar medicine manufacturers in countries where the need for increased access to medicine is the most urgent. The country scope for the research programme follows the same inclusion criteria as set out in the methodology report for the 2022 Access to Medicine Index.[65] As such, the Generic Medicine Manufacturers Research Programme includes 108 LMICs. A full list of the countries included within the scope of the programme can be found in the appendices.

To define the geographic scope, the Foundation outlined three criteria for inclusion: (1) countries' level of income (gross national income per capita); (2) level of development, and; (3) scale and scope of inequality. Assessments for each country were based on data from the World Bank, the United Nations Development Programme (UNDP) and the United Nations Economic and Social Council (ECOSOC).

Defining the geographic scope of the programme

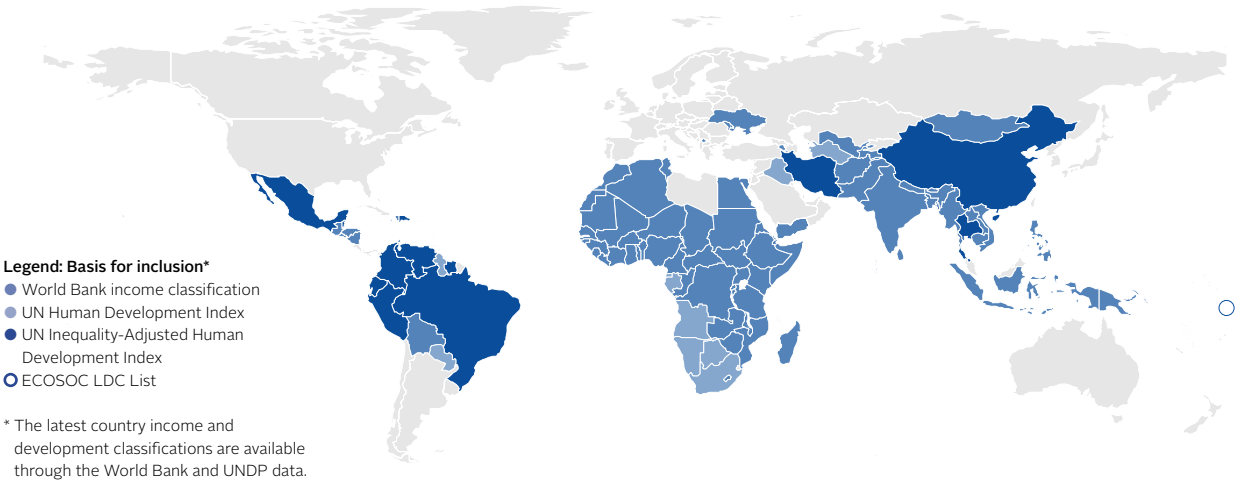
Step 1: All countries classified (according to World Bank data) as low income or lower-middle income were included;[68]

Step 2: All countries defined (according to the UNDP's Human Development Index) as having low or medium human development were included;[69]

Step 3: All high-development countries with a high inequality-adjusted HDI ratio (HiHDI) as defined by the UN Inequality-Adjusted Human Development Index were included;[69]

Step 4: All least developed countries as defined by ECOSOC were included.[70]

FIGURE 5 **Countries in scope of the Generic Medicine Manufacturers Research Programme**



Product scope

The Generic Medicine Manufacturers Research Programme product scope includes 102 essential off-patent generic and biosimilar medicines used to treat a broad set of diseases. The Foundation developed this list following an extensive prioritisation process that included an in-depth review of peer-reviewed literature on each product and consultations with clinical subject matter experts. The products listed within the product scope thereby represent products with pressing accessibility, availability, and/or affordability issues in LMICs.

To guide the inclusion of products for the research programme, the Foundation developed a prioritisation model outlining specific criteria. A full list of the products included within the scope of the programme can be found in the appendices.

Product prioritisation process

For a product to be included within the product scope:

- The product must be a medicine* or a contraceptive device**.
- The product must be listed on the 2021 WHO Model List of Essential Medicines or the 2021 WHO Model List of Essential Medicines for Children***.[71,72]
- The product must be either a first- or second line treatment or indicated as standard of care as per treatment guidelines as listed by either the National Institute for Health and Care Excellence (NICE), Centers for Disease Control and Prevention (CDC) or the WHO.[71–74] Specifically for cancer products, the European Society for Medical Oncology (ESMO) and National Comprehensive Cancer Network (NCCN) guidelines were followed, and for antibiotics, the WHO's 2021 AWaRe classification was used.[75–77]
- The product must be off-patent. To cross-reference the patent status of each product data from MedsPal by the Medicines Patent Pool (MPP), Pat-Informed by the World Intellectual Property Organization (WIPO), the Orange Book by the Food and Drug Administration (FDA) was used.[4,78,79] Additionally, country specific databases were further cross-referenced, which included the Patent register by Health Canada and Intellectual Property Database of South Africa among others.[80,81]
- There must be evidence of access gaps for the product in LMICs. Such information was sourced and cross-referenced through an in-depth review of peer-reviewed literature and public information for each product seeking to uncover robust evidence of access gaps.
- To be eligible for inclusion, the product must have been selected as a priority product by one of the external stakeholders, in-country experts or pharmacists, disease specialists and/or by one of the global health organisations consulted by the Foundation.
- For each company, up to five in-licensed products are also in scope. These have been (or will be) chosen in consultation with the companies. Please see appendix V for further information.

* Vaccines, both preventive and therapeutic, diagnostics, vector control products, microbicides, platform technologies and medicines used only for symptomatic relief are excluded from the product scope.

**For contraceptives, only devices (such as the implant) are considered. Instruments, apparatuses, appliances, and other similar or related articles intended to be used to control contraception (e.g., condoms, diaphragms or hormone-delivery contraceptive rings) are excluded.

*** Certain exceptions were made for a subset of the HIV/AIDS products, as multiple stakeholders emphasised the importance of these products despite them not being listed as fixed combinations on the WHO EML or WHO EML paediatric. Specifically, this refers to (1) dolutegravir (DTG)/lamivudine (3TC) (or emtricitabine (FTC))/tenofovir alafenamide (TAF) (DTG+XTC+TAF); (2) abacavir/lamivudine/dolutegravir (ABC+ 3TC+DTG); and (3) darunavir/ritonavir (DRV/r), all of which are listed on the 22nd WHO EML or the 8th WHO EML for children but not necessarily as combinations.

Analytical framework

The analytical framework identifies and outlines three areas where generic and biosimilar medicine manufacturers have a responsibility to improve access to medicine in low- and middle-income countries (LMICs).

This includes **A) Expanding Access; B) Supply & Quality; and C) Research & Development (R&D)**. These three areas, referred to hereafter as 'Research Areas', represent those where companies have the greatest opportunities to improve access to medicine, and where an assessment of company activity could have the greatest impact. Each Research Area includes specific themes with corresponding assessment parameters to assess manufacturers' actions and to identify tangible opportunities for improvement (see table 3).

TABLE 3 **Overview of Research Areas and themes**

EXPANDING ACCESS
Themes in this research area:
EA1. Access-to-medicine strategy
EA2. Product registration
EA3. Expanding access & pricing strategies
EA4. Engaging in licensing activities
EA5. Improving product availability
SUPPLY & QUALITY
Themes in this research area:
SQ1. Demand planning & data sharing
SQ2. Delivery performance
SQ3. Stockouts & shortages mitigation
SQ4. Manufacturing quality-assured products
SQ5. Safeguarding quality & safety of marketed products
RESEARCH & DEVELOPMENT
Themes in this research area:
RD1. Adaptive R&D
RD2. Access planning

How we assess companies

The framework was developed to measure, analyse and evaluate the various strategies generic and biosimilar medicines manufacturers employ to expand access to medicine in LMICs. In recognition of the heterogeneity amongst manufacturers, a tailored assessment approach dependent on the individual characteristics of each manufacturer will be applied. As such, companies will be assessed against their individual capability to expand access to medicine in LMICs. In addition, the framework will highlight best practices amongst the manufacturers and identify specific opportunities for improvement for each manufacturer.

EXPANDING ACCESS

The Expanding Access Research Area considers the steps that generic and biosimilar medicine manufacturers can take to ensure that their products are registered, produced at scale, and priced affordably to address demand, especially for vulnerable populations in LMICs.

PRIORITY THEMES FOR ASSESSING COMPANIES' ACTIVITIES

Registration as a gateway to improving access

Before a company can launch its product in any given country, the company must first file that product for registration, e.g., with the country's national regulatory authority, or via the World Health Organization (WHO) Collaborative Registration Procedure (CRP). When more products are registered in a country, this enables greater choice – and more equitable access to products – for governments, pooled procurement agencies, and ultimately patients themselves. It can also result in greater market competition, leading to lower prices.

As such, the framework will assess the efforts companies undertake to register quality-assured generic and biosimilar medicines in LMICs. It will consider each company's capacity for registration based on in which of the 108 LMICs in scope it has previously filed at least one product. When assessing companies' registration strategies, particularly for biosimilar products for which registration in LMICs might present specific challenges, the analysis will also consider the regulatory maturity of the country and the availability of a reference product, among others.

The framework will also evaluate companies' engagement in mechanisms designed to facilitate the registration of quality-assured products in LMICs. For instance, this includes generic and biosimilar medicines eligible for the WHO prequalification of Medicines Programme (e.g., trastuzumab, rituximab, and insulin) and/or medicines eligible for the WHO CRP.

Similarly, the framework will assess whether companies engage in other mechanisms to facilitate registration of their products, such as regional joint assessments; the European Medicines Agency's EU-Medicines for all (EU-M4all) procedure; or the Swissmedic Marketing Authorisation for Global Health Products (MAGHP) procedure, which is currently being piloted in the East African Community.

Examining efforts to expand access and product affordability

Generic and biosimilar medicine manufacturers can use a variety of strategies to improve the availability and affordability of their products to maximise patient reach in LMICs, from applying equitable pricing strategies (meaning strategies that take into account payers' ability to pay), to participating in public or private partnerships and/or pooled procurement mechanisms, and donation programmes.

In many countries, the prices of generic medicines are subject to mandatory control mechanisms that result in lower prices compared to originator medicines. However, even when pricing control mechanisms are in place, there is no guarantee that medicines will be accessible and affordable for all patients across the income pyramid. Companies can implement access strategies and enact policies to ensure that their products are available and affordable to most people, including the poorest and most vulnerable. For instance, by pricing their products responsibly and implementing policies that take into account payers' ability to pay, both at the country level and for different populations groups within each country, companies can ensure broad access to their products. The Generic Medicine Manufacturers Research Programme will assess the strategies used by companies to expand access and affordability for their products in the LMICs where access gaps are greatest.

Leveraging licensing opportunities

Until the market exclusivity period for a patented product expires, generic and biosimilar medicine manufacturers are unable to launch an off-patent version (although with certain exceptions, for instance, under the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)). By engaging in licensing agreements directly with originator companies or through organisations such as the Medicines Patent Pool, as well as taking advantage of non-assert declarations, whereby the patent-holder commits not to enforce its patent in certain countries, companies can develop generic version of medicines before the patent expires and potentially expand access to affordable, quality-assured products in LMICs. The Generic Medicine Manufacturers Research Programme will assess and analyse the types of licensing agreements that generic and biosimilar medicine manufacturers are involved in, specifically focusing on companies' actions after signing these agreements. For instance, this may include their efforts to file for registration and improve the availability of patented medicines in the territories within the scope of the license. Exploration into the potential of licensing biologics to support the early entrance of affordable biosimilar medicines in LMICs has also begun.[14] As such, in the future the Generic Medicine Manufacturers Research Programme will track and evaluate how companies with biosimilar products within their portfolios participate and engage in these agreements.

Approaches to improving product availability

Generic and biosimilar medicine manufacturers can employ a variety of strategies to improve product availability in LMICs, including leveraging their manufacturing capabilities and strengthening their supply chain capacity. For instance, they can invest in local manufacturing or further expand their local

and/or regional presence in LMICs. Such efforts may include investing in or setting up manufacturing or packaging facilities in LMICs, which can establish a stronger and more solidified presence ensuring that production occurs closer to where the products will be distributed.[82–84] Similarly, manufacturers can transfer technical knowledge and/or expertise to other manufacturers who have a local or regional presence in LMICs.[85] Supply chain strengthening is another way manufacturers can increase product availability, for example by optimising and investing in their supply chain management skills and logistics or engaging in partnerships with local stakeholders to strengthen their distribution capabilities. Such initiatives are important, as the lack of well-functioning and resilient supply chains may also contribute towards the poor availability of essential medicines in LMICs.[38,86,87] As such, the Generic Medicine Manufacturers Research Programme will examine manufacturers' differing strategies that aim to improve product availability within LMICs.

