RECOGNISING ANTIBIOTICS AS A ‘GLOBAL PUBLIC GOOD’: CHALLENGES AND POSSIBILITIES

Will recognising antibiotics as a ‘global public good’ help the world tide over the double trouble that it faces – of existing antibiotics becoming ineffective on one hand, and research and development on new antibiotics stalling on the other?

October 18, 2023
We are currently facing **three key crisis**

- **Crisis 1**: Antibiotics are becoming ineffective
- **Crisis 2**: The antibiotic development crisis
- **Crisis 3**: The issue of access
Stagnant years! of antibiotic pipeline for priority pathogens

- Priority pathogens = unmet need = most are Gram-negatives

- 12 pathogens categorized into critical, high and medium priority by the WHO in 2017 to guide global antibiotic research

*As per World Health Organization’s priority pathogen list, 2017; ^Number of antibiotic candidates; Source: World Health Organization
Global antibiotic pipeline: weak, fragile, dry, anemic!

In comparison:

>10,000 medicines under active clinical development for cancer

>1,800 for neuropsychiatric conditions

~1,500 for endocrine, blood and immune disorders*

Agents that lack intrinsic antibacterial activity and work through other means; *May not substitute traditional*

Priority pathogens, *M. tuberculosis* and *C. difficile*

Source: WHO database updated till late 2021; *WHO’s Global Health Observatory on Health Research and Development;*
Small firms, big task – Traditional candidates

Clinical development pipeline

<table>
<thead>
<tr>
<th>TRADITIONAL ANTIBIOTIC CANDIDATES: 46</th>
<th>Phase 1: 22</th>
<th>Phase 2: 14</th>
<th>Phase 3: 9</th>
<th>Pre-registration: 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Targeting WHO priority pathogens</td>
<td>28</td>
<td>16</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Developers in Phase 1:</td>
<td>Bugworks Research, Juvabis, Entasis Therapeutics, Pfizer/Aria Pharmaceutical, KDP BioSciences Pharmaceutical Technical, Meiji Seika, Opex Biopharma, Roche, Spero Therapeutics, TASSIS Pharmaceutical, Venaton, Sinoent, Wockhardt</td>
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<tr>
<td>Developers in Phase 2:</td>
<td>Debiopharm International, TenNor Therapeutics</td>
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<td>Developers in Phase 3:</td>
<td>Sichuan Pharmaceutical Holding Group, Glaxo SmithKline (GSK), Entasis Therapeutics, Alere Therapeutics, Wockhardt, Iterum Therapeutics, VendoRx Pharmaceuticals/GLOBAL ANTIBIOTIC RESEARCH AND DEVELOPMENT PARTNERSHIP (GARDP), Entasis Therapeutics/GARDP</td>
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<td>Developers in Pre-registration: Fujifilm Toyama</td>
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<tr>
<td>Targeting Mycobacterium tuberculosis</td>
<td>13</td>
<td>6</td>
<td>7</td>
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<tr>
<td>Developers in Phase 1:</td>
<td>GSK-TB drug accelerator/Bill &amp; Melinda Gates Foundation, Innovative Medicines for Tuberculosis Foundation, TB Alliance, Institute of Medinio Medica, Institute of Medinio Medica/TB Alliance</td>
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<tr>
<td>Developers in Phase 2:</td>
<td>GSK, University of Munich, LogoChem Biosciences/Haiwe Biopharm, Otsuka Pharmaceutical, TB Alliance/Sequella, TB Alliance/Bill and Melinda Gates Foundation, Qurient</td>
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<tr>
<td>Targeting Clostridioides difficile</td>
<td>5</td>
<td>-</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Developers in Phase 2:</td>
<td>Crestone, Deinove, Acux Pharmaceutical, MGB Biopharma, Developers in Phase 3: Summit Therapeutics</td>
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Near-future scenario bleak

- **Only nine** in phase 3
- **None for** *M. tuberculosis*
- **Only two** for critical priority pathogens
- **Solithromycin** is the only one in pre-registration stage
Small firms, big task – Non-traditional candidates

Near-future scenario bleak

- **Only five** in phase 3
- **Only two** in pre-registration stage
- **None for *M. tuberculosis*** (only one in phase 1)

Approximately 80% of new antibiotic discoveries are reported to be from small developers

Source: A 2022 report by biotechnology innovation organisation

<table>
<thead>
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<th>Clinical development pipeline</th>
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<tbody>
<tr>
<td><strong>Non-traditional antibiotic candidates</strong>: 34</td>
</tr>
<tr>
<td>Phase 1: 12</td>
</tr>
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<tr>
<td><strong>Targeting WHO priority pathogens</strong></td>
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<td>Developers in Phase 1:</td>
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Long-term scenario also not promising!

