



# THE CRISIS OF ANTIBIOTIC RESEARCH AND DEVELOPMENT

Challenges and possibilities  
to rejuvenate the antibiotic  
innovation ecosystem







# **THE CRISIS OF ANTIBIOTIC RESEARCH AND DEVELOPMENT**

**Challenges and possibilities to rejuvenate the antibiotic innovation ecosystem**

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# Contents

<b>1. INTRODUCTION</b>	<b>6</b>
<b>2. THE STATE OF ANTIBIOTIC RESEARCH AND DEVELOPMENT</b>	<b>8</b>
2.1 The weak state of antibiotic development pipeline	8
2.2 Research focus of the pharmaceutical industry	10
2.3 Micro, small and medium-scale companies developing antibacterial products	19
2.4. Ongoing initiatives to support antibiotic R&D	22
<b>3. CHALLENGES AND POSSIBILITIES: REJUVENATING THE ANTIBIOTIC INNOVATION ECOSYSTEM</b>	<b>28</b>
3.1 Need for coordinated global response to antibiotic pipeline and access crisis	29
3.2 Supporting small and medium-scale antibiotic developers	32
3.3 Recognising antibiotics as a 'global public good'	34
<b>ANNEXURE</b>	<b>39</b>
<b>REFERENCES</b>	<b>40</b>

# 1. Introduction

Bacteria is becoming resistant to the drugs (antibiotics) used to treat them. This is the cause of a silent crisis; the world is facing. Popularly known as antimicrobial resistance (AMR), but the crisis is largely about antibacterial resistance or antibiotic resistance, i.e., it is about bacteria and antibiotics.

This means antibiotics are becoming ineffective. Bacterial infections cured earlier are becoming untreatable. Beyond health, things like food security, livelihood and development are poised to be negatively and heavily impacted.

At a microbiological level, resistance in bacteria largely happens in the presence of antibiotics, when bacteria fight for survival, and some undergo certain change that does not allow antibiotic to kill them. This change can pass on to other bacteria and in the process one or more types of different antibiotics become ineffective. This kind of relationship between antibiotic and bacteria is quite specific and typical (compared to equation between other illnesses and drugs used to treat them) and therefore makes the crisis and it's handling very complex.

One part of the strategy adopted is to conserve antibiotics that the world has. It is about using them only when really needed to reduce the chances of change in bacteria. In other words, avoiding all unnecessary use. There is a lot of global momentum around it and some success is visible.

Another part is to keep making new antibiotics as resistance against existing antibiotics continues to develop and increase. There is some momentum but very limited success. That there are no new class of antibiotics developed for over the last few decades is a common understanding. Similarly, there are not many developed to kill pathogens that cause lethal infections such as in hospitals and intensive care units and are considered of critical priority.

This report presents the current scenario on where the world stands on its readiness to develop new antibacterial treatment options for future use. It covers both traditional small molecule antibiotics and non-traditional antibacterial products in clinical and preclinical pipeline. The report focusses on pipelines of select high-earning 15 global pharmaceutical companies to know their R&D focus and reflects upon reasons as to why the pharmaceutical have moved away from antibiotic R&D.

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It then presents the role played by micro, small-and medium-scale antibiotic developers who have taken up the responsibility to develop antibiotics and the typical challenges they face. It briefly summarises the global initiatives to stimulate the antibiotic R&D, broadly categorised into two sets i.e., Push and Pull incentives.

The second part of the report, suggests the way ahead in terms critical reforms needed to rejuvenate the antibiotic R&D ecosystem and also reflects on the need to deliberate, if antibiotics (or any other aspect of it) can be considered a 'global public good' to attract greater attention and funding.

Finally, the report presents the key takeaways of a series of expert consultations on the suggested way ahead. This deep-dive exercise adds nuance to the understanding of the crisis and potential solutions; challenges faced by small and medium scale antibiotic developers; and challenges and possibilities of considering antibiotics or any other aspect of it as a 'global public good'.

We hope that the report effectively informs the ongoing global deliberations on measures needed to rejuvenate antibiotic R&D ecosystem with an aim to ensure sustainable and equitable access to effective antibiotic therapies to people of all parts of the world and specifically to those living in global south.

## 2. The state of antibiotic research and development

The present state of antibiotic research and development globally is characterised by a weak antibiotic pipeline, big pharmaceutical companies not keen to develop antibiotics, small and medium scale antibiotic developers facing challenges and initiatives that are ongoing to support antibiotic R&D.

### 2.1 The weak state of antibiotic development pipeline

‘Weak’, ‘anaemic’, ‘fragile’, ‘dry’, are some of the ways the current state of antibiotic development pipeline is described. As per the data updated until late 2021 by the World Health Organization (WHO) for 12 identified priority pathogens, *Mycobacterium tuberculosis* and *Clostridioides difficile*, there are 297 antibiotic candidates in the pipeline, out of which 217 are in preclinical development, 77 are undergoing clinical trials, and three in pre-registration stage (ready for market launch after government approval).<sup>1,2</sup>

Identified by the WHO in 2017, priority pathogens are 12 different kinds of bacteria expected to pose a big threat to human health. Based on the urgency of need for new antibiotics, these are categorised as into **critical**, **high** and **medium** priority.<sup>3</sup> Most are Gram-negative bacteria that have complex cell walls and can cause difficult to treat, life-threatening infections (see *Box: WHO priority pathogens*).

#### Clinical pipeline

Out of the 77 candidates in clinical pipeline, 45 are traditional small molecule candidates and 32 are non-traditional. Traditional small molecules directly inhibit

#### WHO priority pathogens

- Priority 1 (Critical): *Acinetobacter baumannii*, carbapenem-resistant; *Pseudomonas aeruginosa*, carbapenem-resistant; *Enterobacteriaceae*, carbapenem-resistant, ESBL-producing
- Priority 2 (High): *Enterococcus faecium*, vancomycin-resistant; *Staphylococcus aureus*, methicillin-resistant, vancomycin-intermediate and resistant; *Helicobacter pylori*, clarithromycin-resistant; *Campylobacter* spp., fluoroquinolone-resistant; *Salmonellae*, fluoroquinolone-resistant; *Neisseria gonorrhoeae*, cephalosporin-resistant, fluoroquinolone-resistant
- Priority 3 (Medium): *Streptococcus pneumoniae*, penicillin-non-susceptible; *Haemophilus influenzae*, ampicillin-resistant; *Shigella* spp., fluoroquinolone-resistant



the growth of or kill bacteria by targeting components necessary for bacterial growth.<sup>4</sup> Non-traditional candidates lack intrinsic antibacterial activity and work through other approaches. These include bacteriophages and phage-derived enzymes, microbiome modulating agents, antibodies, immune-modulating agents (see *Table 1: Antibacterial clinical pipeline*).

Of the 45 traditional candidates, 28 target WHO’s priority pathogens, which has remained nearly stagnant since 2017 (see *Figure 1: Traditional antibacterial candidates targeting priority pathogens (2017-21)*). There are 13 against *Mycobacterium tuberculosis* and five targeting *Clostridioides difficile*.

In phase 3 of clinical development, there are only nine traditional small molecules targeting priority pathogens, one for *Clostridioides difficile* and none for *Mycobacterium tuberculosis*. Only two target critical priority pathogens.<sup>5</sup> Clearly, near future scenario is bleak.

Among the 32 non-traditional candidates, only five are in phase three, of which three are against priority pathogens. For *Mycobacterium tuberculosis*, there is only one candidate, which is in phase one.<sup>6</sup>

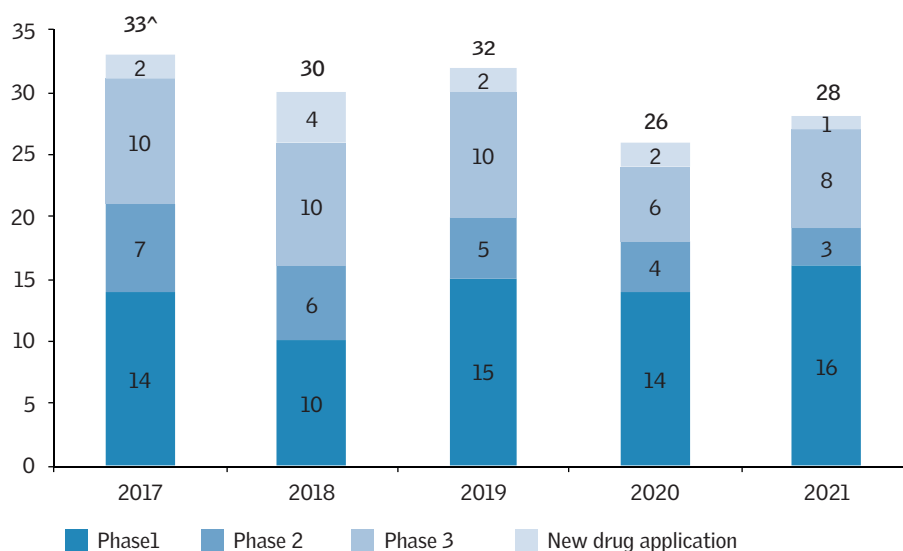
In comparison, as per WHO’s Global Health Observatory on Health Research and Development, currently, there are more than 10,000 medicines in active clinical development for cancer, more than 1800 for neuropsychiatric conditions and about 1500 for endocrine, blood and immune disorders.<sup>7</sup>

**Table 1: Antibacterial clinical pipeline<sup>8</sup>**

	Phase 1	Phase 2	Phase 3	Pre-registration	Total
<b>Traditional candidates</b>	<b>22</b>	<b>14</b>	<b>9</b>	<b>1</b>	<b>46</b>
Priority pathogens	16	3	8	1	28
<i>Mycobacterium tuberculosis</i>	6	7	-	-	13
<i>Clostridioides difficile</i>	-	4	1	-	5
<b>Non-traditional candidates</b>	<b>12</b>	<b>15</b>	<b>5</b>	<b>2</b>	<b>34</b>
Priority pathogens	7	10	3	1	21
<i>Mycobacterium tuberculosis</i>	1	-	-	-	1
<i>Clostridioides difficile</i>	4	5	2	1	12
<b>Total</b>	<b>34</b>	<b>29</b>	<b>14</b>	<b>3</b>	<b>80</b>

Note: this is updated till late 2021; - denotes no candidates

**Figure 1: Traditional antibacterial candidates targeting priority pathogens (2017-21)**



<sup>^</sup>Total number of antibacterial candidates in a particular year. Source: WHO

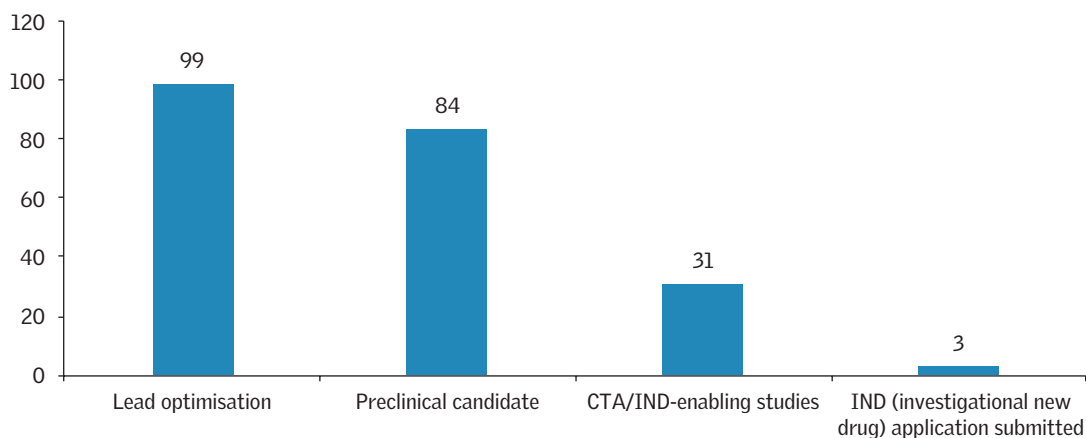
## Preclinical pipeline

Out of the 217 candidates, only 34 (about 15 per cent) are in late-stage preclinical development which are close to getting ready to enter into the clinical trials.<sup>9</sup> For three out of these, investigational new drug application has been submitted. Others are part of clinical trial application/investigational new drug enabling studies. This is too less a pool for clinical trials, considering the high failure risk at this stage. Out of the remaining 183 preclinical products, 99 are in lead optimization and 84 are preclinical candidates (see *Figure 2: Antibacterial preclinical pipeline*).