Theme		Description	Rationale
EA1.	**Access-to-medicine strategy**	The company has a clear long-term strategy for improving access to medicine that is aligned and/or integrated within its corporate strategy and business model. Well integrated and comprehensive strategies will aim to sustainably increase access to medicine with commitments to increase patient reach, will have measurable and time-bound objectives for improving access to medicine that are publicly reported and will have director and/or board level responsibility for access to medicine initiatives.	When companies have well-integrated and comprehensive access-to-medicine strategies, this demonstrates the company's overall commitment to increase access to medicine through sustainable channels and indicates how access is relevant for the long-term growth of the company. When these strategies include measurable and time-bound objectives that are publicly reported, and when such strategies include director and/or board level responsibility for achieving defined access-to-medicine goals, this increases the likelihood of the access-related initiatives being achieved.
EA2.	**Product registration**	The company files its generic and biosimilar* medicines for registration within the LMICs in scope, prioritising countries with the highest disease burden and unmet needs. The company participates in mechanisms designed to facilitate broad product registration in LMICs and seeks approval from authorities such as the European Medicines Agency (EMA) and/or other WHO Listed Authorities (WLAs). Such mechanisms might include: • The WHO Collaborative Registration Procedure for WHO Prequalified products, • The WHO Collaborative Registration Procedure for Stringent Regulatory Authorities (SRAs) approved and/or assessed products, • The Regional Joint Assessments, such as the ASEAN Joint Assessment, The African Regional Joint Assessment initiatives, the CARICOM Joint assessment, • The European Medicines Agency EU-M4all (formerly Article 58), • Swissmedic Marketing Authorisation for Global Health Products (MAGHP) procedure. * Registration of biosimilar medicines requires specific assessment/evaluation defined by the unique characteristics of biological medicinal products and manufacturing processes.	Product registration in local markets is a vital step towards making medicines available in a country. When a company files products for registration in multiple LMICs where the disease burden is high for the particular disease targeted by the product, this demonstrates a commitment to reach patient populations in need and to provide access to its products. Participation in mechanisms designed to facilitate broad product registration, such as WHO's prequalification and collaborative registration procedure (CRP), the EMA EU-Medicines for all process (EU-M4all) and regional joint assessments, can facilitate the timely availability of products while ensuring that they are safe and meet stringent quality standards for international procurement.

Theme		Description	Rationale
EA3.	**Expanding access & pricing strategies**	The company makes efforts to expand access to and ensure affordability of their generic and biosimilar products for people living within the LMICs in scope. The company demonstrates evidence of the following: • Efforts (alone or in partnership) to expand patient access to products through the implementation of access strategies (e.g., pricing strategies, patient assistance programmes and tenders, public or private partnerships, participation in pooled procurement mechanisms, donations) and the geographic scope of these methods. • How the company considers ability to pay of the different payer types in the public sector (reimbursement authority) and/or the private sector (private insurance or self-pay) when setting prices, including the magnitude of price reductions (where applicable). • The number of patients who have benefitted during the period of analysis and evidence of plans to increase patient reach in the coming years.	When a company addresses the accessibility and affordability of its products, this can help improve access and product reach across the income pyramid for people living in LMICs. Generic and biosimilar medicine manufacturers, in most cases, improve product affordability by increasing competition in the market for off-patent medicines. This, however, on its own, offers no guarantee that medicines will be accessible and affordable. Generic and biosimilar medicine manufacturers can use a variety of strategies to improve the products availability and affordability for all segments of a population and ultimately maximise patient reach, for example, by applying pricing strategies that consider different payers' ability to pay, participating in public or private partnerships and/or pooled procurement mechanisms and donation programmes.
EA4.	**Engaging in licensing activities**	The company engages in voluntary licensing agreements, either directly with originator companies or through organisations such as the Medicines Patent Pool (MPP), and leverages non-assert declaration (NADs) opportunities to improve the availability of patented products in LMICs. It also makes efforts to maximise registration and availability of products in the territories covered by these agreements.	While the responsibility to issue voluntary licences and NADs lies with the patent-holder, i.e. the originator company, generic and biosimilar medicine manufacturers have a vital role to play in ensuring that licences and NADs ultimately increase access to medicine in LMICs. When generic and biosimilar medicine manufacturers launch products covered by licences or NADs, and when they engage with originators on agreements that are transparent and include terms that cover the needs of populations in LMICs, this can improve the affordability and availability of medicines. As part of licensing agreements, generic and biosimilar medicine manufacturers may also be the recipients of technology transfers, which may help improve general and/or specific knowledge for the development of products.
EA5.	**Improving product availability**	The company makes efforts (alone or in partnership) to improve the availability of products within the LMICs in scope through activities such as, but not limited to: • Scaling up or developing its local manufacturing presence/capacity in LMICs in scope. This might include, but is not limited to, utilising its established manufacturing presence to improve product availability or setting up new manufacturing and/or packaging facilities in LMICs (for instance with third-party manufacturers). • Engaging in technology transfers, whereby the company transfers knowledge and/or expertise to local manufacturers in LMICs. • Building supply chain capacity in LMICs in scope, in areas such as distribution and logistics. Such efforts can be carried out in partnership with local stakeholders (e.g., ministries of health and public procurement, logistics and distribution agencies). • Other initiatives aimed at improving availability of products in LMICs, whether alone or in partnership.	Ensuring quality-assured products are available to those who need them requires strong supply chains, including timely delivery and proper management and distribution. While the management and distribution of products partly lies under the scope of national authorities and originator companies, generic and biosimilar medicine manufacturers can contribute to strengthening local supply and distribution capabilities by participating in initiatives to localise production or by working with partners to strengthen supply, among others.

SUPPLY & QUALITY

The Supply & Quality Research Area focuses on companies' processes to ensure quality in the manufacturing of their products, as well as processes to ensure continuity of supply. It also captures how generic and biosimilar medicine manufacturers leverage their expertise and resources to address local barriers to access.

PRIORITY THEMES FOR ASSESSING COMPANIES' ACTIVITIES

Collaboration to align supply and demand

Demand for essential products can outstrip supply for various reasons, including inaccurate demand forecasting, disruptions to manufacturing and sudden peaks in demand, like those seen during the COVID-19 pandemic. While stakeholder collaboration is necessary to address these challenges, generic and biosimilar medicine manufacturers can implement specific strategies to improve supply security in low- and middle-income countries (LMICs). Having an internal forecasting and demand planning system allows companies to accurately plan for their production and ensure they have sufficient capability to meet future demand at the global, regional, and local levels. Such systems can also inform companies' processes to scale up production whenever shortages are forecast.

To increase the likelihood that potential shortages are detected and prevented, companies can also take steps to share data and align information on supply and demand with relevant stakeholders, such as governments, procurement agencies and other partners. Data sharing might include information on the company's internal supply plans, their sourcing of key materials (inc. active pharmaceutical ingredients (APIs), key starting materials and excipients) and other potential issues which might affect product supply.

Delivering responsibly on supply commitments

Off-patent medicines in LMICs are largely procured through tendering mechanisms, whereby the procurement agency, often the public sector, purchases large quantities of quality-assured medicines at fixed prices by awarding the contract to the supplier and/or suppliers that are best able to meet the criteria of the tender.[38] International agencies that purchase essential products on behalf of LMICs, such as UNICEF, the Pan-American Health Organization (PAHO) and the Global Fund, also play an important role in making essential products available at affordable prices. Both national and international procurers can increase access to quality-assured generic medicines by streamlining and reducing the administrative burden of tendering procedures, awarding tenders to suppliers in a timely manner, providing adequate lead times based on accurate forecasting of demand and ensuring that suppliers are paid on time.[38]

When manufacturers supply via tenders set-out by governments or national and international procurers, they must ensure that they are able to meet their supply commitments and fulfil the terms of tendering contracts, which includes supplying medicines in the quantities ordered, at the right locations, and following the agreed-upon timeframes. Companies should also work in collaboration with procurement partners by communicating potential delays to deliveries in a timely manner and implement action plans to address them. Such actions are critical to ensure a secure supply of health products in LMICs within tendering agreements, and to allow procurers, alongside local stakeholders, to effectively plan for the distribution of products at the country level. The Generic Medicine Manufacturers Research Programme will assess whether generic and biosimilar medicine manufacturers deliver according to plan on tenders to ensure security of supply of off-patent medicines to LMICs.

Efforts to prevent and mitigate stockouts and shortages of essential medicines

There is a vast array of strategies generic and biosimilar medicine manufacturers can use to ensure people living in LMICs have access to a sufficient supply of quality-assured products. To prevent the risk of shortages, companies can build up safety stocks of APIs and raw materials, while also ensuring that sufficient buffer stocks of finished products are available to serve the regions and countries in which they operate. For instance, steps to decentralise production by producing from regional sites and hubs can strengthen security of supply and reduce the impact of disruptions, as can strategies to engage in multiple sourcing of critical components, and collaboration with partners to be able to meet surges in demand.

Stakeholders consulted by the Foundation recommended a nuanced approach to assessing the activities of manufacturers that have vertically integrated supply chains and control various steps of the production process, such as APIs, formulations, manufacturing, packaging, and distribution processes. This is because they might have greater ability to control and improve the efficiency of the supply chain. The Generic Medicine Manufacturers Research Programme will assess whether and how the manufacturers employ strategies to ensure a continuous supply of products to prevent and mitigate shortages and stockouts.

Manufacturing quality-assured medicines and quality assurance strategies

Well-functioning healthcare systems are reliant on the availability of quality-assured medicines, especially those classed as "essential medicines" by the WHO. Generic and biosimilar medicine manufacturers must therefore ensure that their products are effective, safe and quality-assured.

Companies must implement strategies to ensure their manufacturing sites are consistent with the international

standards on current Good Manufacturing Practice (cGMP) and address any variabilities across their production facilities and manufacturing sites. They can also implement strategies and processes to address product recalls and mitigate the circulation of substandard medicines; take steps to strengthen their quality assurance systems or those of in-country partners; and ensure traceability and transparency of the source of their products. The Generic Medicine Manufacturers Research Programme will assess manufacturers' quality assurance strategies, and their efforts towards ensuring the production of quality-assured medicines.

Theme		Description	Rationale
SQ1.	Demand planning & data sharing	The company has internal forecasting and demand planning systems in place to ensure a stable supply of quality-assured medicines efficient to predict and meet future demand. It engages in bilateral data-sharing with relevant external stakeholders (including government agencies, hospitals, warehouses, wholesalers, or other relevant networks) to align supply and demand. Such data-sharing might include information regarding the company's supply plans, sources and process of sourcing of key materials (including APIs, key starting materials and excipients), and other issues which might affect the supply of its products.	When companies have forecasting and demand planning systems in place it can contribute and lead to appropriately aligned supply and demand. This ensures that the correct quantities of essential medicines are supplied. Similarly, potential supply chain disruptions can be anticipated, and the continuity of supply can be maintained when companies engage with the relevant stakeholders on their forecasting and demand planning systems, share their market intelligence data and outline any potential disruptions.
SQ2.	Delivery performance	The company fulfils supply commitments made to national and international procurement agencies (e.g., UNICEF, the Global Fund, etc.) to ensure the continued and timely delivery of quality-assured products to LMICs. It presents evidence of the following: • Having systems in place to actively monitor and review its internal delivery performance, for instance, by tracking on-time-in-full delivery (OTiF), Line-Item Fill Rate (LIFR) or other metrics. • The extent to which, and how regularly, the company communicates issues that might affect the timely delivery or fulfilment of the contracts' terms to the procurement partner. • The actions that the company implements when delays occur that are within the responsibility of the company or its contracted third-party suppliers (e.g., delays in delivery due to production/paperwork issues, freight issues, export licences).	To ensure the continued and timely supply of quality-assured products to LMICs, companies have an important role in complying with delivery commitments made to procurement agencies. Delivering products in the appropriate quantities and timeframes, as well as disclosing when potential delays occur, helps international and national procurement agencies effectively plan for distribution of products and ensure patients have access to the right medicines, at the right time.
SQ3.	Stockout & shortages mitigation	The company employs a range of strategies to ensure a continuous supply of products and to prevent shortages and stockouts. Such strategies may include: • Maintaining a sufficient stock for critical components and conducting regular audits of its stock. • Holding regional stocks and/or making efforts to decentralise stocks of critical components. • Implementing strategies to promote supplier diversity, for example by working with multiple upstream suppliers and/or sourcing from local suppliers. • When applicable, implementing strategies to scale up production of APIs (when vertical integration is in place). • Other initiatives to fulfil emergency orders and/or surges in demand, alone or in partnership with relevant international, national or local stakeholders.	Supply inefficiencies can be caused by many events occurring upstream and downstream in the supply chain, including failure in manufacturing processes by the main manufacturer or its third-party affiliate, scarcity of APIs and high dependency on just a few API suppliers, as well as external events such as climate disasters or unexpected events affecting different levels of the supply chain. When companies implement specific mechanisms to prevent stockouts and shortages, this can help ensure a sufficient and reliable supply of products in LMICs.