Preclinical pipeline

- **Only 3** out of the 217 have their Investigative New Drug (IND) application submitted
- **31** are in clinical trial application/IND-enabling studies
- Too less a pool, considering the **high failure risk** at this stage
- ~**85% preclinical candidates** developed by micro, small and medium developers

Pre-clinical pipeline as on WHO database updated until late 2021
Hollow pipeline

Industry attributes to antibiotic market failure; venture capitalists also moved away to more profitable areas

Out of 1007 molecules in clinical pipeline of 15 global pharmaceuticals, only 13 are antibacterial candidates, being developed by four companies. 8 out 13 are by one company (GSK).

- **411** candidates were found to be developed for cancer;
- **150** for immunology, allergy, inflammation or respiratory diseases;
- **84** for cardiology, metabolism or renal disease areas.

The BIG EXODUS is not only because of high risk low return (due to often cited market failure) but also because of profits in other areas. As reflected through blockbuster drugs in profitable areas like cancer, autoimmune disorders, metabolic diseases
Big Exodus by high-earning companies

Most of the world’s 15 big pharmaceutical companies* do not have antibiotics in their clinical pipeline.

Many who were developing earlier have exited. Some many years ago; some recently. Only GSK, Roche, Pfizer and AbbVie are currently developing.

Collectively, the 2022 revenue of these 15 companies was about $711 billion, 17.5% of which ($124 billion) was total investment in research and development.

*Selected by Down To Earth to represent a cross-section of high-earning, global pharmaceutical firms; *Includes infectious disease; *Information could not be accessed; *Notes: Data updated till June 2, 2023; Source: Compiled by CSE-DTE Data Centre
Teething Troubles

• Small-medium scale antibiotic developers are struggling to develop antibiotics or making money from what they have developed (bankruptcy issues, diminished values/ exits)

• With the collapse of pharmaceutical companies, it took out of circulation—or sharply reduced the availability of—five of the 15 antibiotics approved by the US FDA since 2010**

• Of the 12 antibiotic companies gone public in the past 10 years, only five are still active today*

• Growing consensus on the need to support antibiotic R&D through investments via, broadly, two types of approaches—push and pull. After about a decade of push incentives, it is clear their success has been less than required; they are not enough and need to be supplemented. On the other hand, the impact of pull incentives initiated in recent years remains to be seen.

*A 2022 report by biotechnology innovation organisation; ** 2020 article of Nature
Way Ahead- Critical reforms needed
To stimulate the antibiotic R&D ecosystem for a sustainable and equitable antibiotic access worldwide

• **Greater public financing and reforms** are needed such as 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.

• **Governments need to come together for a coordinated response** in terms of prioritising antibiotics and developers, testing and piloting incentives and removing access barriers. **Action needed by G20 countries.** Unless major economies come together, individual country efforts will have limited long-term gains.

• **Need to strike the right balance in public-private partnership** for antibiotic development. 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.

• **Time to consider antibiotics as ‘global public goods’?**
Webinar 1 - The crisis in antibiotic research and development

The Antibiotic Webinars: 1

The Crisis in Antibiotic Research and Development

At a time when existing antibiotics are becoming ineffective, pharmaceutical companies are not investing in R&D for new antibiotics. Is the world staring at a serious health emergency in the near future?

Date: Friday, 28 July 2023
Time: 5:00 TO 6:30 PM (IST)
Platform: ZOOM

Our Speakers

Moderator

SUNITA NARAIN
Director General, CSE and Member, Global Leader Group on AMR

JAMES ANDERSON
Executive Director, Global Health, International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), Switzerland

RICHARD LAWSON
Senior Project Manager, Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), USA

LESLEY OGILVIE
Director of the Secretariat, Global AMR R&D Hub, Germany

AMIT KHURANA
Director, Sustainable Food Systems Programme, CSE

RAJESHWARI SINHA
Programme Manager, Sustainable Food Systems Programme, CSE

GAURI ARORA
Programme Officer, Sustainable Food Systems Programme, CSE
Key points emerged
In addition to financing, coordination, collaboration, prioritisation is key

- The crisis of antibiotic research is a **global problem and would need global solutions**.
- Need to build **more robustness and resilience in funding** for antibiotic development pipeline. The current scale of investments is insufficient to meet the growing crisis of AMR.
- Push incentives are working, but have their challenges. **Push and pull incentives need to work together**. Pull incentives like the UK subscription model, would work better if other countries do something similar.
- Only funding is not enough; **coordination, collaboration and communication** is the key to solving the antibiotic R&D crisis. This should include understanding of the gaps in the pipeline, and funding and have a targeted collaborative action
- Need to understand what a good pipeline looks like and **set targets** for achieving it; there is importance of **predictability** to avoid a fragmented response
- **Need to link all measures to support new antibiotic development with access and affordability particularly in LMICs.** The issue of access and antibiotic development cannot be solved without cooperation between countries and stakeholders.
Webinar 2 - Small and medium scale antibiotic developers: Challenges they face and the way forward
Key points emerged
In addition to financing, there is a need to address barriers through non-financing measures