## 2.2 Research focus of the pharmaceutical industry

‘Penicillin’, the first antibiotic was a chance discovery in 1928 by Alexander Fleming, a Scottish bacteriologist in London. It was only in 1941, with the help of pharmaceutical companies in the US, penicillin was mass produced to save countless lives of soldiers in World War II. Hence known as a ‘Miracle Drug’. Then followed the ‘Golden era’ of 1950s and 60s, when many pharmaceutical companies became keen and developed antibiotics of several novel types/classes. But since 1980s, the antibiotic revolution had begun to fade. Antibiotics developed since then are not novel enough. They have less power to kill bacteria, which now have become smarter. Major pharmaceutical companies have left this space of antibiotic development.

**Figure 2: Antibacterial preclinical pipeline**



Note: Updated until September 2021; source: WHO

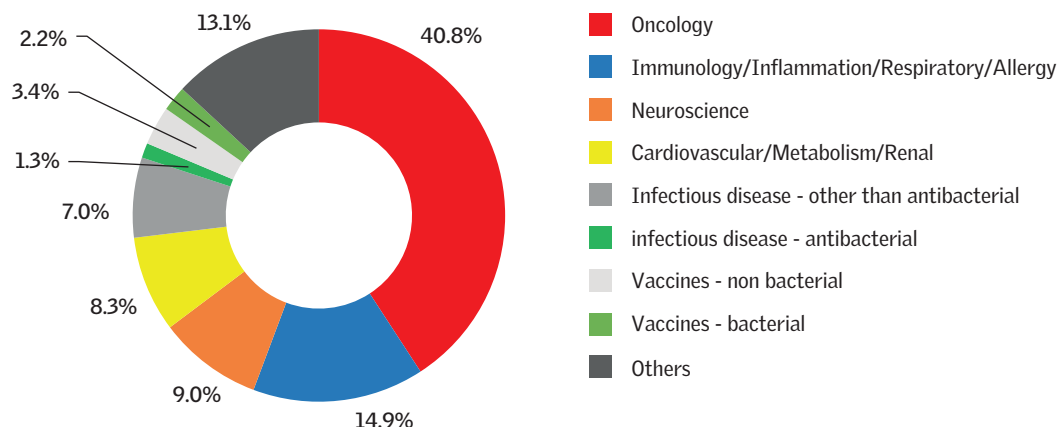
To understand the research focus of big pharmaceutical companies, this report presents analysis of the clinical development pipeline of 15 high-earning global pharmaceutical and biopharma companies based on information available on their websites. Collectively, their 2022 revenue after conversion from different currencies (as per conversion rates on December 31, 2022) was about USD 711 billion and a considerable 17.5 per cent (USD 124 billion) was invested in research and development.

These companies are Astra Zeneca, F Hoffman-La Roche, Bristol Myers Squibb, Pfizer, Novartis, GlaxoSmithKline (GSK), Johnson & Johnson, AbbVie, Gilead Sciences, Sanofi, Eli Lilly and Company, Merck & Co, Amgen, Biogen and Viatris.

### **Collective pipeline of big pharmaceutical companies**

As on June 2023, out of the 1,007 molecules in the clinical pipeline of these companies, only 13 (1.3 per cent) antibacterial candidates were found to be developed by four companies. GSK was developing eight of them. F Hoffmann-La Roche and Pfizer were developing two each and AbbVie was developing one.

In contrast, 411 candidates (41 per cent) were being developed for cancers/ oncology by 13 companies. Almost all companies were involved in developing 150 candidates (15 per cent) in areas of immunology, inflammation, respiratory or allergy. A total of 91 candidates (about 9 per cent) were being developed in

**Figure 3: Pipeline summary of select 15 high-earning pharmaceutical companies**

Source: CSE analysis based on pipeline information of company websites. Note: others include rare blood disorders, rare disease, hematology, ophthalmology, pain, pulmonary hypertension, aesthetics.

areas of neurosciences. A total of 84 candidates (8.3 per cent) candidates were being developed in areas of cardiology, metabolism or renal (see *Figure 3: Pipeline summary of select 15 high-earning pharmaceutical companies*)

Few companies were developing vaccines against bacterial infections (about 2 per cent of total products). These were Sanofi, Merck, Pfizer, GSK and Johnson & Johnson. Unlike antibiotics which are given to those which are sick, vaccines as a preventive measure are administered to large number of people, thereby acting as a promising revenue stream unlikely to be affected by market failure.<sup>10</sup>

### Individual pipeline of big pharmaceutical companies

A closer look at the clinical pipeline of the individual companies shows that almost all focus on areas other than antibacterial candidates. Key focus remains oncology for most companies (see *Figure 4: Products in clinical pipeline of companies*)

**Astra Zeneca** was found to be developing about 56 per cent (95) of the 170 molecules in area of oncology. There are no antibacterial candidates in its pipeline. It's 2022 R&D expenditure was 21.8 per cent (USD 9.7 billion) of revenue.

**F. Hoffmann-La Roche** was developing about 49 per cent (51) of the 104 molecules in area of oncology/hematology. It is developing two antibacterial candidates. It's 2022 R&D expenditure was 22.1 per cent (CHF 14 billion) of revenue.

**Bristol Myers Squibb** was developing about 52 per cent (47) of the 91 molecules in area of solid tumours. There are no antibacterial candidates in its pipeline. It's 2022 R&D expenditure was 20.6 per cent (USD 9.5 billion) of revenue.

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**Pfizer** was developing about 36 per cent (32) of the 89 molecules in area of oncology. It is also developing 14 molecules in the area of inflammation and immunology, 12 molecules for rare diseases and 14 vaccines, out of which six are bacterial. It is developing two antibacterial candidates. It's 2022 R&D expenditure was 11.3 per cent (USD 11.4 billion) of revenue, which was USD 100.3 billion.

**Novartis** was developing about 22 per cent (18) of the 81 molecules in area of solid tumours. It is also developing 15 molecules in areas of immunology and 14 in hematology. There are no antibacterial candidates in its pipeline. It's 2022 R&D expenditure was 19.6 per cent (USD 9.9 billion) of revenue.

**GlaxoSmithKline** was developing about 55 per cent (41) of the 75 molecules for infectious diseases. Out of these, eight are antibacterial candidates and 10 are bacterial vaccines. It is also developing 16 molecules in the area of oncology. It's 2022 R&D expenditure was 18.4 per cent (GBP 5.4 billion) of revenue.

**Johnson & Johnson** was developing about 38 per cent (28) of the 74 molecules in the area of oncology. It is also developing 12 molecules in the area of immunology and 14 molecules in the area of infectious disease and vaccines, global public health. It has no antibacterial candidates but one bacterial vaccine. It's 2022 R&D expenditure was 15.4 per cent (USD 14.6 billion) of revenue.

**Abbvie** was developing about 41 per cent (26) of the 63 molecules in the area of oncology. It is also developing 10 molecules in the area of neurosciences and 10 in aesthetics. It has one antibacterial candidate in its pipeline. It's 2022 R&D expenditure was 12.2 per cent (USD 7.1 billion) of revenue.

**Gilead Sciences** was developing about 63 per cent (38) of the 60 molecules in the area of oncology. It is also developing 17 molecules for viral diseases. It has no antibacterial candidates. It's 2022 R&D expenditure was 18.3 per cent (USD 5.0 billion) of revenue.

**Sanofi** was developing about 28 per cent (15) of the 53 molecules in the area of oncology. It is also developing 14 molecules in immunology and inflammation. It has 10 vaccines out of which three are bacterial. It has no antibacterial candidates. It's 2022 R&D expenditure was 15.6 per cent (EUR 6.7 billion) of revenue.

**Eli Lilly** was developing about 40 per cent (20) of the 50 molecules in the area of diabetes and obesity. It is also developing 10 molecules in immunology and nine for cancers. It has no antibacterial candidates. It's 2022 R&D expenditure was 25.3 per cent (USD 7.2 billion) of revenue.

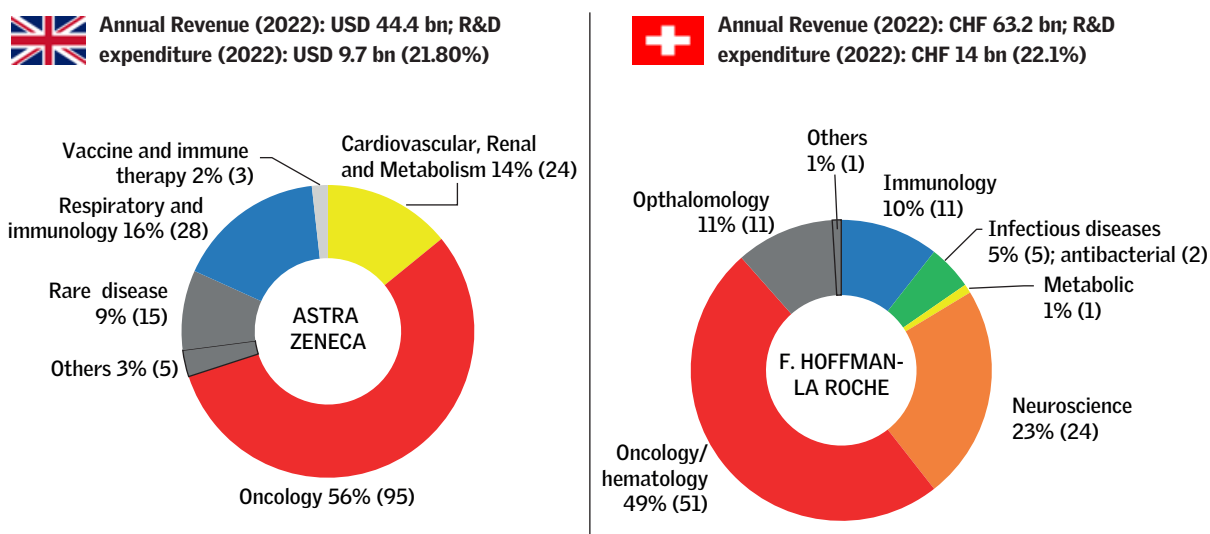
**Merck & Co** was developing about 56 per cent (22) of the 39 molecules in the area of oncology. It has three vaccines out of which two are bacterial. It has no antibacterial candidates. It's 2022 R&D expenditure was 22.8 per cent (USD 13.5 billion) of revenue.

**Amgen** was developing about 50 per cent (18) of the 36 molecules in the area of oncology/hematology. It has no antibacterial candidates. It's 2022 R&D expenditure was 16.7 per cent (USD 4.4 billion) of revenue.

**Biogen** was developing most of its 22 molecules in multiple areas related to neurosciences. It has no antibacterial candidates. It's 2022 R&D expenditure was 21.7 per cent (USD 2.2 billion) of revenue.


**Viatrix**, with an R&D expenditure of about 4 per cent (USD 0.66 billion) of its revenue, its focus areas are cardiovascular, neurology, pain/osteoarthritis, urology, and psychiatry.

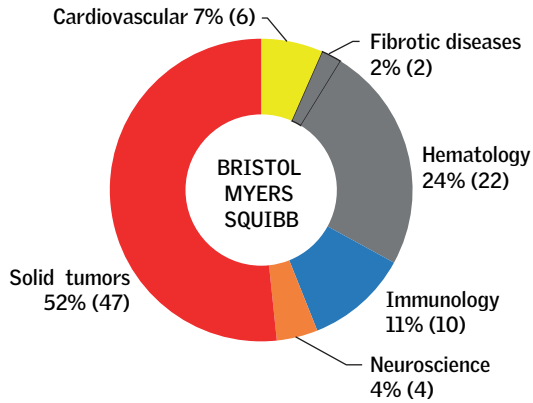
**Figure 4: Products in clinical pipeline of companies**




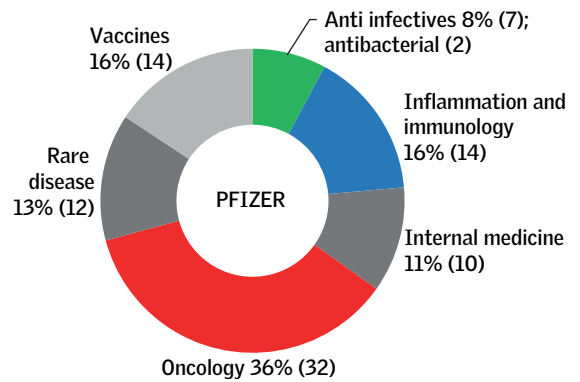
Note: Information on clinical pipeline is updated till June 2, 2023. Red colour in pie denotes oncology/cancer/solid tumours/oncology-hematology; blue denotes immunology/inflammation/respiration/allergy; yellow denotes cardiovascular/renal/nephrology/metabolism/diabetes and obesity/pulmonary hypertension; orange denotes neurology/neurosciences/neurological related conditions; green is used only for companies developing antibacterial candidates as part of respective category such as infectious diseases; light grey are vaccines; dark grey is all others which do not fall under the above categories. In the case of Johnson & Johnson, category infectious diseases and vaccines, global public health is taken as light grey. Percentage values in pies have been rounded off to zero decimal place.