Theme		Description	Rationale
SQ4.	**Manufacturing quality-assured products**	The company has systems in place and employs a range of strategies to ensure, maintain and/or improve the production of quality-assured products at its own and third-party manufacturing sites. Strategies are consistent with the international standards on current Good Manufacturing Practice (cGMP) and are accepted by recognised national and international authorities, such as the US Food and Drug Administration (FDA), European Medicines Agency (EMA) and WHO. It adopts concrete strategies to limit variability in manufacturing processes between manufacturing sites, with the aim of ensuring that quality-assured products are guaranteed for delivery across all geographic regions. It ensures that stringent quality standards are upheld by suppliers and when sublicensing production or specific activities to third-party manufacturers.	When companies implement systems and strategies to ensure that medicines are consistently produced to stringent international standards on cGMP at their own (and third-party) manufacturing sites, this can help minimise the likelihood that substandard medicines will reach patients.
SQ5.	**Safeguarding quality & safety of marketed products**	The company reports concrete systems to ensure the quality and safety of marketed products. It presents evidence of the following: • A process to identify and address complaints concerning potentially substandard products, including a system for recalling products from the market promptly and effectively and alerting the appropriate authorities. • Strategies to mitigate the circulation of substandard and falsified medicines, including reporting of the authorities or organisations to which it reports encounters of substandard or falsified medicines. • Efforts to disclose the source of finished products, including specifying the primary manufacturing plant and disclosure of product components and materials that are third-party sourced.	When companies implement quality assurance strategies, this ensures that the quality of all marketed products is maintained. In the event of a recall, companies must have processes in place to ensure that these happen in a timely and efficient manner. Labelling products with data that enables tracking the source (e.g., final manufacturing plant) allows for the identification and tracking of products for which quality concerns arise. Companies should also implement strategies to mitigate the circulation of substandard and falsified medicines, for example by efficiently alerting the relevant authorities to ensure that timely action is taken.

RESEARCH & DEVELOPMENT

The Research & Development (R&D) Research Area considers companies' R&D activities aimed at adapting products for low- and middle-income settings and vulnerable populations, as well as looking at the plans that companies develop during the R&D phase to make their adapted products accessible in low- and middle-income countries (LMICs) once launched.

PRIORITY THEMES FOR ASSESSING COMPANIES' ACTIVITIES

Capturing companies' R&D activities

For many diseases, the medicines that exist are insufficiently tailored to meet the needs of people living in LMICs; for example, if a product requires access to continuous cold storage, people living in areas without reliable electrical infrastructure will face additional access barriers. While innovative R&D is typically not a core activity for generic and biosimilar medicine manufacturers, some manufacturers have already shown the value they can add within this space by engaging in adaptive R&D to make versions of products more suitable for use in resource-limited settings. Indeed, some companies have begun expanding their R&D capabilities in-house or through new partnerships and strategic acquisitions.

Having reviewed such developments with stakeholders, and drawing on strategic guidance from the Expert Committee, the Generic Medicine Manufacturers Research Programme will highlight specific examples of companies' efforts for adaptive R&D. Adaptive R&D is defined as making adaptations to existing medicines, which may include, but are not limited to: new formulations; new fixed-dose combinations of existing chemical or biological entities; or the repurposing of an existing product for additional indications.

All companies in scope of the programme have R&D facilities in order to perform research to demonstrate the equivalence of new products to the originator or reference product, so all companies potentially have the capacity to engage in adaptive R&D. However, the analysis based on this framework will acknowledge that manufacturers' capabilities and focus on R&D differ and cannot be compared like-for-like. As such, the analysis will focus on and spotlight specific examples of companies' late-stage adaptative R&D projects, including the pathogens, conditions and diseases targeted and the types of adaptations made. When applicable, it will also highlight whether such projects focus on priority R&D gaps defined by WHO and/or Policy Cures Research.

Planning for access to ensure public health needs are considered during product development

Access planning during R&D is important to ensure the availability, accessibility and affordability of products in LMICs once they reach the market. When generic and biosimilar medicine manufacturers develop adaptive R&D projects, either in-house or in partnership, it is crucial that they plan for access during the project development phase to ensure timely access to the products in LMICs. Companies should have an overarching framework or policy in place to ensure that access planning is considered for all R&D projects from Phase II of clinical development (also referred to as late-stage clinical projects). Furthermore, the companies should have project-specific access plans in place for each late-stage R&D project in their pipeline. As such, the Generic Medicine Manufacturers Research Programme will assess whether and how the manufacturers who have adaptive R&D projects in their pipeline have made commitments, implemented strategies or are engaging in efforts that plan for access early in the development phase for these projects.

Theme		Description	Rationale
RD1.	Adaptive R&D	The company has adaptive R&D projects in their pipeline - where applicable – to develop products suited for low- and middle-income settings and for vulnerable populations. Projects can be developed in-house or through collaborative R&D. This can include, but is not limited to: • Adaptations to formulations (e.g., heat-stable formulations, oral formulations, long-acting formulations, new fixed-dose combinations); • Adaptations targeting specific populations (e.g., paediatric populations).	Medicines are only useful when they meet demographic needs and can be deployed effectively in a particular setting. When manufacturers adapt their products to differing environmental conditions (e.g., heat-resistant formulations), specific demographic segments (e.g., children) or create new formulations (e.g., fixed-dose combinations), this can help to address context-specific access issues.

Theme		Description	Rationale
RD2.	**Access planning**	The company considers access planning* for its adaptive R&D projects in their pipeline. This includes whether and how the company: • Has a policy/framework in place during the development phase (i.e., R&D), to ensure that equitable access is planned for all projects in development, both in-house and collaboratively, for people living in LMICs. This is called 'company-wide R&D access planning'.* • Ensures that all late-stage** adaptive R&D projects are supported by project-specific access plans, to ensure future availability, affordability, and/or accessibility of the to-be product in LMICs in scope. This is called 'project-specific R&D access planning'. * Access plans are plans made during the R&D stage to ensure the product will become accessible in LMICs. Access plans can be developed in-house or in collaboration with external stakeholders and include commitments and strategies to increase the availability, affordability and supply of medicines in LMICs in scope. **Late-stage refers to projects in Phase II and III clinical trials and those that were approved during the period of analysis. This theme relates to plans to ensure access upon approval to products in the pipeline.	Companies can ensure that their products quickly reach the people who need them by planning for access during clinical development (starting from Phase II). To strengthen the potential impact on public health, the company's access plans should include not only commitments to filing the product for registration in LMICs, but also measures that go beyond this to ensure affordability and supply. For instance, such measures could include equitable pricing strategies, meaning strategies that consider different payers' ability to pay; sufficient supply commitments; and applying for WHO prequalification. Such planning can help those in LMICs to gain rapid, affordable and reliable access to products following their market entry.

APPENDICES

APPENDIX I. DISEASES IN SCOPE OF THE GENERIC MEDICINE MANUFACTURERS RESEARCH PROGRAMME

The disease scope for the Generic Medicine Manufacturers Research Programme includes 82 diseases, conditions and pathogens as defined in the 2022 Access to Medicine Index.[65] However, in contrast to the Index methodology, Disease X - defined by the World Health Organization (WHO) as a pathogen currently unknown to cause human disease that could cause a serious international epidemic – is excluded,[88] and coronaviral diseases are only considered for in-licensed products. Cancer is counted as one non-communicable disease within the disease list; this encompasses 19 specific sub-types of cancer.

TABLE 4 **Disease scope**

Diseases, conditions and pathogens in scope of the Generic Medicine Manufacturers Research Programme.

	Rationale for inclusion				
Communicable Diseases	Top 10 DALY burden in countries in scope	≥95% disease burden in countries in scope	WHO-identified NTD or MNH condition	R&D priority*	Stakeholder consensus**
Arenaviral haemorrhagic fevers (Lassa fever)				●	
Bunyaviral diseases				●	
Coronaviral diseases*				●	
Enteric diseases	●	●		●	
Diphtheria		●			
Emergent non-polio enteroviruses				●	
Filoviral diseases		●		●	
Henipaviral diseases				●	
HIV/AIDS	●	●		●	
Leptospirosis				●	
Lower respiratory infections	●			●	
Malaria	●	●		●	
Measles	●	●			
Meningitis	●	●		●	
Pertussis	●	●			
Rheumatic fever				●	
Sexually transmitted infections (STIs)†	●	●		●	
Tetanus		●			
Tuberculosis	●			●	
Viral hepatitis (B and C)	●	●		●	
Yellow fever		●			
Zika				●	
Non-Communicable Diseases					
Alzheimer's disease					●
Anxiety disorders	●				
Asthma	●				
Bipolar disorder					●
Cancer‡				●	●
Chronic obstructive pulmonary disease (COPD)	●				
Diabetes mellitus	●				
Endometriosis					●
Epilepsy					●
Hypertensive heart disease	●				●
Ischaemic heart disease	●				
Kidney diseases	●				
Migraine	●				
Schizophrenia					●
Thalassemia		●			●
Sickle cell disease		●			
Stroke	●				
Unipolar depressive disorders	●				

	Rationale for inclusion				
Neglected Tropical Diseases	Top ten DALY burden in countries in scope	≥95% disease burden in countries in scope	WHO-identified NTD or MNH condition	R&D priority*	Stakeholder consensus**
Buruli ulcer			●	●	
Chagas disease			●	●	
Dengue and Chikungunya		●	●	●	
Dracunculiasis		●	●		
Echinococcosis			●		
Food-borne trematodiases		●	●		
Human African Trypanosomiasis		●	●	●	
Leishmaniasis		●	●	●	
Leprosy		●	●	●	
Lymphatic filariasis		●	●	●	
Mycetoma, chromoblastomycosis and other deep mycoses			●	●	
Onchocerciasis		●	●	●	
Rabies		●	●		
Scabies and other ectoparasites		●	●	●	
Schistosomiasis		●	●	●	
Snakebite envenoming		●	●	●	
Soil-transmitted helminthiasis		●	●	●	
Taeniasis/cysticercosis			●	●	
Trachoma		●	●	●	
Yaws		●	●		
Reproductive, Maternal and Newborn Health Conditions					
Birth asphyxia and birth trauma		●	●		
Contraceptive methods			●	●	
Hypertensive disorders of pregnancy		●	●	●	
Abortion and miscarriage		●	●		
Maternal haemorrhage		●	●	●	
Maternal sepsis		●	●		
Neonatal sepsis and infections		●	●		
Obstructed labour		●	●		
Other neonatal conditions		●	●		
Preterm birth complications		●	●		

* Only in scope for in-licensed products.
† Excludes HIV/AIDS.
‡ Includes 19 cancer types: bladder; brain, nervous system; breast; cervical; colorectal; gallbladder; head and neck; Kaposi sarcoma; leukaemia; liver; lung; non-Hodgkin lymphoma; oesophageal; ovarian; prostate; stomach; thyroid; uterine; osteosarcoma.

Priority pathogens

Acinetobacter baumannii (carbapenem-resistant)
Campylobacter spp. (fluoroquinolone-resistant)
Enterobacteriaceae (carbapenem-resistant, 3rd generation cephalosporin-resistant)
Enterococcus faecium (vancomycin-resistant)
Haemophilus influenzae (ampicillin-resistant)
Helicobacter pylori (clarithromycin-resistant)
Neisseria gonorrhoeae (3rd generation cephalosporin-resistant, fluoroquinolone-resistant)
Pseudomonas aeruginosa (carbapenem-resistant)
Salmonella spp. (fluoroquinolone-resistant)
Shigella spp. (fluoroquinolone-resistant)
Staphylococcus aureus (methicillin-resistant, vancomycin-intermediate and vancomycin-resistant)
Streptococcus pneumoniae (penicillin-non-susceptible)

APPENDIX II. COUNTRIES IN SCOPE OF THE GENERIC MEDICINE MANUFACTURERS RESEARCH PROGRAMME

The geographic scope for the Generic Medicine Manufacturers Research Programme consists of 108 low- and middle-income countries (LMICs) as defined and outlined in the 2022 Access to Medicine Index.[65]

TABLE 5 **Geographic scope**

Countries in scope of the Generic Medicine Manufacturers Research Programme.