- Need for regulatory harmonization at global level so that the innovators can use the data generated.
- Need to open up clinical trial testing for innovative drugs; Mechanisms needed to access clinical trial networks, data harmonization and quality approvals; streamlining national regulatory approvals.
- Need to adopt accelerated approval pathways so that it is clear how an antibiotic can qualify as it will spur innovation.
- Need to strike a balance in selecting a project to be supported – b/w a viable and well differentiated product for unmet need in short term and an innovative drug for long term, with more risk of failure.
- Nurture and conserve discovery talent for sustainable long-term innovation; groom and expand pool of antibiotic-discovery scientists
- Developed economies are less interested in funding research and innovation not relevant to their geographies
- Problem of R&D differs from that of commercialisation and are to be systematically addressed; Need to leverage on collaborations, Covid-19 learnings and India’s pandemic response.
Will recognising antibiotics as a ‘global public good’ help the world tide over the double trouble that it faces – of existing antibiotics becoming ineffective on one hand, and research and development on new antibiotics stalling on the other?
What are ‘goods’ and the different types of goods?

‘Goods’ refer to 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.*

From an economic standpoint, goods are of four types: **Public; Common; Club; Private.**

This is commonly understood using two parameters: **Rivalry and Excludability**

<table>
<thead>
<tr>
<th>Rival-Excludable</th>
<th>Non Rival-Excludable</th>
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<tbody>
<tr>
<td><strong>Private goods</strong></td>
<td><strong>Club goods</strong></td>
</tr>
<tr>
<td>E.g., Food, cars, clothing</td>
<td>E.g., Satellite TV</td>
</tr>
<tr>
<td><strong>Rival-Non excludable</strong></td>
<td><strong>Non Rival- Non excludable</strong></td>
</tr>
<tr>
<td><strong>Common goods</strong></td>
<td><strong>Public goods</strong></td>
</tr>
<tr>
<td>E.g., Natural resources like coal</td>
<td>E.g., Air, national defense</td>
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</tbody>
</table>

*Source: EU focus on global public goods, 2002

Non-excludable (meaning they are made available to all) and nonrivalarous (meaning they can be enjoyed over and over again by anyone without diminishing the benefits they deliver to others)
Public goods can be local, regional, national, international, domestic or global......What are Global Public Goods?

**Organization for Economic Cooperation and Development (OECD), 2004**
A Global Public Good is an International Public Good (public goods which provides benefits crossing national borders of the producing country) which, while not necessarily to the same extent, benefits consumers all over the world.

**International Task Force on Global Public Goods, 2006**
Global public goods are those whose benefits could in principle be consumed by the governments and peoples of all states. Examples include mechanisms for ensuring financial stability, the scientific knowledge involved in the discovery of a vaccine and international regulations for civil aviation and telecommunications.

**European Union, 2002**
The goods are global because they range beyond national borders. In reality not all GPGs are truly global in their reach but they are, at least, regional and/or inter national in that their benefits extend across several countries.

**World Health Organisation, 2022**
Global public goods refer to programmes, policies, and services that have a truly global reach (although the distribution of benefits may be unevenly experienced or perceived across countries).
Antibiotics or any aspect of AMR response as a ‘global public good’?

Current global discussions around AMR and global public goods

- **Global Leaders Group on AMR, Summary note, 2023:** ‘Several members urged GLG advocacy in favour of classifying antibiotics as global public goods that are treated differently from other drugs in terms of R&D and access, with an increased focus on public financing and agreements with the private sector on issues such as research coordination and prioritization, and drug pricing and access.’

- **World Bank report, 2017:** ‘As effective antimicrobial treatment is part of the global commons, so containment of AMR is a global public good, which will prolong the availability of effective antimicrobials for all countries.’

- **Final Report of the Review on AMR, 2016:** ‘When it comes to dealing with AMR, countries have three options in how they pay.....One of the option is by working together and paying for global public goods in a pooled way, countries could most efficiently and effectively work to avoid the type of large-scale outbreak of an untreatable infection that nobody wants to see’
Issues/Questions

• Global Public Good or Global Common Good or any other categorization approach?
  • Some aspect may not fit the strictest definition (for example, antibiotics is not non-rivalrous) though antibiotics do have attributes of global public good
  • How do things change if it is public v/s common good

• Which aspects of antibiotics/AMR response can be considered? e.g.,
  • Knowledge linked to antibiotic development
  • Reduced infection as a result of antibiotic use
  • Antibiotic effectiveness
  • Antibiotic research and development
  • Antibiotic access
Thank you!
For more information, contact:

Amit Khurana
Director
Sustainable food systems programme
k_amit@cseindia.org

Rajeshwari Sinha
Programme Manager
s_rajeshwari@cseindia.org

Gauri Arora
Programme Officer
gauri.arora@cseindia.org