Source: Company websites

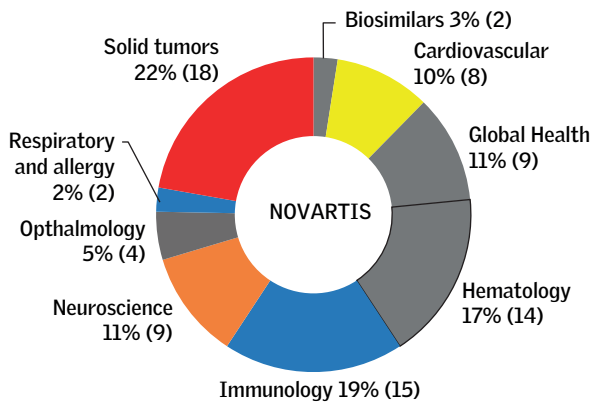
 Annual Revenue (2022): USD 46.1 bn; R&D expenditure (2022): USD 9.5 bn (20.60%)




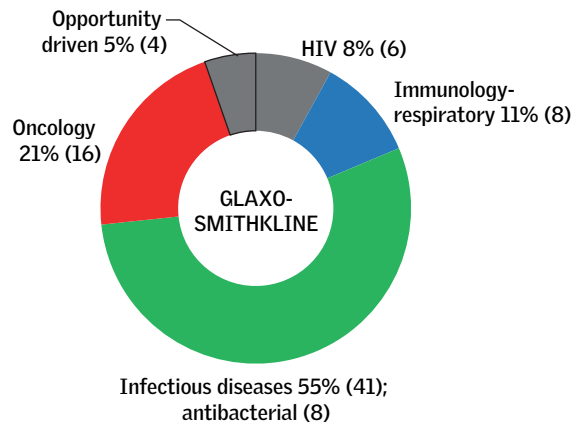
 Annual Revenue (2022): USD 100.3 bn; R&D expenditure (2022): USD 11.4 bn (11.3%)




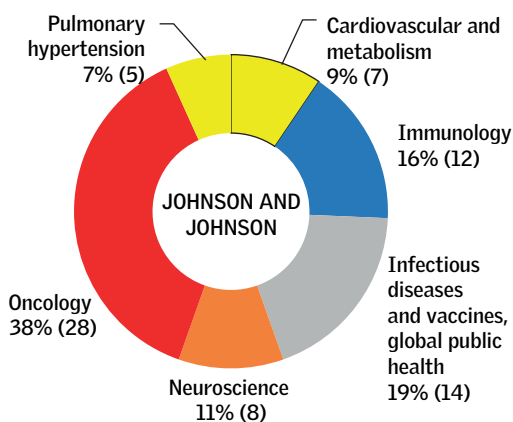
 Annual Revenue (2022): USD 50.5 bn; R&D expenditure (2022): USD 9.9 bn (19.60%)




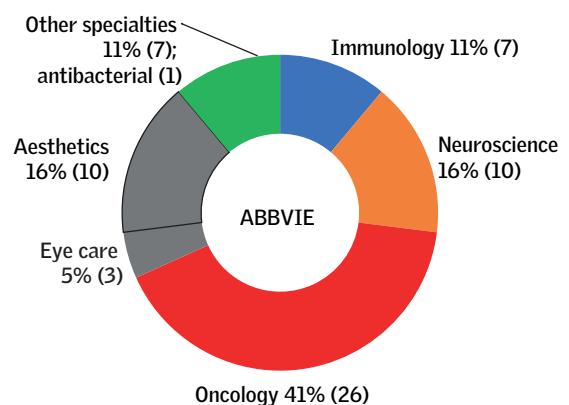
 Annual Revenue (2022): GBP 29.3 bn; R&D expenditure (2022): GBP 5.4 bn (18.40%)




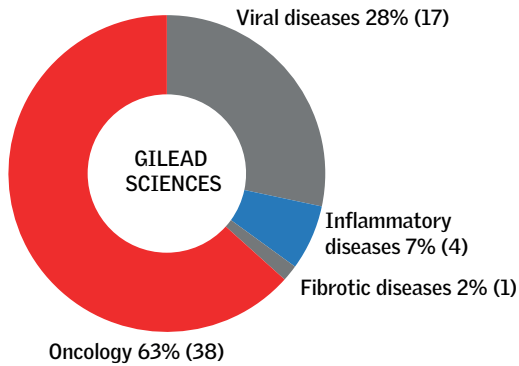
 Annual Revenue (2022): USD 94.9 bn; R&D expenditure (2022): USD 14.6 bn (15.38%)




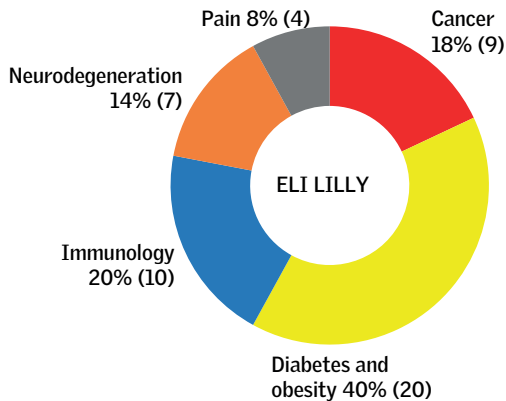
 Annual Revenue (2022): USD 58 bn; R&D expenditure (2022): USD 7.1 bn (12.20%)




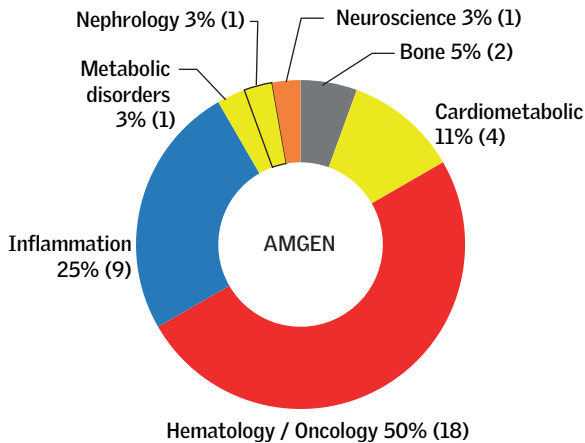
 Annual Revenue (2022): USD 27.3 bn; R&D expenditure (2022): USD 5 bn (18.30%)




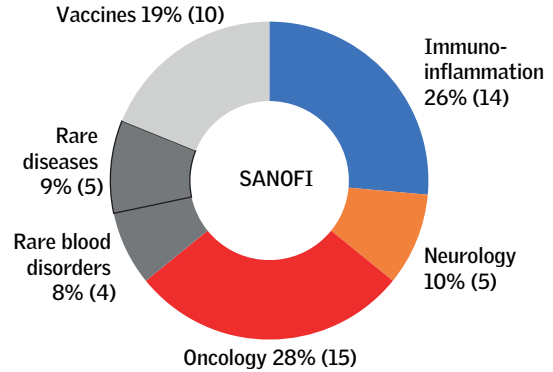
 Annual Revenue (2022): USD 28.5 bn; R&D expenditure (2022): USD 7.2 bn (25.26%)




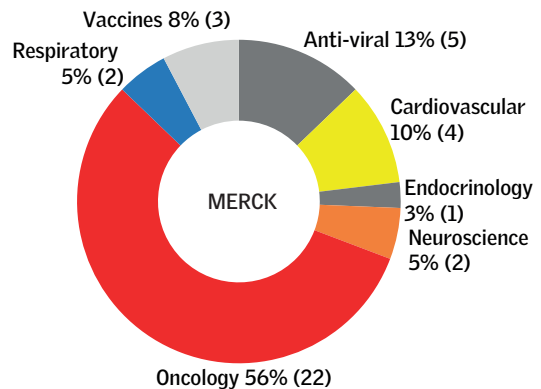
 Annual Revenue (2022): USD 26.3 bn; R&D expenditure (2022): USD 4.4 bn (16.70%)




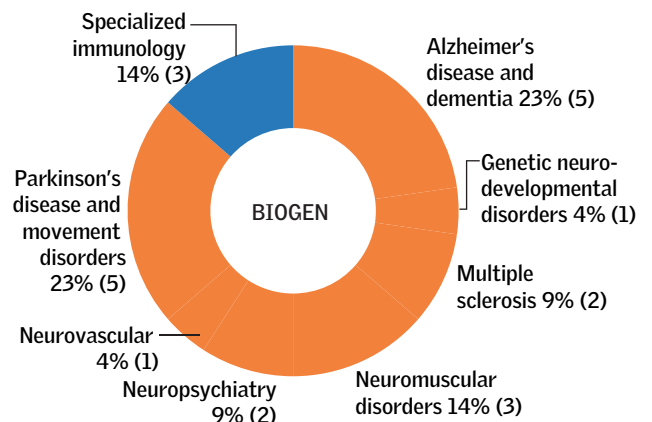
 Annual Revenue (2022) : EUR 42.9 bn; R&D expenditure (2022): EUR 6.7 bn (15.61%)



 Annual Revenue (2022): USD 59.2 bn; R&D expenditure (2022): USD 13.5 bn (22.80%)



 Annual Revenue (2022): USD 10.1 bn; R&D expenditure (2022): USD 2.2 bn (21.78%)





## Shifting focus: The big exodus from antibiotic R&D and M&As in other areas

The research focus that has shifted away from antibiotics and moved towards other areas is marked by companies' exiting the antibiotic development space and entering into mergers and acquisitions (M&As) to strengthen their pipelines in other disease areas. A look at this timeline over the last two decades shows many of these companies were either pioneers or very active in antibiotic R&D. But some have exited many years ago and others more recently (see *Table 2: Timeline of exit from antibiotic R&D and key M&As in other areas*)

### Big exodus: Market failure or blockbuster drugs?

'Market Failure' for antibiotics is often cited as a reason by the pharmaceutical industry for this big exodus. This is one reason, as revenues from selling an

**Table 2: Timeline of exit from antibiotic R&D and key M&As in other areas**

Year	Exit or key M&As
Early 2000s	<ul style="list-style-type: none"> <li>• Bristol Meyers Squibb is reported to have stopped antibiotic development<sup>11</sup></li> <li>• Eli Lilly reported to have stopped antibiotic development<sup>12</sup></li> </ul>
2011	<ul style="list-style-type: none"> <li>• Sanofi acquired Genzyme for USD 20 bn, focussed on rare disease, renal endocrinology, hematology oncology<sup>13</sup></li> </ul>
2013	<ul style="list-style-type: none"> <li>• Roche struck a deal for the license of an experimental antibiotic from Switzerland's Polyphor for USD 560 mn<sup>14</sup></li> </ul>
2015	<ul style="list-style-type: none"> <li>• AbbVie acquired Pharmacyclics for USD 21 bn to strengthen its commercial presence in oncology<sup>15</sup></li> <li>• Roche ended its collaborations with Polyphor<sup>16</sup></li> </ul>
2016	<ul style="list-style-type: none"> <li>• Novartis acquired Reprixys Pharmaceuticals Corporation for USD 332 mn specialising in hematologic and inflammatory disorders<sup>17</sup></li> <li>• AstraZeneca sold the development rights of its late-stage small molecule antibiotics business to Pfizer<sup>18</sup></li> </ul>
2017	<ul style="list-style-type: none"> <li>• Novartis acquired Ziarco Group Limited for USD 420 mn focused on the development of novel treatments in dermatology<sup>19</sup></li> <li>• Novartis acquired Encore Vision for USD 456 mn focused on the development of a novel treatment in presbyopia<sup>20</sup></li> <li>• Johnson &amp; Johnson (J&amp;J) acquired Actelion, for USD 30 bn known for innovative products for pulmonary arterial hypertension<sup>21</sup></li> <li>• Gilead Sciences acquired Kite Pharma for USD 11.9 bn, which is an industry leader in the field of cell therapy<sup>22</sup></li> </ul>
2018	<ul style="list-style-type: none"> <li>• Novartis shut down its antibacterial and antiviral research<sup>23</sup></li> <li>• Sanofi outsourced its anti-infective R&amp;D to Evotec<sup>24</sup></li> <li>• Sanofi acquired Ablynx for EUR 3.9 bn and Bioverativ for USD 11.6 bn, to strengthen its leadership in rare diseases<sup>25,26</sup></li> <li>• Johnson &amp; Johnson scraps development of cadazolid, a phase 3 antibiotic for treating <i>C difficile</i><sup>27</sup></li> </ul>
2019	<ul style="list-style-type: none"> <li>• Bristol Meyers Squibb acquired Celgene for USD 74 bn a company focussing primarily on oncology and also immunology, inflammation and cardiovascular disease<sup>28</sup></li> <li>• Eli Lilly acquired LoxoOncology for USD 6.92 bn<sup>29</sup></li> </ul>
2020	<ul style="list-style-type: none"> <li>• Last antibiotic in Astra Zeneca's pipeline seen<sup>30</sup></li> </ul>
2021	<ul style="list-style-type: none"> <li>• Novartis acquired GSK's cephalosporin antibiotics business of three established brands (Zinnat, Zinacef and Fortum) for USD 500 mn.<sup>31</sup> This was for generic manufacturing.</li> </ul>
2023	<ul style="list-style-type: none"> <li>• Sanofi acquired Provention Bio, Inc. for USD 2.9 bn to bolster its immune-mediated diseases pipeline<sup>32</sup></li> <li>• Novartis acquired Chinook Therapeutics for USD 3.2 bn to bolster innovative medicines strategy and renal pipeline<sup>33</sup></li> </ul>

Note: Text in red denotes an exit of company from antibiotic development space or a similar event/activity.

antibiotic are often low and unpredictable due to reasons like short duration of most antibacterial treatments compared to treatment for chronic conditions and uncertain nature of the need. Due to stewardship concerns, antibiotic developers also cannot push to sell their drugs at least in the first few years and by the time a new antibiotic becomes the first or second line of treatment in a country, there is a risk of losing revenues to the low-cost generic options.