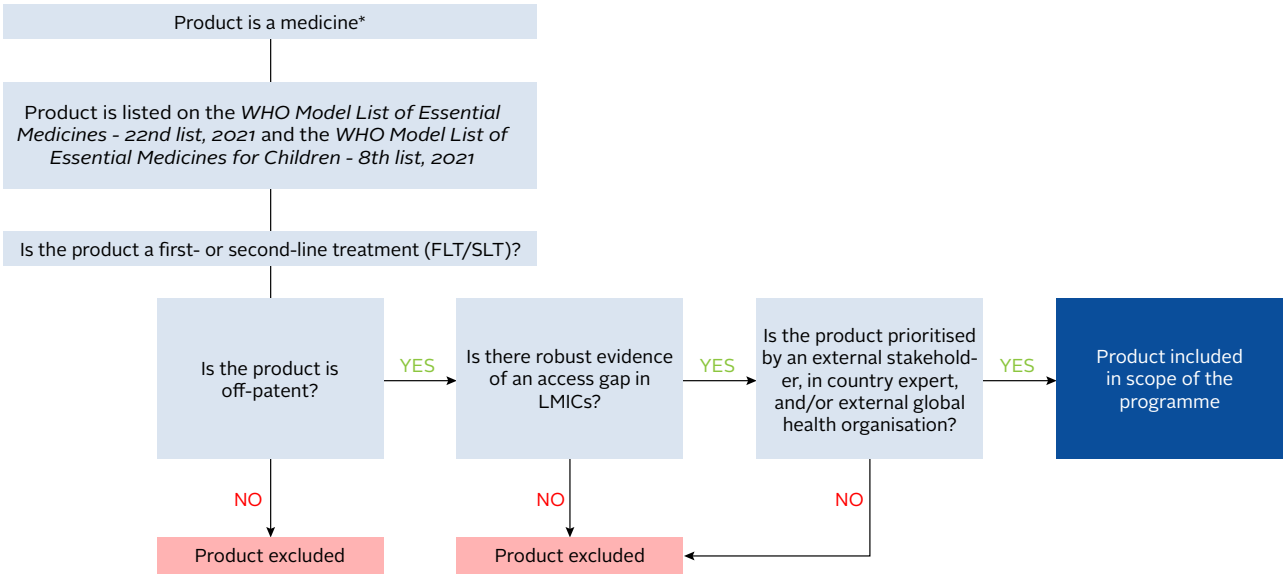
East Asia & Pacific		Peru	HiHDI	Guinea	LIC
Cambodia	LMIC	Suriname	HiHDI	Guinea-Bissau	LIC
China	HiHDI	Venezuela	HiHDI	Kenya	LMIC
Indonesia	LMIC			Lesotho	LMIC
Kiribati	LMIC	**Middle East & North Africa**		Liberia	LIC
Korea, Dem. People's Rep.	LIC	Algeria	LMIC	Madagascar	LIC
Lao PDR	LMIC	Djibouti	LMIC	Malawi	LIC
Micronesia, Fed. Sts.	LMIC	Egypt, Arab Rep.	LMIC	Mali	LIC
Mongolia	LMIC	Iran	HiHDI	Mauritania	LMIC
Myanmar	LMIC	Iraq	MHDC	Mozambique	LIC
Papua New Guinea	LMIC	Morocco	LMIC	Namibia	MHDC
Philippines	LMIC	Palestine, State of/ West Bank Gaza	LMIC	Niger	LIC
Samoa	LMIC	Syrian Arab Republic	LMIC	Nigeria	LMIC
Solomon Islands	LMIC	Tunisia	LMIC	Rwanda	LIC
Thailand	HiHDI	Yemen, Rep.	LIC	São Tomé and Principe	LMIC
Timor-Leste	LMIC			Senegal	LIC
Tonga	LMIC	**South Asia**		Sierra Leone	LIC
Tuvalu	LDC	Afghanistan	LIC	Somalia	LIC
Vanuatu	LMIC	Bangladesh	LMIC	South Africa	MHDC
Vietnam	LMIC	Bhutan	LMIC	South Sudan	LIC
		India	LMIC	Sudan	LMIC
Europe & Central		Maldives	HiHDI	Swaziland/Eswatini	LMIC
Armenia	LMIC	Nepal	LMIC	Tanzania	LIC
Kosovo	LMIC	Pakistan	LMIC	Togo	LIC
Kyrgyz Republic	LMIC	Sri Lanka	LMIC	Uganda	LIC
Moldova	LMIC			Zambia	LMIC
Tajikistan	LMIC	**Sub-Saharan Africa**		Zimbabwe	LIC
Turkmenistan	MHDC	Angola	LHDC		
Ukraine	LMIC	Benin	LIC		
Uzbekistan	LMIC	Botswana	MHDC		
		Burkina Faso	LIC		
Latin America & Caribbean		Burundi	LIC		
Belize	HiHDI	Cabo Verde	LMIC		
Bolivia	LMIC	Cameroon	LMIC		
Brazil	HiHDI	Central African Republic	LIC		
Colombia	HiHDI	Chad	LIC		
Dominican Republic	HiHDI	Comoros	LIC		
Ecuador	HiHDI	Congo, Dem. Rep.	LIC		
El Salvador	LMIC	Congo, Rep	LMIC		
Guatemala	LMIC	Côte d'Ivoire	LMIC		
Guyana	MHDC	Equatorial Guinea	MHDC		
Haiti	LIC	Eritrea	LIC		
Honduras	LMIC	Ethiopia	LIC		
Mexico	HiHDI	Gabon	MHDC		
Nicaragua	LMIC	Gambia	LIC		
Paraguay	MHDC	Ghana	LMIC		

LIC	Low-income country World Bank income classifications
LMIC	Lower-middle income country World Bank income classifications
LDC	Least Developed Country ECOSOC LDC List
LHDC	Low Human Development Country UN Human Development Index
MHDC	Medium Human Development Country UN Human Development Index
HiHDI	High Human Development Country with high inequality UN Inequality-Adjusted Human Development Index

APPENDIX III. PRODUCT PRIORITISATION PROCESS AND PRODUCT SCOPE FOR THE GENERIC MEDICINE MANUFACTURERS RESEARCH PROGRAMME

The product prioritisation process for the Generic Medicine Manufacturers Research Programme outlines and identifies the inclusion and exclusion criteria for the product scope of the programme.

TABLE 6 **Product prioritisation process**



* Excludes vaccines and diagnostics but includes contraceptive devices.

APPENDIX IV. PRODUCTS IN SCOPE OF THE GENERIC MEDICINE MANUFACTURERS RESEARCH PROGRAMME

The product scope for the Generic Medicine Manufacturers Research Programme includes 102 off-patent essential health products. Products were identified through the Research Programme's product prioritisation process and are listed following the WHO's latest list of recommended International Non-proprietary Names (INN). [89] The product scope will be updated for future iterations of the analysis, considering updates to the WHO Model List of Essential Medicines (EML) and shifting priorities within the global health community.

TABLE 7 **Product scope**

Products in scope of the Generic Medicine Manufacturers Research Programme.

International Non-proprietary Name (INN)	Disease
bevacizumab	Cervical, ovarian, colorectal and liver cancer
capecitabine	Breast, colorectal and stomach cancer
carboplatin	Cervical, breast, ovarian, head and neck, lung, osteosarcoma, prostate, brain, nervous system and bladder cancer
cisplatin	Cervical, head and neck, brain and nervous system, lung, osteosarcoma, ovarian and stomach cancer
cyclophosphamide	Leukaemia, breast, brain and nervous system and non-hodgkin lymphoma
docetaxel	Breast, prostate and stomach cancer
doxorubicin	Leukaemia, kaposi sarcoma, breast and non-hodgkin lymphoma cancer
etoposide	Leukaemia, lung, osteosarcoma and ovarian cancer
fluorouracil	Breast, colorectal and stomach cancer
gemcitabine	Ovarian, lung and breast cancer
hydroxyurea (hydroxycarbamide)	Leukaemia and sickle cell disease
methotrexate	Leukaemia, osteosarcoma and breast cancer
oxaliplatin	Colorectal and stomach cancer
paclitaxel	Cervical, ovarian, breast, kaposi sarcoma and lung cancer
rituximab	Leukaemia and non-hodgkin lymphoma cancer
tamoxifen	Breast cancer
trastuzumab	Breast and stomach cancer
amlodipine	Hypertensive heart disease
amlodipine/lisinopril	Hypertensive heart disease
enalapril	Hypertensive heart disease
hydrochlorothiazide	Hypertensive heart disease
lisinopril	Hypertensive heart disease
lisinopril/hydrochlorothiazide	Hypertensive heart disease
telmisartan	Hypertensive heart disease
telmisartan/amlodipine	Hypertensive heart disease
telmisartan/ hydrochlorothiazide	Hypertensive heart disease
valsartan	Hypertensive heart disease
bisoprolol	Hypertensive heart disease and ischaemic heart disease
metoprolol	Hypertensive heart disease and ischaemic heart disease
atorvastatin	Ischaemic heart disease
warfarin	Stroke
fluoxetine	Unipolar depressive disorders, anxiety disorders
sertraline	Unipolar depressive disorders, anxiety disorders
diazepam	Anxiety disorders, epilepsy
fluphenazine	Schizophrenia
paliperidone	Schizophrenia
haloperidol	Schizophrenia, bipolar affective disorder
risperidone	Schizophrenia, bipolar affective disorder
lamotrigine	Epilepsy
sodium valproate	Epilepsy, bipolar affective disorder
carbamazepine	Epilepsy, bipolar affective disorder
sumatriptan	Migraine
beclometasone	Asthma, chronic obstructive pulmonary disease
budesonide	Asthma, chronic obstructive pulmonary disease
formoterol/budesonide	Asthma, chronic obstructive pulmonary disease
ipratropium bromide	Asthma, chronic obstructive pulmonary disease
salbutamol	Asthma, chronic obstructive pulmonary disease
tiotropium	Asthma, chronic obstructive pulmonary disease
gliclazide	Diabetes mellitus
insulin injection (soluble)	Diabetes mellitus
intermediate-acting insulin	Diabetes mellitus
long-acting insulin analogues	Diabetes mellitus
metformin	Diabetes mellitus
misoprostol	Maternal haemorrhage
oxytocin	Maternal haemorrhage
tranexamic acid	Maternal hemorrhage
calcium gluconate	Hypertensive disorders of pregnancy
hydralazine	Hypertensive disorders of pregnancy
magnesium sulfate	Hypertensive disorders of pregnancy
methyldopa	Hypertensive disorders of pregnancy
dexamethasone	Preterm birth complications
ethinylestradiol/levonorgestrel	Contraceptive methods
etonogestrel (implant)	Contraceptive methods
levonorgestrel	Contraceptive methods
tenofovir disoproxil fumarate	Hepatitis B
daclatasvir	Hepatitis C
daclatasvir/sofosbuvir	Hepatitis C

International Non-proprietary Name (INN)	Disease
ribavirin	Hepatitis C
sofosbuvir	Hepatitis C
sofosbuvir/velpatasvir	Hepatitis C
abacavir/lamivudine (ABC+3TC)	HIV/AIDs
abacavir/dolutegravir/lamivudine (ABC+DTG+3TC)***	HIV/AIDs
darunavir/ritonavir (DRV/r)***	HIV/AIDs
dolutegravir (DTG)/lamivudine (3TC) (or emtricitabine (FTC))/tenofovir alafenamide (TAF) (DTG+XTC**+TAF)***	HIV/AIDs
dolutegravir (DTG)/lamivudine (3TC) (or emtricitabine (FTC))/tenofovir disoproxil fumarate (DTG+XTC**+TDF)	HIV/AIDs
artemether/lumefantrine	Malaria
azithromycin*	Trachoma, yaws, enteric diseases and sexually transmitted infections (STIs)
ivermectin	Lymphatic filariasis, onchocerciasis (river blindness), scabies and other ectoparasitoses, soil transmitted helminthiasis
amphotericin B	Leishmaniasis, antifungal infections
praziquantel	Schistosomiasis, taeniasis/cysticercosis
amikacin	Bacterial infection
ampicillin	Bacterial infection
benzathine-benzylpenicillin	Bacterial infection
benzylpenicillin	Bacterial infection
cefalexin	Bacterial infection
cefazolin	Bacterial infection
chloramphenicol	Bacterial infection
clindamycin	Bacterial infection
cloxacillin	Bacterial infection
doxycycline	Bacterial infection
gentamicin	Bacterial infection
nitrofurantoin	Bacterial infection
phenoxymethylpenicillin	Bacterial infection
procaine-benzylpenicillin	Bacterial infection
spectinomycin	Bacterial infection
sulfamethoxazole/trimethoprim	Bacterial infection
trimethoprim	Bacterial infection
metronidazole	Bacterial infection and parasitic infection
isoniazid	Tuberculosis
linezolid	Tuberculosis
rifampicin	Tuberculosis
sulfamethoxazole/trimethoprim/isoniazid/pyridoxine hydrochloride	Used for prevention of HIV-related opportunistic infections such as tuberculosis