However, this big exodus is not just because of market failure but is also due to high revenues and profitability in other disease areas. A look at the top 10 blockbuster drugs (drugs that generate annual sales of at least USD 1 billion) sold in 2021 shows how profitable drugs for cancer, autoimmune diseases and diabetes related complications can be and why pharmaceutical industry is not keen to invest in antibiotic R&D<sup>34,35</sup> (see *Table 3: Top ten drugs by worldwide sales in 2021*).

**Table: 3 Top ten drugs by worldwide sales in 2021**

Drug	Molecule	Companies	2021 sales (billion USD)	Indication(s)
Comirnaty	Vaccine	Pfizer, BioNTech	36.8	COVID-19
Humira	Monoclonal antibody	AbbVie	20.7	Rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, plaque psoriasis and more
Spikevax	Vaccine	Moderna	17.7	COVID-19
Keytruda	Humanized antibody	Merck & Co.	17.2	Melanoma, non-small cell lung cancer, head and neck cancer, Hodgkin lymphoma, urothelial carcinoma, gastric cancer
Eliquis	Anticoagulant	Bristol Myers Squibb, Pfizer	16.73	Nonvalvular atrial fibrillation, deep vein thrombosis and pulmonary embolism
Revlimid	Small molecule drug	Bristol Myers Squibb	12.8	Myelodysplastic syndrome, multiple myeloma, lymphoma, follicular lymphoma
Imbruvica	Small molecule drug	AbbVie, Johnson & Johnson	9.8	Mantle cell lymphoma, chronic lymphocytic leukemia, Waldenstrom's macroglobulinemia, marginal zone lymphoma, chronic graft-versus-host disease
Stelara	Monoclonal antibody	Johnson & Johnson	9.1	Plaque psoriasis, psoriatic arthritis, Crohn's disease, ulcerative colitis
Eylea	Glycoprotein	Regeneron Pharmaceuticals, Bayer	8.9	Wet age-related macular degeneration, diabetic macular edema, diabetic retinopathy, macular edema
Biktarvy	Small molecule drug	Gilead Sciences	8.6	HIV (Human immunodeficiency viruses)

Source: Fierce Pharma

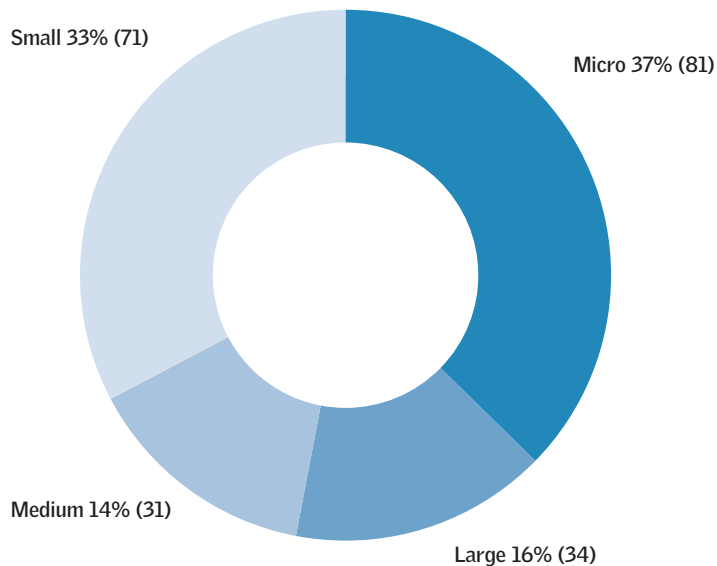
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## 2.3 Micro, small and medium-scale companies developing antibacterial products

While the big pharmaceutical companies are moving out, the micro, small and medium-scale companies are becoming active in antibiotic R&D. As per WHO database, out of 217 antibacterial preclinical candidates, developer institutions of 183 candidates (84 per cent) are micro ( $\leq 10$  employees), small (11-50 employees), or of medium-scale (51-500 employees). Importantly, 70 per cent candidates are being developed by micro and small-scale developers (see *Figure 5: Preclinical candidates by micro, small and medium-scale developers*).

The scenario is similar for the clinical pipeline. A look at developers of 77 candidates shows that there are several small and medium-scale companies involved in both traditional and non-traditional products across all three clinical phases. Their active presence is not limited to priority pathogens but also extends to *Mycobacterium tuberculosis* and *Clostridioides difficile* (see *Table 4: Developers of antibacterial products in clinical pipeline*).

**Figure 5: Preclinical candidates by micro, small and medium-scale developers**



Source: WHO

**Table 4: Developers of antibacterial products in clinical pipeline**

	Developers - Phase 1	Developers - Phase 2	Developers - Phase 3
<b>Traditional products</b>			
Priority pathogens	<ul style="list-style-type: none"> <li>• Bugworks Research</li> <li>• Juvabis</li> <li>• Entasis Therapeutics</li> <li>• Pfizer/ Arixa Pharmaceutical</li> <li>• KBP BioSciences Pharmaceutical Technical Co.Ltd</li> <li>• MicuRX</li> <li>• Meiji Seika</li> <li>• Qpex Biopharma</li> <li>• Roche</li> <li>• Spero Therapeutics</li> <li>• TAXIS pharmaceutical</li> <li>• Venatorx</li> <li>• Sinovent</li> <li>• Wockhardt Ltd.</li> </ul>	<ul style="list-style-type: none"> <li>• Debiopharm International SA</li> <li>• Tendor Therapeutics</li> </ul>	<ul style="list-style-type: none"> <li>• Sichuan Pharmaceutical Holding Group Ltd.</li> <li>• Glaxo SmithKline (GSK)</li> <li>• Entasis Therapeutics Inc.</li> <li>• Allecra Therapeutics</li> <li>• Wockhardt, Iterm Therapeutics</li> <li>• VenatoRx Pharmaceuticals Inc./ GARDP</li> <li>• Entasis Therapeutics Inc./ GARDP</li> </ul>
<i>Mycobacterium tuberculosis</i>	<ul style="list-style-type: none"> <li>• GSK-TB drug accelerator/Bill &amp; Melinda Gates Foundation</li> <li>• Innovative Medicines for Tuberculosis Foundation</li> <li>• TB Alliance</li> <li>• Institute of Mediria Medica</li> <li>• Institute of Mediria Medica/TB Alliance</li> </ul>	<ul style="list-style-type: none"> <li>• GSK</li> <li>• University of Munich</li> <li>• LegoChem Biosciences/Haihe Biopharm</li> <li>• Otsuka Pharmaceutical Co</li> <li>• TB alliance/ Sequella</li> <li>• TB alliance/Bill and Melinda Gates Foundation</li> <li>• Qurient Co.</li> </ul>	
<i>Clostridioides difficile</i>		<ul style="list-style-type: none"> <li>• Crestone</li> <li>• Deinove</li> <li>• Acurx Pharmaceutical</li> <li>• MGB Biopharma</li> </ul>	<ul style="list-style-type: none"> <li>• Summit Therapeutics Inc.</li> </ul>
<b>Non-traditional</b>			
Priority pathogens	<ul style="list-style-type: none"> <li>• Mabwell Biosciences</li> <li>• Aptorum Group</li> <li>• Eagle Pharmaceuticals</li> <li>• GSK</li> <li>• Locus Biosciences</li> <li>• Servatus</li> <li>• Trellis Bioscience</li> </ul>	<ul style="list-style-type: none"> <li>• Armata Pharmaceuticals</li> <li>• Aridis Astra Zeneca/ MedImmune</li> <li>• BiomX</li> <li>• Gamaleya Research Institute of Epidemiology and Microbiology</li> <li>• Lumen Bioscience</li> <li>• Riovant Sciences/ inTron Biotechnology</li> <li>• AlgiPharma AS</li> <li>• Adaptive Phage Therapeutics</li> <li>• BioAegis Therapeutics</li> <li>• Felix Biotechnology/Yale University</li> </ul>	<ul style="list-style-type: none"> <li>• Tashkent Pediatric Medical Institute</li> <li>• Aridis Pharmaceutical Inc.</li> <li>• Contrafect</li> </ul>
<i>Mycobacterium tuberculosis</i>	<ul style="list-style-type: none"> <li>• Bioversys/GSK</li> </ul>	-	-
<i>Clostridioides difficile</i>	<ul style="list-style-type: none"> <li>• Artugen Therapeutics</li> <li>• Lumen Bioscience</li> <li>• Nubiyota/Takeda</li> <li>• Ferring (Ribiotx)</li> </ul>	<ul style="list-style-type: none"> <li>• Finch Therapeutics</li> <li>• Da Volterra</li> <li>• ImmuniMed</li> <li>• Synthetic Biologics</li> <li>• Vedanta Biosciences</li> </ul>	<ul style="list-style-type: none"> <li>• Ferring Pharmaceuticals</li> <li>• Seres Therapeutics</li> </ul>

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## Challenges

The micro, small and medium-scale companies however struggle to develop antibacterial products or make money from ones they have developed. In the recent past, there are examples of some filing for bankruptcy and others facing diminished values or exits. For example,

- The US based Melinta Therapeutics, founded in 2000, focussed on developing novel broad-spectrum antibiotics for treatment of antibiotic-resistant infections. In 2011, it collaborated with Sanofi and received an upfront amount of USD 10 million. However, due to financial troubles, it filed for bankruptcy in 2019. It later recovered to and continues to develop antibiotics.<sup>36</sup>
- Achaogen, another US-based antibiotic drug developer filed for bankruptcy in 2019. This is after its antibiotic Plazomicin (Zemdri) was approved by the FDA in 2018 for the treatment of complicated urinary tract infections (UTIs) caused by multidrug-resistant *Enterobacteriaceae* but was not approved for bloodstream infections. The company had to lay off staff and seek a buyer for its business.<sup>37</sup>
- Aradigm also announced bankruptcy in 2019 while pursuing regulatory approval of its inhaled antibiotic.<sup>38</sup>
- Ireland based developer Nabriva Therapeutics announced closure in 2023.<sup>39</sup>
- The valuation of Tetrphase Pharmaceuticals, another US based antibiotic developer, which in 2015 had an evaluation of USD 1.8 billion was acquired for a mere USD 43 million by US' La Jolla Pharma, a biotech focusing on infectious disease.<sup>40</sup>
- In 2022, Spero Therapeutics, a biotech focussing on infectious disease, halted its commercialisation activities of its late-stage drug for urinary tract infections and laid off 75 per cent of its staff.<sup>41</sup>

A 2020 *Nature* article notes that with the collapse of companies like Achaogen, Aradigm, Melinta Therapeutics and Tetrphase Pharmaceuticals, availability of five of the 15 antibiotics approved by the US FDA since 2010 was sharply reduced.<sup>42</sup>

There are some examples of addressing these challenges. Bugworks Research India Pvt. Ltd. which started out with a sole focus on developing antibiotics have started developing drugs for oncology in parallel.<sup>43</sup> GangaGen Biotechnologies Pvt. Ltd.,

which develops non-traditional molecules for human use, have also shifted their focus on developing bacteriophages that can be used as probiotics in feed additives in poultry.<sup>44</sup>

## 2.4 Ongoing initiatives to support antibiotic R&D

Currently, there is a growing consensus on the need to support antibiotic R&D through investments among others. Broadly two types of approaches exist - Push and Pull.

### Push incentives

Push incentives involve funding the early stage of antibiotic development, from discovery to clinical trials. These provide direct support through grants, loans and tax incentives, and involve the role of non-profits, industry and government largely aimed to support small- and medium-scale companies. These incentives can help bring down development costs and the funder shares the risk of failure.

Ongoing push strategies differ w.r.t. areas of focus and stages of funding. Some focus on discovery and early-stage funding such as Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), others support late-stage development like the Global Antibiotic Research and Development Partnership (GARDP) and AMR Action Fund. Those which support end-to-end product development include Biomedical Advanced Research and Development Authority (BARDA). Initiatives like the Joint Programming Initiative on AMR (JPIAMR) support basic exploratory research. Support includes those for antibacterial products, vaccines and diagnostics (see *Table 5: Examples of key push incentive projects*).

Push funders face challenges as well. For example, in the case of CARB-X, because of the high level of innovation of many programs that it supports, there is little to no precedence with many preclinical models, particularly animal models of infection, as well as clinical development and regulatory strategies. There is limited expertise in drug discovery and development within innovators who apply for funding. CARB-X helps developers address challenges through support from their internal R&D team, network of global subject matter experts, as well as by providing in-kind services.

Similarly in case of GARDP, new antibiotic development becomes more challenging when the clinical development is to be conducted in diverse geographies and populations. Another challenge is ensuring access to new as well as existing antibiotics. New antibiotic development for newborns and children

**Table 5: Examples of key push incentive projects**

Funder	Launch year and type	Focus area	Stage of development supported	Details on projects and funding
Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) <sup>45</sup>	2016; Public-private partnership	Development of new antibiotics, vaccines, and rapid diagnostics to fight drug-resistant bacteria (WHO and Centers for Disease Control and Prevention (CDC) bacterial threats lists)	Early-stage development (discovery, preclinical and phase 1)	<ul style="list-style-type: none"> <li>• Invested &gt; USD 400 mn since 2017</li> <li>• Total 93 projects: 29 currently active</li> <li>• 14/29 active projects on antibacterials (traditional and non-traditional)<sup>46</sup></li> </ul>
Global Antibiotic Research and Development Partnership (GARDP) <sup>47</sup>	2016 as non-profit; independent PPP since 2019	Children's antibiotics; serious bacterial infections in adults; sexually transmitted infections (all drug development projects target priority pathogens)	Late-stage development	<ul style="list-style-type: none"> <li>• Raised EUR 178 million from inception to end of 2022;</li> <li>• Total expenditure since inception is EUR 100.4 million; Expenditure in 2022 was EUR 24.3 million with 77 per cent on R&amp;D and access</li> <li>• Major initiative "5BY25" which aims to deliver 5 new treatments by 2025</li> <li>• SECURE initiative to accelerate access to essential antibiotics, while ensuring their sustainable use</li> </ul>
AMR Action Fund <sup>48</sup>	2020, Public-private partnership	To bring 2-4 new antibiotics to market by 2030 against WHO and CDC bacterial threats lists	Largely late-stage funding	<ul style="list-style-type: none"> <li>• USD 1 billion fund</li> <li>• Currently investing in five companies<sup>49</sup></li> </ul>
Biomedical Advanced Research and Development Authority (BARDA) <sup>50</sup>	2011, Govt. of USA	Innovative technologies against drug-resistant infections determined by the CDC and WHO	End to end product development from early research to licensure and commercialization	<ul style="list-style-type: none"> <li>• USD 1.8 billion since launch.</li> <li>• 22 products in current AMR related portfolio; four of these are approved<sup>51</sup></li> </ul>
Global AMR Innovation Fund (GAMRIF) <sup>52</sup>	2011, Government of UK	One Health focus	Early-stage R&D in underfunded areas of AMR, tailored for low- and middle-income countries	Portfolio includes different work packages through which it funds bilateral partnerships (e.g., UK-China), global research initiatives ( e.g., CARB-X), product development partnerships (e.g., GARDP) <sup>53</sup>

is also not easy as it cannot be based on trials in adults. GARDP is addressing these challenges through collaborations, identification of new treatments for children and enabling better access in low and middle-income countries through its SECURE initiative.

While push incentives have been operational for several years now, it has also become clear that they alone would not be enough to stimulate the antibiotic innovation ecosystem. This is largely because the small and medium players who were supported in the early stages of product development through push incentives, struggled to take the product forward into the later stages and the market. Pull incentives therefore came into play.

### **Pull incentives**

Pull incentives, provide a known return on investment to those who have developed a novel antibiotic, and help bring it into the market. These are applicable when an antibiotic has passed through clinical trials. These do not address the risk of failure in the early-stage development of products and are largely driven by governments. Countries which have initiated one or the other pull incentives include the United Kingdom (UK), Japan, Sweden, France, Germany and the United States of America. They are at different levels and the overall impact of pull incentives on stimulating antibiotic R&D remains to be seen.

### **Examples of pull incentives**

**‘Subscription model’ of the UK<sup>54</sup>:** In June 2020, the UK launched a fully delinked subscription style payment model for antibiotics. It involved payment of a fixed price per drug per year to the company, like a subscription, in return for an antibiotic for the UK’s health system. It is also called the ‘Netflix’ model. It involved an assessment of the full value of new antibacterial to the entire health and social care system as part of the Health Technology Assessment that was based on parameters such as the spectrum, transmission, enablement, diversity, and insurance value (acronym STEDI). The project announced in 2019, selected two antibacterials for testing this model cefiderocol (manufactured by Shionogi; new to market) and ceftazidime-avibactam (manufactured by Pfizer; existing product). Each manufacturer was offered, and signed, a contract for an initial 3-year period, with the option of extending for up to 10 years. Ten million pounds per annum per antibacterial was considered a fair share for England based on published estimates of a reasonable ‘pull incentive’ given the development costs and UK’s 2-3 per cent share of the global market.



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While the impact remains to be seen but the model is seen as promising by many. However, some experts argue that instead of rewarding innovation, this model seems to support the antibiotic portfolios of two large pharmaceutical companies. There is a future risk of companies lobbying together to hike the amount quoted in the subscription or push for older formulations being used. The huge sum of public financing involved will also call for greater transparency in the long-term.<sup>55</sup>

**‘Reimbursement model’ of Sweden<sup>56</sup>:** The Public Health Agency of Sweden (PHAS) has piloted a partially de-linked reimbursement model (July 2020-Dec 2022) for procurement of antibiotics used in hospitals. In this, contracts have been signed with four pharmaceutical companies for supply of five antibiotic products. A compensation of at least four million Swedish Krona (SEK) per product per year was guaranteed to these companies in return for keeping a defined security stock in Sweden and guaranteeing delivery to hospitals within 24 hours of ordering. If the revenue for a certain antibiotic was lower than the guaranteed amount, the state paid the difference to the companies. In case of higher sales, the companies received the committed amount in return for continuing to comply with the contractual requirements.

Evaluation of the pilot showed that the model worked well by ensuring antibiotic availability when needed, and that too for use in a limited group of critically ill patients. There was reduction in sales of certain old antibiotics and large cancellation of unsold products. On May 2023, PHAS received a new government commission to continue strengthening the availability of certain antibiotics through this model.

**PASTEUR Act of the US:** The US is considering ‘The Pioneering Antimicrobial Subscriptions to End Upsurging Resistance (PASTEUR), Act’. Originally introduced in 2020, this is a subscription style model of payment which, if passed, would involve upfront payment to companies for access to promising, medically important new antibiotic candidates. The subscription contract ranges from USD 750 million to three billion for upto 10 years.

There are concerns around whether antibiotics brought to the market through this would help improve overall public health outcomes. In November 2022, a group of academics and advocacy organizations sent a letter to Congress arguing why the PASTEUR Act has “fatal flaws” that could aggravate the antimicrobial resistance (AMR) problem.<sup>57,58</sup> While it would award billions to pharmaceutical companies as a financial incentive for newly developed antimicrobials, it does not address the overarching problem that recent antimicrobials approved by the FDA have not

## TYPES OF PULL INCENTIVES

Market entry rewards (MERs) are monetary rewards provided when the antimicrobial enters the market. When reward is not linked to the number of units sold, it is a fully delinked reward. When a part of this reward still comes from the number of units sold, it is a partially delinked model.

Tradeable exclusivity vouchers if offered, can be used by companies to extend the exclusivity period of another more profitable drug or to accelerate regulatory review and approval of a more profitable drug, enabling quicker market entry. Both types of vouchers can be sold to other firms.

Market exclusivity extension gives protection to a branded drug from generic drugs for an extended period.

been proven to work against resistant infections or are not more beneficial than other available and less expensive alternative treatments.

Other examples of pull incentives in the US includes the DISARM (Developing an Innovative Strategy for Antimicrobial-Resistant Microorganisms) Act of 2021, which is based on a reimbursement model. It removes the current incentive for hospitals to choose lower-cost antibiotics under the bundled payment system. It increases payment for certain novel AMR products by carving out payment from existing Medicare Severity-Diagnosis Related Group (MS-DRG) and reimbursing based on the average sales price.<sup>59</sup> The Generating Antibiotic Incentives Now (GAIN) Act of 2012 is based on market exclusivity. Antibiotics that are designated a 'Qualified Infectious Disease Product' are eligible to receive an additional five years of market exclusivity.<sup>60</sup>

**Transferable data exclusivity vouchers of the EU:** The proposed revision of the EU pharmaceutical legislation mentions about providing '**transferable data exclusivity vouchers**' to developers of novel antimicrobials. The voucher will offer an additional year of data protection from competition for the medicine that the voucher applies to. The vouchers will be provided in limited numbers over a limited period (10 vouchers in 15 years).<sup>61</sup> However this transferable exclusivity voucher has been critiqued for multiple reasons some of which are mentioned here. Firstly, it is believed to be an expensive incentive, also hampering access to other blockbuster drugs that the voucher would be applied to, when prices are kept high for those drugs for additional years. Secondly, it is unlikely to be effective, even if implemented because there are hardly any drug candidates in late stage of development deserving of such a big innovation reward.<sup>62</sup>

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## **Commitments at the G7 level**

In 2021, the **G7 Finance Ministers** committed to take necessary steps to address antibiotic market failure and creating the right economic conditions to strengthen antibiotic R&D and bring new drugs to market which meet unmet public health needs.<sup>63</sup> The **G7 Shared Principles for the Valuation of Antimicrobial Therapeutics** in 2021 also outlines a set of guiding principles for more sustainable antimicrobial drug development.<sup>64</sup> Some of these are linked to aspects like access, stewardship and affordability particularly in low- and middle-income countries (LMICs). The G7 Finance Ministers and Central Bank Governors reaffirmed their 2021 commitments in 2022 and 2023 as well.<sup>65,66</sup>

The **G7 Health Ministers' Communiqué** published in May 2022 recognized the need for fostering innovation and accelerating development of new antibiotics, vaccines, alternative therapeutics and diagnostics.<sup>67</sup> It recognizes the need to address the broken market as well as ensure the commercialisation and provision of existing and new antibiotics while also taking care of access and stewardship needs. The Ministers committed to exploring possible market incentive options aligned to the country needs, with focus on supporting pull incentives. In 2023, the G7 Health Ministers similarly recognised the need for sufficient incentives to ensure a sustainable market for new antimicrobials that meet public health needs.<sup>68</sup> They also committed to exploring and implementing push and pull incentives, as well as promoting solutions to address pipeline issues. Similar commitment is also evident in the **2023 G7 Hiroshima Leaders' Communiqué**.<sup>69</sup>

### 3. Challenges and possibilities: Rejuvenating the antibiotic innovation ecosystem

Based on the assessment findings as presented in chapter 2 of this report, **it is clear there is a need for reforms and measures at the global level to stimulate the antibiotic R&D ecosystem for a sustainable and equitable access to effective antibiotics across the world including in low and middle-income countries.**

At a broad level, this would need:

1. **Greater public financing and reforms** on aspects related to market, reimbursements, regulatory approvals, cost of new antibiotics and clinical trials. **Governments will have to play a greater role.** Policymakers need to be aware about the financing rationale and needs.
2. **Governments need to come together for a coordinated response** in terms of prioritizing antibiotics and developers, testing and piloting incentives and removing access barriers. **Action is needed by major economies such as G20 countries**, as individual country efforts will have limited long-term gains.
3. There is a **need to strike the right balance in public-private partnership** for antibiotic development. The notion that governments should take up the entire antibiotic development is not backed by many. On the other hand, public financing should not just be about bring back the big pharma companies.
4. It is also perhaps time to **start discussing if antibiotics or any other aspect of AMR response can be considered as a global public good.** While antibiotics may not fit the strictest economic definition of a ‘global public good’ but it does have attributes of it. There is therefore a need to explore further what ‘global public good’ would actually mean in the context of antibiotics; what are the feasibility, challenges and implications, if antibiotics are designated as global public good, and how it can help in the global AMR response, including addressing the pipeline and access crisis.

The suggested way ahead was further discussed with a larger set global and national stakeholders across a series of webinars – ‘The Antibiotic Webinars’ during July-

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Oct 2023. Details are mentioned in the Annexure. The key takeaways from the three deliberations are presented below.