* Antibiotic not listed in the Access category as per the WHO AWaRe classification, but indicated for the treatment of certain Neglected Tropical Diseases in scope: Trachoma & Yaws

** XTC indicates that the X could be an F for emtricitabine or a 3 for lamivudine

*** Not on WHO EML but high priority for SH and strong evidence to include

APPENDIX V. METHOD OF PRODUCT SPECIFIC ANALYSIS FOR THE GENERIC MEDICINE MANUFACTURERS RESEARCH PROGRAMME

For the first evaluation of companies under this framework, the Foundation will carry out an in-depth analysis of a subset of 10 of the products in scope, per company. This analysis will look at the company's actions and initiatives to expand access to each of these products in LMICs. Each company will be provided with the opportunity to collaboratively select these products in consultation with the Foundation. The company-specific product selection will include off-patent medicines as identified in the programme's product portfolio and that represent the different therapeutic areas in which the company is active and, if applicable, cover non-communicable diseases, communicable diseases, neglected tropical diseases, and maternal health products.

Additionally, a maximum of five in-licensed products will be included for an analysis of companies' activities and efforts to expand access in their role as licensees. These are products for which the generic or biosimilar medicine manufacturer has entered into a licence via the Medicines Patent Pool and/or directly with the originator company.

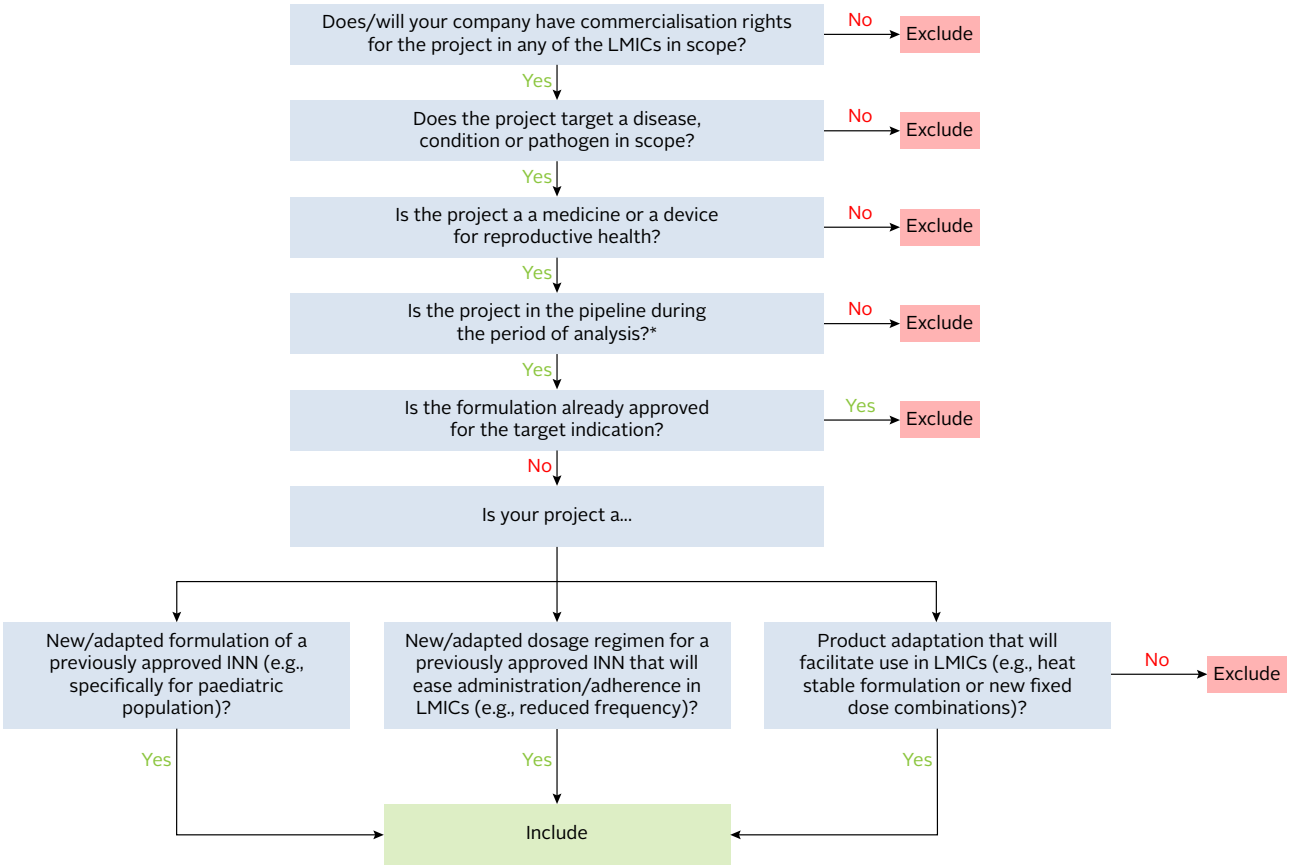
APPENDIX VI. ELIGIBILITY OF R&D PROJECTS FOR INCLUSION IN THE GENERIC MEDICINE MANUFACTURERS RESEARCH PROGRAMME

To determine the eligibility of the R&D projects, the following inclusion criteria apply, and as further outlined in figure Appendix VI, Table 8:

1. The company must have commercialisation rights in at least one country in scope of the programme;
2. The project must target a disease, condition or pathogen listed within the disease scope of the programme;
3. The project should fall within the product types in scope of the programme;
4. The project must be in the pipeline during the period of analysis;
5. Projects should be adaptations for existing products (for example: new/adapted formulations; new/adapted dosage regimens; or adaptations to facilitate use in LMICs, such as heat stable/fixed dose combinations).

Note: the Generic Medicine Manufacturers Research Programme considers projects that meet the criteria outlined above. When applicable, examples of late-stage adaptive R&D projects that target priority product gaps identified by WHO and/or Policy Cures Research (as defined in APPENDIX VII) will be highlighted.

TABLE 8 **R&D inclusion and exclusion criteria**



* The period of analysis is 1 January 2020 - 30 April 2023.

APPENDIX VII. R&D PRIORITY PRODUCT GAPS FOR THE GENERIC MEDICINE MANUFACTURERS RESEARCH PROGRAMME

The Generic Medicine Manufacturers Research Programme considers R&D priorities as those identified and listed by the WHO and/or Policy Cures Research, an independent research group. The following lists were used to determine priority product gaps:

- WHO Priority Pathogen List;[90]
- WHO R&D Blueprint;[91]
- Policy Cures Research G-FINDER emerging infectious diseases;[92]
- Policy Cures Research G-FINDER sexual & reproductive health;[93]
- Policy Cures Research G-FINDER neglected diseases.[94]

TABLE 9 **Priority gaps for R&D**

Gap identified
Restricted gap*

Group	Disease	Specific disease target	R&D Priority Lists: Medicines	Devices (for reproductive health only)	G-FINDER Neglected Diseases	G-FINDER Sexual & Reproductive Health	G-FINDER Emerging Infectious Diseases	WHO R&D Blueprint	WHO Priority Pathogens List
R&D priorities: R&D analysis	Arenaviral haemorrhagic fevers (Lassa fever)						●	●	
	Bunyaviral diseases	Crimean-Congo haemorrhagic fever					●	●	
		Rift Valley fever					●	●	
		Severe fever with thrombocytopenia syndrome (SFTS)					●		
		Other bunyaviral diseases					●		
	Buruli ulcer				●				
	Cancer	HPV-related cervical cancer (1)				●			
	Chagas disease				●				
	Contraceptive methods (2)					●			
	Coronaviral diseases	Middle East respiratory syndrome coronavirus (MERS-CoV)					●	●	
		Severe acute respiratory syndrome (SARS)					●	●	
		Coronavirus disease 2019 (COVID-19)					●		
		Other highly pathogenic coronaviral diseases					●		
	Dengue and Chikungunya	Chikungunya					●		
		Dengue			●				
	Enteric infections	Cholera (3)			●				
		Cryptosporidiosis (3)			●				
		Shigellosis (3)			●				
		Typhoid and paratyphoid fever (*S. typhi, S. paratyphi* A)			●				
		Non-typhoidal S. enterica (NTS)			●				
	Emergent non-polio enteroviruses (including EV71, D68)						●		
	Filoviral diseases	Ebola					●	●	
		Marburg					●	●	
		Other filoviral diseases					●		
	Henipaviral diseases	Nipah					●	●	
		Other henipaviral diseases					●	●	
	HIV/AIDS (4)				●				
	Human African trypanosomiasis				●				
	Hypertensive disorders of pregnancy	Pre-eclampsia (5)				●			
	Leishmaniasis				●				
	Leprosy				●				
	Lymphatic filariasis				●				
	Malaria	*P. falciparum*			●				
		P. vivax			●				
	Maternal haemorrhage	Postpartum haemorrhage (6)				●			
		Cryptococcal meningitis			●				
	Mycetoma, chromoblastomycosis and other deep mycoses	Mycetoma			●				

* A restricted gap is defined as the situation in which a gap for a therapeutic area exists, but the gap is restricted to certain circumstances. For example, a restricted gap may solely refer to certain subtypes of a disease or for a specific population. R&D projects that target indications with restricted gaps are only considered as 'priority R&D' if they address these specific gaps.

Gap identified
Restricted gap

Group	Disease	Specific disease target	R&D Priority Lists: Medicines	Devices (for reproductive health only)	G-FINDER Neglected Diseases	G-FINDER Sexual & Reproductive Health	G-FINDER Emerging Infectious Diseases	WHO R&D Blueprint	WHO Priority Pathogens List
R&D priorities: R&D analysis	Onchocerciasis				●				
	Scabies				●				
	Schistosomiasis				●				
	Sexually transmitted infections (STIs)	Gonorrhoea (7)				●			
		HSV-2				●			
		HTLV-1				●			
		Syphilis (8)				●			
		Other STIs (9)				●			
	Soil transmitted helminthiasis	Hookworm diseases			●				
		Strongyloidiasis			●				
		Trichuriasis			●				
		Ascariasis			●				
	Snakebite envenoming (10)				●				
	Taeniasis/cysticercosis				●				
	Tuberculosis (13)				●				
	Viral hepatitis (B and C)	Hepatitis B (11)			●				
		Hepatitis C (12)			●				
	Zika						●	●	
	Other prioritised antibacterial-resistant infections (13)	*Acinetobacter baumannii* (carbapenem-resistant)							●
		Campylobacter (fluoroquinolone-resistant)							●
		Enterobacteriaceae (carbapenem-resistant, 3rd generation cephalosporin-resistant)							●
		Enterococcus faecium (vancomycin-resistant)							●
		Haemophilus influenzae (ampicillin-resistant)							●
		Helicobacter pylori (clarithromycin-resistant)							●
		Neisseria gonorrhoeae (3rd generation cephalosporin-resistant, fluoroquinolone-resistant)							●
		Pseudomonas aeruginosa (carbapenem-resistant)							●
		Salmonella spp. (fluoroquinolone-resistant)			●				●
		Shigella spp. (fluoroquinolone-resistant)			●				●
		Staphylococcus aureus (methicillin-resistant, vancomycin intermediate and resistant)							●
		Streptococcus pneumoniae (penicillin-non-susceptible)							●

General notes:
• In addition to the above diseases and specific targets, the priority lists also include products targeting multiple included diseases.
• In some cases of duplicates (an R&D gap has been identified on more than one list) one list may define specific restriction for this gap. The Research Programme will consider projects targeting either the general gap or restricted gap equally.
• Where WHO priority pathogens are linked to specific diseases without reference to a specific form of antibacterial resistance, these gaps are defined separately for both the disease and for the antibacterial-resistant priority pathogen.
• Priority R&D product gaps may be updated as new iterations of priority lists are updated. Any changes that would result in the exclusion of a priority R&D project will be discussed internally, with any resulting changes communicated to companies.