### 3.1 Need for coordinated global response to antibiotic pipeline and access crisis

The first deliberation with global stakeholders aimed to develop a deeper understanding on the crisis in antibiotic research and development, ongoing initiatives, and potential solutions. The key takeaways are:

1. **The crisis of AMR is not limited to the crisis of antibiotic R&D. It is in fact a triple crisis.** On one hand, the burden of antimicrobial resistance is rising and antibiotics are becoming ineffective. On the other, new antibiotics that can meet the current public health need are not being adequately developed.

But most important is the crisis of access existing antibiotics as well as those which are developed in recent years to everyone in need at all times and at affordable prices. Access issues are relevant in many countries but are more prominent in LMICs and in the case of antibiotics developed recently.

2. **Society and healthcare systems place a low value on antibiotics.** This is despite the high public health risk of AMR. This low value, which in a way, directs or attracts investment into R&D for future generation of medicines, therefore sends a clear signal to companies that investing in them is not a priority. The way to solve this is through the use of incentives.
3. **In addition to the antibiotic pipeline being weak and stagnant, it is fragmented and lacks predictability.** If this was not the case, it would have encouraged the development of a more sustainable and healthier pipeline.
4. **In addition to funding, coordination and collaboration is key to solving the R&D crisis and avoiding a fragmented response.** Collectively, these are critical to take the antibiotics beyond the R&D phase. In addition to cooperation and coordination between countries, stakeholders include big, small and medium scale antibiotic developers, academia, funders and civil society. This can help sustain a global conversation, support developer predictability, develop products that are really needed to mitigate the impacts of AMR, ensure access and affordability.

An interesting example is the development of a novel antibiotic candidate by Bugworks Research Inc., which was initially supported by CARB-X since 2017,

from lead optimization to phase 1 clinical trials. Subsequently it was taken up by GARDP for further support.

5. **The current scale of investments is insufficient to meet the growing AMR crisis. There is need for sustainable and predictable financing.** This includes further financing of public private partnerships as single initiative cannot do everything. In addition, the financing should be robust and resilient, so that the process of antibiotic innovation does not get impacted due to adverse external situations.

As per the Global AMR R&D Hub, only 23 per cent of the USD 1.8-2 billion – invested every year in AMR R&D from the public and philanthropic sector globally – is going into new antibiotic development.

6. **Push incentives are working but they cannot serve the entire purpose alone.** They have multiple challenges like limited expertise in drug discovery and development within innovators who apply for funding, clinical development in diverse geographies and populations. However, one of the big risks is that these will advance projects to a cliff, where there is no taker or no downstream funding to work towards. Push incentives therefore cannot work alone and have to be tied up with pull incentives as well. Push and pull incentives need to work together.
7. **Pull incentives are relatively more recent and there is a need to build on the experience of countries currently implementing pull incentives.** This includes examples like the UK's subscription model, the PASTEUR Act of the US. The UK subscription model, for example, is seen as a successful initiative, but it would have limited gains if it remains limited to UK.

It is important for national governments, especially the major economies to coordinate and come together. While different countries may not have the same structure, each country will need to adapt the model a bit so that it fits with their structure. In addition, there is also a need for mechanisms for implementing pull incentives or other innovative financing mechanisms.

8. **Targets for new antibiotics should be developed and abundantly informed by public health needs.** These should be realistically set based on a process or a framework, to identify and prioritize how many or what kind of high impact antibiotics are needed to be developed over a particular period of time, and how much money is available or being invested for this.

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Developers, funders and governments should collectively agree on priorities and design appropriate incentives. This process is laden with many uncertainties, it is however important to prioritize based on priority pathogens, disease syndromes, or burden of disease in order to manage the pipeline better.

This should also include understanding of the gaps in the pipeline (e.g., priority pathogens for which the pipeline has no antibiotic under development) and having a targeted collaborative action through involvement of academia, small and medium companies and then big companies.

Another option that could be explored is to evolve **the Priority Pathogens List into a Priority Indications List**. This should be backed-up by indication-specific target product profiles to guide researchers and developers in their selection of projects and in the development and execution their project plans. Examples can be provided of feasible clinical trial designs with which to evaluate new products in each of the indications. Aligning research with priority indications and feasible clinical trials can help improve productivity of the pipeline.

In addition, there is a need to leverage the infrastructure created during COVID for the use of AMR.

There is also a need to understand what a ‘good pipeline’ looks like when compared to the current weak pipeline, and set targets for achieving it accordingly.

9. **Sustainable and equitable access to antibiotics should be an integral part of all measures to support new antibiotic innovation ecosystem.** Vast parts of the world need access to antimicrobials, and they need to get this at affordable costs. The development of new antimicrobials has therefore to be linked with the issue of affordability and access.
10. **Access and predictability in demand are linked.** For e.g., new antibiotics which are being developed are targeting the critical priority pathogens and will be kept in ‘reserve’ category and used only when needed, in order to avoid resistance from emerging quickly against them. However, if companies are assured of predictability, there could be a possibility of ensuring access of such antibiotics in LMICs as well, provided these are used judiciously with appropriate stewardship.

11. **The Global Leaders Group on AMR has an important role to play.** It is in a very important position to convene and bring together these conversations ahead of the High-level meeting on AMR which is to be held at the 2024 United Nations General Assembly, an important political milestone.

### 3.2 Supporting small and medium-scale antibiotic developers

The second deliberation with Indian stakeholders aimed to understand the challenges faced by Indian small and medium-scale antibiotic developers and potential solutions. The key takeaways presented below focused on non-financial measures and would also largely be applicable to scenario in other geographies.

1. **Need to harmonise global regulatory aspects during clinical development phase and in approval stages for antibiotics.** Different regulatory systems across countries could hinder development or access to antibiotics. For example, phase 3 clinical trials require the drug to be tested across different ethnicities, geographies and therefore requires developers to get approvals from different countries. Due to lack of similar protocols, requirements and time taken, the developer needs to wait for approvals from concerned countries and till the time that happens the drug is stuck at that stage of development.

Areas where harmonization can be achieved include scientific and technical requirements, analytical procedure development and validation, quality risk management, study design/sampling, cohort recruitment for quality, safety, and efficacy assessment.

Benefits of harmonisation include ensuring favourable marketing conditions to support early access to medicinal products, promoting competition and efficiency, and reducing unnecessary duplication of clinical testing.

2. **Adoption of accelerated approval pathways for antibiotics can spur antibiotic innovation.** A clear matrix/criterion needs to be developed and adopted at the national level to help identify and select a drug like an antibiotic that can be given an accelerated approval. The matrix/criteria also need to be made clear to developers that how a life-saving drug like an antibiotic can qualify.

Some countries have clear pathways for accelerated drug approval. For example, the accelerated approval program by the US FDA, which is a drug



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development pathway that offers an approval based on a “surrogate” marker in a clinical trial.<sup>70</sup>

National regulatory agencies can customise and build upon global best practices. In addition, regulatory approval processes at the national level should be streamlined to reduce approval time and remove bottlenecks.

3. **Important to strike a right balance while selecting an antibiotic development project to be supported.** Considering resource constraints, public health needs and failure risks of the project, such a balance is the need of the hour.

For example, balance between a viable and well differentiated product for the unmet need in the short-term and an innovative drug carrying more failure risk for the longer term. Prioritization effort needs to be matched with the challenge.

4. **Nurturing and conserving the discovery talent for sustainable long-term innovation of antibiotics is a must.** There is a need to groom and expand the pool of scientists who can discover antibiotics. Considering that antibiotic R&D is no longer the focus for several decades, the expertise available has been reducing and shifting to research in other areas. The renewed interest in financing and support needs to be complemented by dedicated efforts to nurture and conserve this expertise. Unless it is done, the discovery talent will likely not be available in the long-term.
5. **Clinical trials for innovative drugs need to be supported.** This can be achieved such as through opening up of clinical trials, expanding clinical trial network and capacity, through Centres of excellence to help in accessing networks, clinical isolates, patients as well as in harmonising data and quality approvals. Regulatory bodies can also support innovators to conduct clinical trials in other countries.
6. **Big funding depends on the scale of resistance problem at the local level.** Funding sources from western/developed countries are less keen to fund research against resistance problems not present there. This means, for resistance problem in India (but not in western countries), small antibiotic R&D firms may have to solely depend upon Indian sources and neighbouring countries for funding.

7. **Collaborations in antibiotic development are to be explored and leveraged.** Between academic institutes and pharmaceutical companies, similar understanding of what is required and what needs to be done is important. Between big companies and small developers, gaps need to be bridged such as by creating a platform - wherein they can engage and interact - with the help of funding agencies
8. **Challenges across each development stage vary.** For example, those related to commercialization or at the translational level are different and are to be systematically addressed.

### 3.3 Recognising antibiotics as a 'global public good'

The third deliberation aimed to discuss the challenges and possibilities of considering antibiotics or any other aspect of AMR response as a 'global public good' and what would it mean to address AMR. The key takeaways are:

#### *About global public goods*

1. **The concept of global public goods is not new, but presently there is a renewed interest in this concept.** This is because of the wide array of emerging trans-national health challenges, which, if not acted upon timely, will not only cost lives but also adversely impact economy. There is a need for international collective action for health (ICAH) to address these challenges. While the cost of investing in these actions could be large, the return on investment is quite high. Discussions and debate around global public goods are also gaining momentum.
2. **The conventional definition of global public goods is narrow and has its own challenges.** Usually, a global public good is understood as being non-rival (if one person consumes it, this does not reduce its availability to others) and non-excludable (no one can be denied access). But this definition does not capture the full array of health actions that are collectively required to address wider supra-national health challenges. There are ongoing discussions at global platforms like the United Nations (UN) and Organization for Economic Cooperation and Development (OECD) on these definitional issues, around whether there is a need to define things further and if so, how.
3. **There has been a global push for a broader concept of public goods.** This is because if narrow definitions are continued to be followed, there is a possibility of missing on the critical functions. Globally, there is also an awareness on

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the need to do better tracking action towards those. In the academic way, definitions will not be helpful alone. It has to be tied to actual policy action. More definitional clarity is therefore needed. There are some alternative ways to look at how public goods can be defined.

- o One, is the concept of **common goods**. As per the WHO, ‘common goods for health’ are public goods or have large social externalities, and thus will not arise through market forces alone – therefore, they require both public financing and public action. This concept has emerged after the observed failures (e.g. in surveillance, leadership, advocacy) exposed by Ebola, SARS, Zika, and other communicable diseases as well as by other health and environmental risk factors.
- o Another concept is ‘**global functions**’, which capture the broad array of activities critical in preparing for and responding to transnational challenges. These include supplying global public goods, managing cross border externalities (e.g., AMR response) and exercising leadership. In terms of funding, it is only about a fifth of external health financing which is dedicated to global needs, of which only 4 per cent is going to cross border externalities that includes AMR.
- o There is a trend that cycles of ‘panic and neglect’ such as a disease outbreak (E.g., Ebola) leads to increase in this proportion of this financing globally, following which the proportion again falls after the outbreak recedes. Global functions approach therefore not only helps clarify, define and classify essential IACH activities, it also helps identify priorities, know the amount being spent, recognize gaps, tracking the financing for these activities

**4. Antibiotics do not fit the conventional definition of global public goods. But there could be different dimensions or characteristics which could fit.** This can include, for e.g., patent for an antibiotic shared in an open patent pool, AMR containment, knowledge linked to antibiotic development, reduced infection as a result of antibiotic use, antibiotic effectiveness, antibiotic R&D, antibiotic access. It can also include aspects linked to antibiotics such as supply, appropriate use, registration, affordability etc. Awareness, surveillance, Water, Sanitation and Hygiene (WASH) and Infection Prevention and Control (IPC) could also be framed as global public goods.

*Additionally,*

5. **Global collaborative action and global governance is crucial for addressing cross border threats such as AMR.** This could be expedited through measures like a binding agreement, putting more accountability on government, strengthening existing AMR governance models. There is a shared responsibility to secure this co-owned global resource so that it can continue to be effective. It is also a right as people should have access to it when needed.
6. **While the dry pipeline is a concern, it is also true that putting too much focus on antimicrobial development would not be very useful.** This is because on one hand bacteria are rapidly evolving to develop resistance and even newly developed antimicrobials become ineffective soon. Moreover, overly focusing on antimicrobials and the role of the public sector may be putting too much pressure on the official development assistance (ODA) and may be linked with limitations like ‘tragedy of the commons’ and ‘free rider problem’.

It is therefore important to go back to the root causes of the problem and look at AMR containment issue more holistically, which is today a human and sustainable development issue. There is a need to address aspects like access to clean water, infection prevention, appropriate antimicrobial use in agriculture which is linked to better and sustainable development.

Similarly, an AMR lens on investments in areas such as water and sanitation, livestock and agriculture, healthcare systems and strengthening public health systems needs to be applied.

*About funding,*

7. **Existing financing models like the push and pull incentives have limitations when looked at from a ‘global public good’ perspective.**

For example, pull incentives like subscription models operational in the UK or being planned in the US may not work in LMICs unless effective mechanisms are developed that enable these countries to pay. **Antibiotics will otherwise remain as only a regional good or a national public good.** It will also not drive innovation. Even if subscription mechanisms developed in different countries are applied globally, the priorities that would guide developers would be those countries who can pay the most.

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Another Pull mechanism, which could be linked to creation of global public goods effectively is a prize (for example, a ‘milestone prize’ during clinical development or an end-stage prize/market exclusivity reward for a product when it comes to market). But this can happen provided right conditions are in place such as a company willing to give up its intellectual property in exchange for a prize, affordability is ensured and supply is enough etc.

Push funders like the GARDP face concerns such as whether companies and public sector are willing to share or license their compounds to GARDP to take forward its development, the territory provided in case license is available, if product developed in the right presentation as required in LMICs.

- 8. In terms of funding, there has been an increased amount of spending over time on health through development budgets, in particular infectious diseases.** A 2023 working paper by the OECD notes that bilateral aid spending on provision of global public goods by members of the OECD Development Assistance Committee (DAC) has grown from an estimated 37 per cent of average bilateral official development assistance (ODA) in 2007-11 to around 60 per cent in 2017-21. Subsequently, expenditure on national government priorities has dropped.<sup>71</sup>

It is however difficult to measure flows going to AMR. This is more so in case of LMICs, which are most impacted w.r.t health challenges. It is also imperative to know the use and mobilization of domestic resources, such as in areas like pandemic prevention and preparedness, AMR and One Health.

- 9. Compulsory financing at country level could also be explored, though there has not been much political appetite for it.** This could involve innovative financing mechanisms such as global taxes, along the lines of the airline tax which have earlier helped.

## WHAT ARE GLOBAL PUBLIC GOODS

'Goods' in the case of global public goods (GPG) can be referred to as the advantages to society from the provision of certain utilities and from satisfying particular wants and needs such as the eradication of disease or the elimination of pollution.<sup>72</sup> From an economic stand point, goods can be of four types-private goods, club goods, common goods and public goods. These are commonly understood using two parameters – rivalry and excludability.<sup>73</sup>

Public goods, for example, are non-excludable (meaning they are made available to all) and non-rivalrous (meaning they can be enjoyed over and over again by anyone without diminishing the benefits they deliver to others).<sup>74</sup> Examples of public goods include air, national defense. Public goods have positive externalities (exists when a benefit spills over to a third-party) such as police protection or public health funding. However, because they are designed to be accessible by the public, public goods tend to also experience a negative impact from use, which affects all users equally, something known as the 'free rider problem'.<sup>75</sup>

From a geographical stand point, public goods can be local, regional, national, international, domestic or global.<sup>76</sup>

With regard to global public goods, there are also discussions which argue that the economic definition is a narrow one. And therefore, over the years, many prominent organisations have articulated the concept of global public goods in different ways in their reports and documents.

These include the OECD<sup>77</sup>, WHO<sup>78</sup>, International task force on global public goods<sup>79</sup>, EU<sup>80</sup>, among others.

### Types of goods from an economic perspective

<p><b>Rival-excludable</b></p> <p><b>Private goods</b> E.g., Food, cars, clothing</p>	<p><b>Non rival-excludable</b></p> <p><b>Club goods</b> E.g., Satellite TV</p>
<p><b>Rival-non excludable</b></p> <p><b>Common goods</b> E.g., Natural resources like coal</p>	<p><b>Non rival-non excludable</b></p> <p><b>Public goods</b> E.g., Air</p>

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# Annexure

List of experts who shared their perspective through the three webinars:

**Amit Khurana**, Director, Sustainable Food Systems Programme, CSE

**Anna Sjöblom**, Director ReAct Europe

**Frank Berthe**, The Pandemic Fund Secretariat, Washington DC

**Gauri Arora**, Programme Officer, Sustainable Food Systems Programme, CSE

**Gavin Yamey**, Director, Center for Policy Impact in Global Health, Duke Global Health Institute

**James Anderson**, Executive Director, Global Health, International Federation of Pharmaceutical Manufacturers and Associations (IFPMA)

**Jitendra Kumar**, Managing Director, Biotechnology Industry Research Assistance Council (BIRAC)

**Kerri Elgar**, Senior Policy Analyst, Development Co-operation Directorate, OECD

**Lesley Ogilvie**, Director of the Secretariat, Global AMR R&D Hub

**Rajeshwari Sinha**, Programme Manager, Sustainable Food Systems Programme, CSE

**Richard Lawson**, Senior Project Manager, Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X)

**Rohit Malpani**, Independent Consultant

**Sachin Bhagwat**, Senior Vice President, Drug Discovery, Wockhardt Research Centre

**Sunita Narain**, Director General, CSE and Member, Global Leaders Group on AMR

**T.S. Balganes**, President, GangaGen Biotechnologies Pvt. Ltd.

**Vasan Sambandamurthy**, Senior Vice President, Global Operations, Bugworks Research India Pvt. Ltd.

# References

1. Antibacterial products in clinical development for priority pathogens. World Health Organisation. <https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/antibacterial-products-in-clinical-development-for-priority-pathogens> Accessed on November 17, 2023.
2. WHO antibacterial preclinical pipeline review. World Health Organisation. <https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/who-antibacterial-preclinical-pipeline-review> Accessed on November 17, 2023.
3. WHO publishes list of bacteria for which new antibiotics are urgently needed. World Health Organisation. <https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed> Accessed on November 17, 2023.
4. 2021 Antibacterial Agents In Clinical And Preclinical Development. World Health Organisation. <https://iris.who.int/bitstream/handle/10665/354545/9789240047655-eng.pdf?sequence=1> Accessed on November 17, 2023.
5. Antibacterial products in clinical development for priority pathogens. World Health Organisation. <https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/antibacterial-products-in-clinical-development-for-priority-pathogens> Accessed on November 17, 2023.
6. Ibid
7. Ibid
8. Health products in the pipeline from discovery to market launch for all diseases. World Health Organisation. <https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/health-products-in-the-pipeline-from-discovery-to-market-launch-for-all-diseases> Accessed on November 17, 2023.



- 
9. WHO antibacterial preclinical pipeline review. World Health Organisation. <https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/who-antibacterial-preclinical-pipeline-review> Accessed on November 17, 2023.
  10. David A. Kennedy and Andrew F. Read. Why does drug resistance readily evolve but vaccine resistance does not? Proceedings of the Royal Society B, 2017, Volume 284, issue 1851 <https://royalsocietypublishing.org/doi/10.1098/rspb.2016.2562> Accessed on November 17, 2023.
  11. E. Power. Impact of antibiotic restrictions: the pharmaceutical perspective. Clinical Microbiology and Infection, 2006, Volume 12, Pages 25-34 <https://www.sciencedirect.com/science/article/pii/S1198743X14613306#:~:text=In%202001%2C%20Eli%20Lilly%20and,threat%20of%20emerging%20infectious%20diseases>. Accessed on November 17, 2023.
  12. Ibid
  13. Sanofi to buy Genzyme for more than \$20 billion. Reuters. 2011 <https://www.reuters.com/article/us-genzyme-sanofi-idUSTRE71E4XI20110216/> Accessed on November 17, 2023.
  14. Roche in \$550 million deal for superbug-fighting antibiotic. Reuters. 2013. <https://www.reuters.com/article/us-roche-polyphor-idUKBRE-9A307L20131104/> Accessed on November 17, 2023.
  15. AbbVie to Acquire Pharmacyclics, including its blockbuster product Imbruvica®, Creating an Industry Leading Hematological Oncology Franchise. Abbvie New Centre. 2015 <https://news.abbvie.com/news/abbvie-to-acquire-pharmacyclics-including-its-blockbuster-product-imbruvica-creating-an-industry-leading-hematological-oncology-franchise.htm> Accessed on November 17, 2023.
  16. Roche Ends Antibiotic Collaboration with Polyphor. Genetic Engineering & Biotechnology News. 2015. <https://www.genengnews.com/news/update-roche-ends-antibiotic-collaboration-with-polyphor/#:~:text=Roche%20has%20ended%20a%20two,the%20multidrug%2Dresistant%20Pseudomonas%20species>. Accessed on November 17, 2023.

17. US securities & Exchange Commission Form 20-F 2018, Novartis. <https://www.sec.gov/Archives/edgar/data/1114448/000137036819000002/a19013020f.htm>. Accessed on November 18, 2023.
18. AstraZeneca to sell small molecule antibiotics business to Pfizer. 2016. <https://www.astrazeneca.com/media-centre/press-releases/2016/AstraZeneca-to-sell-small-molecule-antibiotics-business-to-Pfizer-24082016.html#modal-historic-confirmation>, Accessed on November 18, 2023.
19. Novartis AG completed the acquisition of Ziarco Group Limited from New Enterprise Associates, Lundbeckfond Invest A/S, BVF Partners LP, Amgen Ventures, Sofinnova Ventures, Inc. and Pfizer Venture Investments for \$420 million. 2017 <https://www.marketscreener.com/quote/stock/NOVARTIS-AG-9364983/news/Novartis-AG-completed-the-acquisition-of-Ziarco-Group-Limited-from-New-Enterprise-Associates-Lundbe-35223978/>. Accessed on November 18, 2023.
20. Novartis bolsters ophthalmology pipeline through acquisition of Encore Vision, Inc. 2016. <https://www.novartis.com/news/media-releases/novartis-bolsters-ophthalmology-pipeline-through-acquisition-encore-vision-inc>. Accessed on November 18, 2023.
21. Johnson & Johnson to Acquire Actelion for \$30 Billion With Spin-Out of New R&D Company. 2017. <https://www.jnj.com/media-center/press-releases/johnson-johnson-to-acquire-actelion>. Accessed on November 18, 2023.
22. Gilead Sciences Closes Acquisition of Cell Therapy Specialist Kite Pharma. 2017. <https://www.thefreelibrary.com/Gilead+Sciences+Closes+Acquisition+of+Cell+Therapy+Specialist+Kite...-a0507894561>. Accessed on November 18, 2023.
23. Novartis Exits Antibiotics Research, Cuts 140 Jobs in Bay Area. 2018. <https://www.bloomberg.com/news/articles/2018-07-11/novartis-exits-antibiotics-research-cuts-140-jobs-in-bay-area>. Accessed on November 18, 2023.
24. Evotec and Sanofi in exclusive talks to create an Evotec-led Infectious Disease open innovation R&D platform. 2018. <https://www.sanofi.com/en/me>

---

dia-room/press-releases/2018/2018-03-08-06-46-35-1418077. Accessed on November 18, 2023.

25. Sanofi to acquire Ablynx for € 3.9 Billion. 2018. <https://www.sanofi.com/en/media-room/press-releases/2018/2018-01-29-07-19-03-1313306>. Accessed on November 18, 2023.
26. Sanofi to Acquire Bioverativ for \$11.6 Billion. 2018. <https://www.sanofi.com/en/media-room/press-releases/2018/2018-01-22-06-00-00-1298161>. Accessed on November 18, 2023.
27. Johnson & Johnson scraps phase 3 antibiotic program acquired in \$30B Actelion takeover. 2018. <https://www.fiercebiotech.com/biotech/j-j-scrap-phase-3-antibiotic-program-acquired-30b-actelion-takeover#:~:text=takeover%20%7C%20Fierce%20Biotech-,Johnson%20%26%20Johnson%20scraps%20phase%203%20antibiotic%20program,in%20%2430B%20Actelion%20takeover&text=Johnson%20%26%20Johnson%20has%20halted%20development,takeover%20of%20Actelion%20last%20year>. Accessed on November 18, 2023
28. Bristol Myers to Buy Celgene in \$74 Billion Cancer-Drug Bet. 2019. <https://www.bloomberg.com/news/articles/2019-01-03/Bristol-Myers-squibb-to-buy-celgene-in-74-billion-pharma-deal>. Accessed on November 18, 2023.
29. Lilly Announces Agreement To Acquire Loxo Oncology. 2019. <https://investor.lilly.com/news-releases/news-release-details/lilly-announces-agreement-acquire-loxo-oncology>. Accessed on November 18, 2023.
30. What science can do: Annual Report and Form 20-F Information 2020, AstraZeneca. 2020. <https://www.astrazeneca.com/investor-relations/annual-reports/annual-report-2020.html>. Accessed on November 18, 2023.
31. Novartis' Sandoz doubles down on antibiotics with \$500M deal for GSK brands, FIERCE Pharma. 2021. <https://www.fiercepharma.com/pharma/novartis-sandoz-snaps-up-gsk-s-antibiotics-business-doubling-down-commitment#:~:text=Novartis%20Sandoz%20is%20doubling%20down,in%20more%20than%20100%20countries>. Accessed on November 18, 2023.