(1) HPV-related cancer priority R&D restrictions are in place for medicines (ONLY includes medicines to clear or prevent HPV infection; anti-neoplastic drugs for cervical cancer are EXCLUDED). Includes devices that either clear HPV infection or treat cervical lesion.
(2) Contraceptive methods are restricted to on-demand (requiring action at the time of intercourse or pericoitally for efficacy [e.g., emergency contraception]), short-acting (working for <1 year but do not require action at the time of intercourse [e.g., injectable hormones]), long-acting reversible (working for ≥1 year [e.g., implants; IUDs]) and permanent (irreversible) methods.
(3) Restrictions for cholera, cryptosporidiosis and shigellosis are in place for medicines (ONLY includes pharmacological interventions that target the pathogen. Supportive therapies [e.g., zinc treatment, oral rehydration therapy, or other fluid and nutritional supplements] are EXCLUDED).
(4) HIV/AIDS priority R&D restrictions for medicines only includes LMIC-specific label expansions of new medicines (e.g., changes in manufacturing, recommended patient population and/or formulation for medicines after they have been approved) and formulations for LMIC use (e.g., paediatric or slow-release formulations; fixed-dose combinations; low-dose drug formulations for prophylaxis; long-acting injectables for treatment or prophylaxis).
(5) ONLY includes R&D for medicines to prevent and/or treat pre-eclampsia and/or eclampsia that offer improvements over existing products and therapies. This includes R&D for novel or existing (re-purposed) drugs, as well as research into magnesium sulphate dosing regimens.
(6) R&D for postpartum haemorrhage devices ONLY includes devices to treat PPH by targeting the underlying pathophysiology (e.g., uterine atony).
(7) Medicines for gonorrhoea MUST prevent or treat antimicrobial-resistant gonorrhoea.
(8) Medicines for syphilis MUST prevent or treat late latent, tertiary, maternal or congenital syphilis.
(9) Other STIs are defined as STIs that disproportionately affect populations in LMICs, including but not limited to trichomoniasis, chancroid, Mycoplasma genitalium, lymphogranuloma venereum and granuloma inguinale (donovanosis).
(10) Snakebite envenoming priority R&D is restricted for medicines (ONLY includes medicines being developed specifically for LMIC needs [e.g., antivenoms incorporating small-molecule inhibitors, heat-stable venom-agnostic oral medicines to slow neurotoxicity and antivenom immunoglobulins based on the venom of snakes from LMICs]).
(11) Medicines for hepatitis B ONLY include LMIC-specific label expansions of new medicines and formulations for LMIC use (e.g., curative therapies; medicines for preventing mother-to-child transmission of HBV; long-acting treatment formulations). Medicines that are biologics must at a minimum provide coverage across HBV genotypes prevalent in LMICs (A, B, C, D, E, F, H and/or I).
(12) Medicines for hepatitis C ONLY include LMIC-specific label expansions of new medicines and formulations for LMIC use (e.g., fixed-dose combinations).
(13) While M. tuberculosis has been listed as a priority pathogen by WHO, this pathogen is assessed separately as tuberculosis.

APPENDIX VIII. DEFINITIONS FOR THE GENERIC MEDICINE MANUFACTURERS RESEARCH PROGRAMME

Access plans*
Access plans are plans made during the R&D stage to ensure the product will become accessible in low- and middle-income countries (LMICs). Access plans can be developed in-house or in collaboration with external stakeholders and include commitments and strategies to increase the availability, affordability and supply of medicines in LMICs in scope.

Active pharmaceutical ingredient (API)*
The active pharmaceutical ingredient (API) is the active pharmaceutical component of a medicine that carries out its intended effects. Some medicines, such as combination therapies, have multiple active ingredients that target multiple disease pathways and/or symptoms. The inactive ingredients of a medicine are referred to as excipients.

Access-to-medicine strategy*
A strategy specifically intended to improve access to medicine, that includes all the typical elements of a strategy (a clear rationale, targets, objectives and expected outcomes). In LMICs where the company operates, the strategy may apply to a defined set of diseases, products or therapeutic areas, or to the whole pipeline and portfolio.

Ad hoc donation programmes*
A gift of products that does not form part of a clear, defined long-term strategy to control, eliminate or eradicate a disease. This may include a company donating a range of medicines based on the explicit needs of a country. Donations made during emergency situations, such as conflicts and natural disasters, are also included here..

Adaptive R&D*
R&D adaptations to existing medicines. This includes new formulations, new fixed-dose combinations of existing chemical or biological entities, a new target demographic, or the repurposing of an existing product for additional indications.

Affordability*
A measure of the payer's ability to pay for a product (whether or not they are the end user).

Affordability*
A measure of the payer's ability to pay for a product (whether or not they are the end user). Pharmaceutical companies use many different criteria to assess affordability.

Base of the income pyramid*
The base of the income pyramid, also referred to sometimes as the working poor, designates the four billion people living on an average of USD 1-5 per day.

Biosimilar*
A biosimilar medicine is a biological product that is highly similar in terms of its efficacy, clinical benefits and safety to an already licensed biological medicine referred to as the reference product. Biosimilar medicines are not referred to as generic medicines, due to the natural variability as well as the greater complexity in the development and manufacturing processes which prevents biosimilar medicines from being replicated exactly.

Branded generic*
A generic medicine which is branded and marketed under a specific trade name.

Conflict of interest*
A conflict of interest is the conflict that arises when the commercial interests of a company are potentially at odds with the interests of the partnership, the partner (i.e. local stakeholders), or the health and well-being of the population the partnership intends to help.

Demographic factors*
Characteristics of a population such as age, sex, income level, education level, employment, etc.

Disability-Adjusted Life Year (DALY)*
The disability-adjusted life year (DALY) is a measure of disease burden that combines disease-associated mortality and morbidity. It is the sum of the number of years of life lost (YLLs) and years lived with disability (YLDs). DALYs allow comparison of disease burden across different populations and health conditions across time. One DALY equals one lost year of healthy life.

EU-Medicines for all (EU-M4all)
The EU-M4all procedure is a mechanism in which the European Medical Agency (EMA) issues opinions in cooperation with the World Health Organization (WHO) on medicines intended for use in LMICs outside the EU to address public health priorities. (Definition from EMA, 2022)

Essential medicine
Essential medicines are those that satisfy the priority healthcare needs of the population. They are selected with due regard to disease prevalence and public health relevance, evidence of efficacy and safety and comparative cost-effectiveness by the WHO. They are intended to be available in functioning health systems at all times, in appropriate dosage forms, of assured quality and at prices individuals and health systems can afford. (Definition from WHO, 2022)

* Working definition, used for analysis.

Exclusive licence*
Exclusive licences are licensing agreements where the licensor (usually the patent-holder) grants the licensee (usually the generic medicine manufacturer) permission to manufacture and supply generic versions of a patented medicine. This is granted on an exclusive basis, and according to the terms of the licence.

Equitable pricing strategies*
A targeted pricing strategy which aims at improving access to medicine for those in need by taking affordability for individuals and healthcare systems into account in a manner that is locally appropriate.

Falsified medicine*
A medicine which is deliberately and fraudulently mislabelled with respect to identity and/or source. Falsified medicines may contain no active ingredient, the wrong active ingredient or the wrong amount of the correct active ingredient.

Generic medicine*
Pharmaceutical product developed and manufactured to be identical to the originator medicine already authorised. Generic medicines offer the same therapeutic and clinical benefits containing the same active pharmaceutical ingredient (API), dose, strength, and route of administration. Generic medicines are manufactured in compliance with the same stringent rules and regulations regarding quality, safety and efficacy as the originator medicine.

Generic manufacturing*
Manufacturing of pharmaceutical products by a generic medicine manufacturer which does not hold the patent for the product (produced under voluntary license or based on Trade-Related Aspects of Intellectual Property Rights (TRIPS) flexibilities etc.), or to a product whose patent has expired.

Good Manufacturing Practices*
Good manufacturing practice (GMP) is a system employed to ensure that products are consistently produced and controlled according to appropriate quality standards. Within pharmaceutical production this serves to minimise risks such as unexpected contamination, incorrect labelling or incorrect dose of the active ingredient. GMP covers all aspects of pharmaceutical production (e.g., starting materials, premises, equipment, training and personal hygiene of staff) and includes processes that provide documented proof that correct procedures are consistently followed at each step of the manufacturing process. GMP guidelines are established and overseen by regulatory agencies in individual countries or regions, as well as the WHO.

International Non-proprietary Name (INN)*
A name given to pharmaceutical products and active pharmaceutical ingredients for identification purposes. All INNs are unique and are globally utilised.

National Regulatory Authority
National Regulatory Authorities (NRAs) are the national agencies responsible for ensuring that pharmaceutical products released for public distribution are evaluated properly and meet international standards of quality and safety and efficacy. (Definition from WHO, 2022)

National reimbursement authorities*
Governmental bodies with the authority to control, approve and determine pricing and reimbursement of medicinal products in a country.

Non-assert declaration*
A declaration where a rights holder commits not to enforce their patents in certain stated countries allowing generic medicines manufacturers to produce or supply the medicine in those countries without the fear of an infringement suit. Immunity from suit is an alternative agreement to non-assert declaration, whereby the patent holder waives the right to sue, subject to certain terms and conditions.

Non-exclusive voluntary licences*
Non-exclusive voluntary licences are defined as the licences which enable - on a non-exclusive basis, and according to the terms of the licence agreed - the manufacture and supply of generic versions of patented medicines by other manufacturers.

Off-patent medicine*
A medicine whose granted patent protection has expired and is no longer protected by or exclusive marketing rights. Patent protection typically lasts for 20 years and is specific to each country.

On-patent/patented medicine*
A patented or on-patent medicine is one which has received exclusivity rights, allowing the patent holder to prevent or stop others from making, using, selling or importing the medicine within the country that granted the patent.

Patient assistance programmes*
Programmes initiated by pharmaceutical companies which provide financial assistance or free of charge medicines for a defined patient population with limited ability to pay.

* Working definition, used for analysis.

Period of analysis*
For the first iteration of company profiles, the time period for which data will be analysed covers company activities which must have been ongoing between January 2020 and April 2023. Projects that have ended before January 2020 and projects initiated after April 2023 are not included.

Priority R&D*
R&D that addresses product gaps that are needed by people living in LMICs due to ineffective, maladaptive or non-existent products for certain diseases, conditions and pathogens in the scope of the Research Programme. These product gaps are defined as being those listed in a series of six priority lists developed by WHO and Policy Cures Research, an independent research group.

Product Development Partnership*
Product Development Partnerships (PDPs) take the form of centralised non-profit organisations that facilitate financial risk-sharing across the public and private sectors by pooling and sharing resources, both tangible and intangible, for the development of medicines, vaccines and other health tools.

Pooled procurement*
A process through which a buyer pulls together demand to increase the total quantity of a specific product to include in a tender, in order to benefit from better procurement conditions and economy of scale.

Public-private partnership*
A public-private partnership (PPP) is a partnership between one or more public organisations and the private sector for providing a public asset or service, in which the private party bears significant risk and management responsibility, and remuneration is linked to performance. The Benchmark also considers a partnership between a non-profit organisation and the private sector to be a PPP.

Structured donation programmes*
A gift of products for which a defined strategy exists as to the type, volume and destination of donated products. Structured donation programmes are long-term, are targeted based on country needs, and are usually targeted to control, eliminate or eradicate a disease.

Substandard medicines*
Also called 'out of specification', these are authorised medical products that fail to meet either their quality standards or specifications, or both. [Based on WHO, 2017]

Un-branded generic*
A generic medicine which is sold and marketed under the International Non-propriety Name (INN).

Universal healthcare coverage
Universal healthcare coverage means that all people have access to the health services they need, when and where they need them, without financial hardship. It includes the full range of essential health services, from health promotion to prevention, treatment, rehabilitation, and palliative care. [Definition from WHO, 2022]

Vulnerable populations*
Vulnerable populations represent people at greater risk of facing stigma and additional barriers to access due to social, economic or health considerations. These can include, but are not limited to, children, girls and women, members of the LGBTQIA+ community, people living with HIV, etc.