32. Sanofi Agrees to Pay \$2.9 Billion For Provention Bio. 2023. <https://www.bloomberg.com/news/articles/2023-03-13/sanofi-agrees-to-pay-2-9-billion-for-provention-bio>. Accessed on November 18, 2023.
33. Novartis bolsters innovative medicines strategy and renal pipeline with agreement to acquire Chinook Therapeutics for USD 3.2bn upfront (USD 40 / share). 2023. <https://www.novartis.com/news/media-releases/novartis-bolsters-innovative-medicines-strategy-and-renal-pipeline-agreement-acquire-chinook-therapeutics-usd-32bn-upfront-usd-40-share#:~:text=Pursuant%20to%20the%20terms%20of,achievement%20of%20certain%20regulatory%20milestones>. Accessed on November 18, 2023.
34. What Is a Blockbuster Drug? The Motley Fool. 2016. <https://www.fool.com/knowledge-center/what-is-a-blockbuster-drug.aspx>. Accessed on November 18, 2023.
35. The top 20 drugs by worldwide sales in 2021 FIERCE Pharma. 2021. <https://www.fiercepharma.com/special-reports/top-20-drugs-worldwide-sales-2021>. Accessed on November 18, 2023.
36. Melinta's Bankruptcy Underlines Problems with the Antibiotics Market. 2020. <https://www.biospace.com/article/deerfield-wins-melinta-assets-after-chapter-11-bankruptcy/#:~:text=Melinta%20Therapeutics%20filed%20for%20Chapter,it%20had%20provided%20the%20company>. Accessed on November 18, 2023.
37. Achaogen bankruptcy raises worry over antibiotic pipeline. 2019. <https://www.cidrap.umn.edu/antimicrobial-stewardship/achaogen-bankruptcy-raises-worry-over-antibiotic-pipeline> Accessed on November 18, 2023.
38. End of the line looms for Aradigm as it files for bankruptcy. 2019. <https://www.fiercebiotech.com/biotech/end-line-looms-for-aradigm-as-it-files-for-bankruptcy> Accessed on November 18, 2023.
39. Antibiotic developer Nabriva to wind down. 2023. <https://cen.acs.org/pharmaceuticals/antibiotics/Antibiotic-developer-Nabriva-wind-down/101/i2> Accessed on November 18, 2023.

- 
40. La Jolla Pharmaceutical Company to Acquire Tetrphase Pharmaceuticals, Inc. 2020. <https://www.globenewswire.com/news-release/2020/06/24/2052639/0/en/La-Jolla-Pharmaceutical-Company-to-Acquire-Tetrphase-Pharmaceuticals-Inc.html> Accessed on November 18, 2023.
  41. Spero to lay off 75% of workforce, change strategy after FDA challenges study results. 2022. <https://www.biopharmadive.com/news/spero-therapeutics-restructuring-layoffs-fda/623179/> Accessed on November 18, 2023.
  42. The antibiotic paradox: why companies can't afford to create life-saving drugs, Nature, 2020. <https://www.nature.com/articles/d41586-020-02418-x>. Accessed on November 18, 2023.
  43. Project Portfolio-R&D. Pipeline in a Product. Bugworksresearch. 2023. <https://bugworksresearch.com/project-portfolio/>. Accessed on November 18, 2023.
  44. Bacteriophages: Novel Applications. GangaGen. 2023. <https://gangagen.com/novel-applications/>. Accessed on November 18, 2023.
  45. CARB-X Combating ANTibiotic-Resistant Bacteria. 2023. <https://carb-x.org/>. Accessed on November 18, 2023.
  46. CARB-X Complete Portfolio, as of 9/13/23. 2016. <https://carb-x.org/wp-content/uploads/2023/09/CARB-X-Pipeline-2023.9.13.pdf>. Accessed on November 20, 2023.
  47. Global Antibiotic Research & Development Partnership (GARDP). 2023. <https://gardp.org/>. Accessed on November 18, 2023.
  48. Enabling Breakthroughs in Antimicrobials, 2 TO 4 NOVEL ANTIBIOTICS BY 2030. AMR ACTION Fund. 2023. <https://www.amractionfund.com/>. Accessed on November 18, 2023.
  49. AMR action fund. 2023. <https://www.amractionfund.com/investments#our-portfolio>. Accessed on November 20, 2023.

50. Biomedical Advanced Research and Development Authority (BARDA). 2023. <https://medicalcountermeasures.gov/barda/>. Accessed on November 18, 2023.
51. BARDA's Expanding-CBRN Medical Countermeasure Portfolio. 2023. <https://www.medicalcountermeasures.gov/barda/cbrn#portfolio>. Accessed on November 20, 2023.
52. The Global AMR Innovation Fund (GAMRIF). 2023. <https://www.gov.uk/government/groups/the-global-amr-innovation-fund>. Accessed on November 18, 2023.
53. Projects supported by DHSC through the Global AMR Innovation Fund.2020.[https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/886146/projects-funded-by-GAMRIF.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/886146/projects-funded-by-GAMRIF.pdf). Accessed on November 20, 2023.
54. Outterson, K., Rex, J.H. Global Pull Incentives for Better Antibacterials: The UK Leads the Way. *Appl Health Econ Health Policy* 21, 361–364 .2023. <https://link.springer.com/article/10.1007/s40258-023-00793-w>. Accessed on November 18, 2023.
55. Rebecca E Glover et al. The antibiotic subscription model: fostering innovation or repackaging old drugs? *Lancet Microbe*. an;4(1):e2-e3. 2023. [https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247\(22\)00235-X/fulltext](https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(22)00235-X/fulltext). Accessed on November 18, 2023.
56. The Public Health Agency of Sweden. Availability of antibiotics. 2023. <https://www.folkhalsomyndigheten.se/the-public-health-agency-of-sweden/communicable-disease-control/antibiotics-and-antimicrobial-resistance/availability-of-antibiotics/#:~:text=The%20Public%20Health%20Agency%20of%20Sweden%20considers%20that%20a%20model,made%20permanent%20to%20ensure%20the>. Accessed on November 18, 2023.
57. <http://freepdfhosting.com/6d498304d6.pdf>. Accessed on November 18, 2023.
58. Ibid

59. Dzintars Gotham et al. Reimbursement models to tackle market failures for antimicrobials: Approaches taken in France, Germany, Sweden, the United Kingdom, and the United States. <https://www.sciencedirect.com/science/article/pii/S0168851020302980>. Accessed on November 20, 2023.
60. Ibid
61. Proposal for a Regulation laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency. European Commission. 2023. [https://health.ec.europa.eu/publications/proposal-regulation-laying-down-union-procedures-authorisation-and-supervision-medicinal-products\\_en](https://health.ec.europa.eu/publications/proposal-regulation-laying-down-union-procedures-authorisation-and-supervision-medicinal-products_en). Accessed on November 18, 2023.
62. Information based on responses received from ReACT on email
63. G7 Finance Ministers' Statement on Actions to Support Antibiotic Development, G7 United Kingdom 2021. [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/1040016/AMR\\_-\\_G7\\_Finance\\_Ministers\\_statement\\_on\\_supporting\\_antibiotic\\_development\\_-\\_final\\_-\\_13\\_Dec\\_2021.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1040016/AMR_-_G7_Finance_Ministers_statement_on_supporting_antibiotic_development_-_final_-_13_Dec_2021.pdf). Accessed on November 18, 2023.
64. G7 Shared Principles for the Valuation of Antimicrobial Therapeutics G7 United Kingdom 2021. [https://assets.publishing.service.gov.uk/media/61b366ca8fa8f5037b09c79e/AMR\\_-\\_G7\\_Health\\_Ministers\\_-\\_shared\\_valuation\\_principles\\_-\\_final\\_-\\_17\\_Nov\\_2021.pdf](https://assets.publishing.service.gov.uk/media/61b366ca8fa8f5037b09c79e/AMR_-_G7_Health_Ministers_-_shared_valuation_principles_-_final_-_17_Nov_2021.pdf). Accessed on November 18, 2023.
65. G7 Finance Ministers and Central Bank Governors' Communiqué | Page 1 G7 Finance Ministers and Central Bank Governors' Petersberg Communiqué. Petersberg, 20 May 2022. [https://globalamrhub.org/wp-content/uploads/2022/05/G7-Finance\\_Ministers\\_Meeting-Bonn-Koenigswinter-Communique-En.pdf](https://globalamrhub.org/wp-content/uploads/2022/05/G7-Finance_Ministers_Meeting-Bonn-Koenigswinter-Communique-En.pdf). Accessed on November 18, 2023.
66. G7 Finance Ministers and Central Bank Governors Meeting Communiqué . Niigata, Japan, 2023. <https://www.consilium.europa.eu/media/64307/g7-communiqué-20230513.pdf>. Accessed on November 18, 2023.

67. G7 Health Ministers' Communiqué. Berlin. 2022. [https://globalamrhub.org/wp-content/uploads/2022/05/G7\\_Health\\_Ministers\\_Communique\\_20220520\\_English.pdf](https://globalamrhub.org/wp-content/uploads/2022/05/G7_Health_Ministers_Communique_20220520_English.pdf). Accessed on November 18, 2023.
68. G7 Nagasaki Health Ministers' Communiqué Nagasaki, Japan. 2023. <https://www.mhlw.go.jp/content/10500000/001096403.pdf>. Accessed on November 18, 2023.
69. G7 Hiroshima Leaders' Communiqué. Hiroshima. 2023. <https://www.mofa.go.jp/files/100506878.pdf>. Accessed on November 18, 2023.
70. Accelerated Approval Program. US Food & Drug Administration. <https://www.fda.gov/drugs/nda-and-bla-approvals/accelerated-approval-program>. Accessed on November 18, 2023.
71. Development co-operation and the provision of global public goods. OECD iLibrary. 2023. <https://www.oecd-ilibrary.org/docserver/aff8cba9-en.pdf?expires=1698821176&id=id&accname=guest&checksum=EB910C-6233C80070BB11CBA2C33F31E2>. Accessed on November 18, 2023.
72. EU focus on global public goods. European Union. 2023. <https://wayback.archive-it.org/12090/20201014214533/https://ec.europa.eu/environment/archives/wssd/pdf/publicgoods.pdf>. Accessed on November 18, 2023.
73. Club Goods. A subset of public goods that possess one of the two key factors of public goods. CFI 2023. <https://corporatefinanceinstitute.com/resources/economics/club-goods/>. Accessed on November 18, 2023.
74. Jason Fernando. What Are Public Goods? Definition, How They Work, and Example. Investopedia. 2022. <https://www.investopedia.com/terms/p/public-good.asp>. Accessed on November 18, 2023.
75. Public Goods, Goods that are commonly available to all people within a society or community that are non-excludable and non-rivalrous. CFI. 2023. <https://corporatefinanceinstitute.com/resources/economics/public-goods/>. Accessed on November 18, 2023.



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76. Regional Public Goods in Asia and Europe. Asian Development Bank. 2021. <https://www.adb.org/sites/default/files/publication/666906/regional-public-goods-asia-europe.pdf>. Accessed on November 18, 2023.
77. Financing Global And Regional Public Goods Through Oda: Analysis And Evidence From The Oecd Creditor Reporting System. OECD Development Centre. 2004. <https://web-archiv.e.oecd.org/2012-06-15/158605-24482500.pdf>. Accessed on November 18, 2023.
78. Global Public Goods for Health. World Health Organization. 2002. <https://iris.who.int/bitstream/handle/10665/42518/9241590106.pdf> Accessed on November 18, 2023.
79. Summary Report of the International Task Force on Global Public Goods. 2006. [https://www.keionline.org/misc-docs/socialgoods/International-Task-Force-on-Global-Public-Goods\\_2006.pdf](https://www.keionline.org/misc-docs/socialgoods/International-Task-Force-on-Global-Public-Goods_2006.pdf). Accessed on November 18, 2023.
80. EU focus on global public goods. European Commission. <https://wayback.archive-it.org/12090/20201014214533/https://ec.europa.eu/environment/archives/wssd/pdf/publicgoods.pdf> Accessed on November 18, 2023.

Conserving antibiotics has been one part of the strategy to contain AMR. Another part is to keep making new antibiotics as resistance against existing antibiotics continues to develop and increase. This report presents the current scenario on where the world stands on its readiness to develop new antibacterial treatment options for future use. It focusses on pipelines of select high-earning 15 global pharmaceutical companies to know their R&D focus and reflects upon reasons as to why the pharmaceutical have moved away from antibiotic R&D.

It then presents the role played by micro, small and medium-scale antibiotic developers who have taken up the responsibility to develop antibiotics and the typical challenges they face. It also suggests the way ahead in terms critical reforms needed to rejuvenate the antibiotic R&D ecosystem. Finally, the report presents the key takeaways of a series of expert consultations on the suggested way ahead.



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