WHO Collaborative Registration Procedure (CRP)
The WHO Collaborative Registration Procedure (CRP) is a procedure launched by the WHO which aims to expedite registration of prequalified finished pharmaceutical products. It accelerates registration through improved information sharing between the WHO prequalification system and national regulatory authorities (NRAs). By leveraging assessment and inspection outputs already produced by WHO prequalification, and thereby eliminating duplicative regulatory work, it speeds up in-country registration of quality-assured products and contributes to their wider availability. (Definition from WHO, 2022)

WHO Model List of Essential Medicines (WHO EML)
The WHO EML is a list published every two years by the WHO, which lists all essential medicines recommended to be available in functioning health systems at all times. (Definition from WHO, 2022)

WHO prequalification*
A scheme run by the WHO, which certifies (i.e., prequalifies) products for a limited number of diseases including HIV/AIDS, malaria, tuberculosis, neglected tropical diseases, diarrhoea, influenza and reproductive health. The assessment consists of a dossier assessment for the specific product and a site inspection against international GMP standards. UN Organizations and other major international entities involved in purchasing medicines for consumption in Africa require WHO prequalification when procuring all of the products in the categories covered.

* Working definition, used for analysis.

REFERENCES

1 International Generic and Biosimilar Medicines Association. A Vision for the Global Generic and Biosimilar Medicines Industry. Published online 2021. Accessed November 9, 2022. https://www.igbamedicines.org/doc/IGBA_Whitepaper_A%20Vision%20for%20the%20Global%20Generic%20and%20Biosimilar%20Medicines%20Industry_registered-user.pdf

2 World Health Organization. *Ten Years in Public Health, 2007-2017—Report by Dr Margaret Chan, Director-General—Access to Medicines: Making Market Forces Serve the Poor.*; 2017. Accessed November 3, 2022. https://apps.who.int/iris/handle/10665/255355

3 Schultz M, McDole J. *Essential Medicines and Patents: Recent Trends in the Latest Editions of the World Health Organization Essential Medicines List.*; 2020. Accessed January 26, 2023. https://geneva-network.com/research/essential-medicines-and-patents-recent-trends-in-the-latest-editions-of-the-world-health-organization-essential-medicines-list/

4 Medicines Patent Pool. Medspal. 2023. Accessed November 24, 2022. https://www.medspal.org/?page=1

5 World Health Organization. *Progress Report on Access to Hepatitis C Treatment: Focus on Overcoming Barriers in Low- and Middle-Income Countries.*; 2018. Accessed November 9, 2022. https://apps.who.int/iris/bitstream/handle/10665/260445/WHO-CDS-HIV?sequence=1

6 World Health Organization. Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Published online 2018. Accessed November 13, 2022. https://www.who.int/publications/i/item/9789241550345

7 Clinton Health Access Initiative. HCV Market Intelligence Report 2021 and Preliminary HBV Market Insights. Published online 2021. Accessed November 13, 2022. https://www.globalhep.org/sites/default/files/content/resource/files/2021-09/Hepatitis-C-Market-Report_2021-FINAL-1.pdf

8 Horby P. Dexamethasone in Hospitalized Patients with Covid-19. *New England Journal of Medicine*. 2021;384(8):693-704. doi:10.1056/NEJMoa2021436

9 Medicines Patent Pool. 27 generic manufacturers sign agreements with MPP to produce low-cost versions of COVID-19 antiviral medication molnupiravir for supply in 105 low- and-middle-income countries. Published 2022. Accessed November 14, 2022. https://medicinespatentpool.org/news-publications-post/27-generic-manufacturers-sign-agreements-with-mpp-to-produce-molnupiravir.

10 Medicines Patent Pool. 35 generic manufacturers sign agreements with MPP to produce low-cost, generic versions of Pfizer's oral COVID-19 treatment nirmatrelvir in combination with ritonavir for supply in 95 low- and middle-income countries. Published 2022. Accessed November 17, 2022. https://medicinespatentpool.org/news-publications-post/27-generic-manufacturers-sign-agreements-with-mpp-to-produce-molnupiravir.

11 Silverman E. Gilead signs licenses for generic companies to make and sell remdesivir in 127 countries. Published 2020. Accessed November 17, 2022. https://www.statnews.com/pharmalot/2020/05/12/gilead-generics-remdesivir-covid19-coronavirus-licenses/.

12 World Health Organization. Biosimilars. Published 2023. Accessed January 25, 2023. https://www.who.int/teams/health-product-policy-and-standards/standards-and-specifications/sbp

13 Patel KB, Arantes Jr LH, Tang WY, Fung S. The role of biosimilars in value-based oncology care. Cancer Manag Res. 2018;Volume 10:4591-4602. doi:10.2147/CMAR.S164201

14 Morin S, Segafredo G, Piccolis M, et al. Expanding access to biotherapeutics in low-income and middle-income countries through public health non-exclusive voluntary intellectual property licensing: considerations, requirements, and opportunities. Lancet Glob Health. 2023;11(1):e145-e154. doi:10.1016/S2214-109X(22)00460-0

15 Hikma Pharmaceuticals. Press release, Hikma announces licensing agreement with Celltrion. Published online 2022. Accessed January 13, 2023. https://www.hikma.com/newsroom/article-i5806-hikma-and-celltrion-sign-exclusive-licensing-agreement-for-yufly-matm-for-the-middle-east-and-north-africa-region/

16 Cipla Ltd. Cipla deal to ensure affordable access to biosimilars. Published online 2022. Accessed January 13, 2023. https://www.cipla.co.za/press-releases/cipla-deal-to-ensure-affordable-access-to-biosimilars

17 Biocon Biologics. Biocon Biologics Out-Licenses Two Biosimilar Assets to Yoshindo for Commercialization in Japan. Published online 2022. Accessed January 13, 2023. https://www.biocon.com/biocon-biologics-out-licenses-two-biosimilar-assets-to-yoshindo-for-commercialization-in-japan/

18 GlobalNewswire. The global biosimilar contract manufacturing market is expected to grow at a CAGR of 16.19% during 2022-2027. Published 2023. Accessed January 13, 2023. https://www.globenewswire.com/news-release/2023/01/12/2588208/0/en/The-global-biosimilar-contract-manufacturing-market-is-expected-to-grow-at-a-CAGR-of-16-19-during-2022-2027.html.

19 Food and Drug Administration. Generic Drug Facts .Published 2021. Accessed January 13, 2023. https://www.fda.gov/drugs/generic-drugs/generic-drug-facts

20 European Medicines Agency. Biosimilar medicines: Overview. Published 2022. Accessed November 7, 2022. https://www.ema.europa.eu/en/human-regulatory/overview/biosimilar-medicines-overview

21 Food and Drug Administration. Overview of Biosimilar Products. Published online 2017. Accessed November 9, 2022. https://www.fda.gov/media/151058/download#:~:text=A%20biosimilar%20has%20no%20clinically,biologic%2C%20called%20a%20reference%20product.&text=Biosimilars%20are%20made%20with%20the,effects%20as%20the%20reference%20product.

22 Food and Drug Administration. Biosimilar Development, Review, and Approval. Published online 2022. Accessed November 9, 2022. https://www.fda.gov/drugs/biosimilars/biosimilar-development-review-and-approval

23 Seiter A. *A Practical Approach to Pharmaceutical Policy.*; 2010. Accessed November 28, 2022. https://documents1.worldbank.org/curated/en/751541468325451548/pdf/552030PUB0Phar10Box349442B-01PUBLIC1.pdf

24 International Generic and Biosimilar Medicines Association. *Market Penetration of Generic Medicines.*; 2021. Accessed January 17, 2023. https://www.igbamedicines.org/doc/20211015_Data.pdf

25 Preston C, King C, Hinds M, Burnett F, Extavour RM. Pharmaceutical procurement among public sector procurers in CARICOM. *Revista Panamericana de Salud Pública.* 2021;45:1. doi:10.26633/RPSP.2021.57

26 Invest India National Investment Promotion & Facilitation Agency. Indian pharmaceuticals - a formula for success. Published 2022. Accessed November 3, 2022. https://www.investindia.gov.in/sector/pharmaceuticals#:~:text=The%20pharmaceutical%20industry%20in%20India%20is%20currently%20valued%20at%20%2450,served%20by%20Indian%20pharma%20exports.

27 Market Data Forecast. *Latin America Generic Drugs Market Research Report - Segmented By Type, Application, & Country.*; 2022. Accessed November 28, 2022. https://www.marketdataforecast.com/market-reports/latin-america-generic-drugs-market

28 Market Data Forecast. *Global Generic Drugs Market Size, Share, Trends, Growth & COVID-19 Impact Analysis Report.*; 2022. Accessed November 28, 2022. https://www.marketdataforecast.com/market-reports/global-generic-drugs-market

29 Market Data Forecast. *Middle East and Africa Generic Drugs Market Research Report - Segmented By Type, Application, & Country.*; 2022. Accessed November 28, 2022. https://www.marketdataforecast.com/market-reports/middle-east-and-africa-generic-drugs-market

30 IMARC group. Generic Drugs Market: Global Industry Trends, Share, Size, Growth, Opportunity and Forecast 2022-2027. Published March 2022. Accessed October 31, 2022. https://www.researchandmarkets.com/reports/5562613/generic-drugs-market-global-industry-trends?utm_source=GNOM&utm_medium=PressRelease&utm_code=25r36w&utm_campaign=1524675+-+Worldwide+Generic+Drugs+Industry+to+2026+-+Players+Include+Mylan%2c+Novartis+and+Pfizer+Among+Others&utm_exec=jamu273prd

31 Rathore AS, Bhargava A. Regulatory considerations in biosimilars: Middle East and Africa regions. *Prep Biochem Biotechnol.* 2021;51(8):731-737. doi:10.1080/10826068.2021.1959346

32 Rathore AS, Bhargava A. Regulatory considerations in biosimilars: Latin America region. *Prep Biochem Biotechnol.* 2021;51(2):201-206. doi:10.1080/10826068.2021.1876729

33 IMARC group. Biosimilar Market: Global Industry Trends, Share, Size, Growth, Opportunity and Forecast 2022-2027. Published 2022. Accessed October 31, 2022. https://www.imarcgroup.com/biosimilar-market

34 Moorkens E, Jonker-Exler C, Huys I, Declerck P, Simoens S, Vulto AG. Overcoming Barriers to the Market Access of Biosimilars in the European Union: The Case of Biosimilar Monoclonal Antibodies. *Front Pharmacol.* 2016;7. doi:10.3389/fphar.2016.00193

35 International Generic and Biosimilar Medicines Association. *Effective Strategies to Advance Access to Biologic Therapies for Non-Communicable Diseases.*; 2021. Accessed November 9, 2022. https://www.globalbiosimilarsweek.org/2021/doc/A-Biosimilar-medicines-Access-Policy-Blueprint-IGBA.pdf

36 Medicines Patent Pool. Medspal - Pembrolizumab. Medspal. Published 2023. Accessed January 25, 2023. https://www.medspal.org/?keywords=Pembrolizumab&page=1

37 Fundytus A, Sengar M, Lombe D, et al. Access to cancer medicines deemed essential by oncologists in 82 countries: an international, cross-sectional survey. *Lancet Oncol.* 2021;22(10):1367-1377. doi:10.1016/S1470-2045(21)00463-0

38 Silverman R, Madan Keller J, Glassman A, Chalkidou K. *Tackling the Triple Transition in Global Health Procurement. Promoting Access to Essential Health Products through Aid Eligibility Changes, Epidemiological Transformation, and the Progressive Realization of Universal Health Coverage.*; 2019. Accessed January 5, 2023. https://www.cgdev.org/sites/default/files/better-health-procurement-tackling-triple-transition.pdf

39 Ocran Mattila P, Ahmad R, Hasan SS, Babar ZUD. Availability, Affordability, Access, and Pricing of Anti-cancer Medicines in Low- and Middle-Income Countries: A Systematic Review of Literature. *Front Public Health.* 2021;9. doi:10.3389/fpubh.2021.628744

40 Haque M, Islam S, Kamal ZM, et al. Ongoing efforts to improve the management of patients with diabetes in Bangladesh and the implications. *Hosp Pract.* 2021;49(4):266-272. doi:10.1080/21548331.2021.1906083

41 Ewen M, Joosse HJ, Beran D, Laing R. Insulin prices, availability and affordability in 13 low-income and middle-income countries. *BMJ Glob Health.* 2019;4(3):e001410. doi:10.1136/bmjgh-2019-001410

42 Conrad R, Lutter R. *Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Generic Drug Prices.*; 2019. Accessed January 5, 2023. https://www.fda.gov/media/133509/download

43 Kaplan D A. Generic drug price tags: Too high. And too low. Competition can help create an in-between.

Published online 2021. Accessed December 14, 2022. https://www.managedhealthcareexecutive.com/view/generic-drug-price-tags-too-high-and-too-low-competition-can-help-create-an-in-between-

44 World Health Organization. Median availability of selected generic medicines. Global Health Observatory data repository. Accessed January 10, 2023. https://apps.who.int/gho/data/node.main.488?lang=en

45 Cameron A, Roubos I, Ewen M, Mantel-Teeuwisse AK, Leufkens HG, Laing RO. Differences in the availability of medicines for chronic and acute conditions in the public and private sectors of developing countries. *Bull World Health Organ.* 2011;89(6):412-421. doi:10.2471/BLT.10.084327

46 World Health Organization. *WHO Good Regulatory Practices.* World Health Organization; 2022. Accessed January 10, 2023. https://www.paho.org/sites/default/files/20220601-oms_1.pdf

47 Kaplan W. *Policy Options for Promoting the Use of Generic Medicines in Lowand Middle-Income.*; 2016. Accessed November 13, 2022. https://haiweb.org/wp-content/uploads/2017/02/HAI_Review_generics_policies_final.pdf

48 International Alliance of Patients' Organisations, International Federation of Pharmaceutical Manufacturers and Association. *Biologic Medicines: Delivering on Their Potential for Patients.*; 2018. Accessed November 13, 2022. https://www.iapo.org.uk/sites/default/files/files/mainreport-in-office(pages).pdf

49 World Health Organization. Medicines Prequalification. WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control). Published 2021. Accessed January 17, 2023. https://extranet.who.int/pqweb/medicines

50 World Health Organization. First human insulins prequalified. Published 2022. Accessed November 28, 2022. https://extranet.who.int/pqweb/news/first-human-insulins-prequalified#:~:-text=27%20September%202022%20-%20The%20first,from%20Novo%20Nordisk%20A%2FS.

51 World Health Organization. WHO prequalifies first biosimilar medicine to increase worldwide access to life-saving breast cancer treatment.https://www.who.int/news/item/18-12-2019-who-prequalifies-first-biosimilar-medicine-to-increase-worldwide-access-to-life-saving-breast-cancer-treatment. Published 2019. Accessed November 28, 2022.

52 Conway M, Holt T, Sabow A, Sun I. Y. *Should Sub-Saharan Africa Make Its Own Drugs?* Mckinsey; 2019. Accessed November 2, 2022. https://www.mckinsey.com/industries/public-and-social-sector/our-insights/should-sub-saharan-africa-make-its-own-drugs

53 Gatticchi G. Covid Causes Shortage of Psychiatric Drugs in South Africa. Bloomberg. Published 2020. Accessed November 2, 2022. https://www.bloomberg.com/news/articles/2020-12-15/covid-causes-shortage-of-psychiatric-drugs-in-south-africa#xj4y7vzkg

54 World Health Organization. *Regulatory Guidance for Assessment and Management of Applications for Marketing Authorization of Oxytocin.*; 2021. Accessed November 11, 2022. https://www.who.int/publications/i/item/9789240022133

55 Torloni M, Gomes Freitas C, Kartoglu U, Metin Gülmezoglu A, Widmer M. Quality of oxytocin available in low- and middle-income countries: a systematic review of the literature. *BJOG.* 2016;123(13):2076-2086. doi:10.1111/1471-0528.13998

56 Lambert P, Nguyen TH, McEvoy C, et al. Quality of oxytocin ampoules available in health care facilities in the Democratic Republic of Congo: an exploratory study in five provinces. *J Glob Health.* 2018;8(2). doi:10.7189/jogh.08.020415

57 Bassat Q. The Unmet Needs of Paediatric Therapeutics in Poor Countries. *J Trop Pediatr.* Published online November 20, 2015. https://academic.oup.com/tropej/article/61/6/403/2380235?login=false

58 Williams SR, Nix DA, Patel KH. Drug Storage and Stability. In: *Wilderness Medicine.* Elsevier; 2007:2251-2260. doi:10.1016/B978-0-323-03228-5.50103-8

59 Cronk R, Bartram J. Environmental conditions in health care facilities in low- and middle-income countries: Coverage and inequalities. *Int J Hyg Environ Health.* 2018;221(3):409-422. doi:10.1016/j.ijheh.2018.01.004

60 Golumbeanu R, Knuckles J. Powering health facilities in the aftermath of the pandemic. Published 2022. Accessed December 14, 2022. https://blogs.worldbank.org/energy/powering-health-facilities-aftermath-pandemic

61 Ivanovska V, Rademaker CMA, van Dijk L, Mantel-Teeuwisse AK. Pediatric Drug Formulations: A Review of Challenges and Progress. *Pediatrics.* 2014;134(2):361-372. doi:10.1542/peds.2013-3225

62 Godman B, McCabe H, D Leong T, et al. Fixed dose drug combinations – are they pharmacoeconomically sound? Findings and implications especially for lower- and middle-income countries. *Expert Rev Pharmacoecon Outcomes Res.* 2020;20(1):1-26. doi:10.1080/14737167.2020.1734456

63 World Health Organization. *Global Burden of Mental Disorders and the Need for a Comprehensive, Coordinated Response from Health and Social Sectors at the Country Level.*; 2011. Accessed December 14, 2022. https://apps.who.int/gb/ebwha/pdf_files/EB130/B130_9-en.pdf

64 Access to Medicine Foundation. *Workshop on Expanding Access to Generic Medicine – Meeting Report.*; 2022. Accessed January 5, 2023. https://accesstomedicinefoundation.org/resource/workshop-on-expanding-access-to-generic-medicine-meeting-report

65 Access to Medicine Foundation. *Methodology for the 2022 Access to Medicine Index.*; 2021. Accessed November 24, 2022. https://accesstomedicinefoundation.org/resource/the-methodology-for-the-2022-access-to-medicine-index

66 Institute for Health Metrics and Evaluation. 2019 Global Burden of Disease (GBD) study. Published 2019. Accessed November 24, 2022. https://vizhub.healthdata.org/gbd-results/

67 Global Cancer Observatory. Global Cancer Observatory 2020. Published 2020. Accessed November 24, 2022. https://gco.iarc.fr/today/online-analysis-table?v=2020&mode=cancer&mode_population=continents&population=900&populations=900&key=asr&sex=0&cancer=39&type=0&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&group_cancer=1&include_nmsc=0&include_nmsc_other=1

68 The World Bank. World Bank Country and Lending Groups. Published 2022. Accessed November 17, 2022. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-worldbank-country-and-lending-groups

69 United Nations Development Programme. *The Next Frontier: Human Development and the Anthropocene. Human Development Report 2020.*; 2020. Accessed November 17, 2022. https://hdr.undp.org/content/human-development-report-2020

70 United Nations Department of Economic and Social Affairs. LDCs at a Glance. Published 2022. Accessed November 17, 2022. https://www.un.org/development/desa/dpad/least-developed-country-category/ldcs-at-a-glance.html

71 World Health Organization. *WHO Model List of Essential Medicines - 22nd List, 2021.*; 2021. Accessed November 24, 2022. https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.02

72 World Health Organization. *WHO Model List of Essential Medicines for Children - 8th List, 2021.*; 2021. Accessed November 24, 2022. https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.03

73 National Institute for Health And Care Excellence. National Institute for Health And Care Excellence. 2023. Accessed November 24, 2022. https://www.nice.org.uk/

74 Centers for Disease Control and Prevention. Centers for Disease Control and Prevention. 2023. Accessed November 24, 2022. https://www.cdc.gov/

75 World Health Organization. 2021 AWaRe classification. Published 2021. Accessed December 21, 2022. https://www.who.int/publications/i/item/2021-aware-classification

76 European Society for Medical Oncology. European Society for Medical Oncology. 2023. Accessed November 24, 2022. https://www.esmo.org/

77 National Comprehensive Cancer Network. National Comprehensive Cancer Network. 2023. Accessed November 24, 2022. https://www.nccn.org/

78 Food and Drug Administration. Orange Book . 2023. Accessed November 24, 2022. https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book

79 World Intellectual Property Organization. Pat-Informed. 2023. Accessed November 24, 2022. https://www.wipo.int/patinformed/

80 Health Canada. Patent Register. 2023. Accessed November 24, 2022. https://pr-rdb.hc-sc.gc.ca/pr-rdb/index-eng.jsp

81 Companies and Intellectual Property Commission. Intellectual Property Online South Africa's official portal for IP services. Published 2023. Accessed November 24, 2022. https://iponline.cipc.co.za/

82 Velásquez G. *Vaccines, Medicines and COVID-19.* Springer International Publishing; 2022. doi:10.1007/978-3-030-89125-1

83 Kaplan W. *Local Production of Pharmaceuticals : Industrial Policy and Access to Medicines, An Overview of Key Concepts, Issues and Opportunities for Future Research.*; 2005. Accessed January 17, 2023. https://openknowledge.worldbank.org/handle/10986/13723

84 United Nations. *Local Production of Pharmaceuticals and Related Technology Transfer in Developing Countries: A Series of Case Studies by the UNCTAD Secretariat.*; 2011. Accessed January 17, 2023. https://unctad.org/system/files/official-document/diaepcb2011d7_en.pdf

85 International Federation of Pharmaceutical Manufacturers and Associations. *Technology Transfer: A Collaborative Approach to Improve Global Health.*; 2021. Accessed January 17, 2023. https://www.ifpma.org/resource-centre/technology-transfer-a-collaborative-approach-to-improve-global-health-2/

86 UNICEF. *Leveraging the Power of Public Supply Chains to Drive Change for Children Every Day.*; 2021. Accessed January 17, 2023. https://www.unicef.org/supply/media/8301/file/Leveraging-Power-Public-SC-reduced.pdf

87 Vledder M, Friedman J, Sjöblom M, Brown T, Yadav P. Improving Supply Chain for Essential Drugs in Low-Income Countries: Results from a Large Scale Randomized Experiment in Zambia. *Health Syst Reform.* 2019;5(2):158-177. doi:10.1080/23288604.2019.1596050

88 World Health Organization. Prioritizing diseases for research and development in emergency contexts. Published 2022. Accessed November 24, 2022. https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts

89 World Health Organization. *INN Recommended List 88.*; 2022. Accessed January 17, 2023. https://www.who.int/publications/m/item/inn-rl-88

90 World Health Organization. *Prioritization of Pathogens to Guide Discovery, Research and Development of New Antibiotics for Drug-Resistant Bacterial Infections, Including Tuberculosis.*; 2017. Accessed November 24, 2022. https://apps.who.int/iris/handle/10665/311820

91 World Health Organization. R&D Blueprint. Published 2022. Accessed November 24, 2022. https://www.who.int/teams/blueprint

92 Policy Cures Research. *Emerging Infectious Disease R&D Scope.*; 2022. Accessed January 17, 2023. https://gfinder.policycuresresearch.org/staticContent/pdf/G-FINDER_EID_R%26D_scope.pdf

93 Policy Cures Research. *Sexual and Reproductive Health R&D Scope.*; 2022. Accessed January 17, 2023. https://gfinder.policycuresresearch.org/staticContent/pdf/SRH_R%26D_scope.pdf

94 Policy Cures Research. *Neglected Disease R&D Scope.*; 2022. Accessed January 17, 2023. https://gfinder.policycuresresearch.org/staticContent/pdf/Y12_2019_G-FINDER_ND_R&D_scope.pdf

Report Design
Scribble Design

Photo Disclaimer
The Access to Medicine Foundation gratefully respects the permission granted to reproduce the copyright material in this report. Every reasonable effort has been made to trace copyright holders and to obtain their permission for the use of copyright material. Should you believe that any content in this report does infringe any rights you may possess, please contact us at info@accesstomedicinefoundation.org or + 31 (0) 20 21 53 535.

Disclaimer
As a multi-stakeholder and collaborative project, the findings, interpretations and conclusions expressed herein may not necessarily reflect the views of all members of the stakeholder groups or the organisations they represent. The report is intended to be for information purposes only and is not intended as promotional material in any respect. The material is not intended as an offer or solicitation for the purchase or sale of any financial instrument. The report is not intended to provide accounting, legal or tax advice or investment recommendations. Whilst based on information believed to be reliable, no guarantee can be given that it is accurate or complete.

Access to Medicine Foundation
Naritaweg 227A
1043 CB Amsterdam
The Netherlands

www.accesstomedicinefoundation.org
info@accesstomedicinefoundation.org
+31 (0)20 21 53 535