THE ROLE OF ‘TEAM INDIA’ IN GLOBAL HEALTH R&D
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INTRODUCTION

In a world that is increasingly G20 rather than G8, led in large part by the economic and political emergence of Asia, India stands at the epicentre of a massive shift in global economic power. At the same time it is a country confronting its own significant internal transitions.

India, like many increasingly affluent countries, is seeing an explosion in its levels of non-communicable diseases, which are predicted to account for two-thirds of all deaths by 2030. At the same time it remains home to a significant burden of neglected diseases; India accounts for a quarter of all global tuberculosis cases, for example, with 2.5 million notified cases in 2011. It is also home to an emerging pharmaceutical industry that has become an integral part of the global research and development (R&D) picture, but which – despite promise – is still yet to prove itself as a source of innovative products.

As the global economic powershift accelerates and middle-income economies play an increasing role in international trade and development, more attention is being paid to India’s contribution to global health R&D. And with three key strengths to leverage – an emerging economy, a strong scientific base, and an active and growing pharmaceutical sector – India has the potential to be a global leader in the field.

A strong economy

India’s economy is both large and growing rapidly; in 2013, its gross domestic product (GDP) stood at $1,877 billion, ahead of both Canada and Australia in the top ten global economies. India’s GDP grew by 6.6% in the period 2010 to 2013, and is forecast to grow by a further 10.5% between 2015 and 2025 – outperforming the global average for each of these periods. Together, the combined GDP of India and China is predicted to exceed that of the seven major OECD economies by 2040. In recent years India has also been transitioning from an aid recipient to an aid donor, and has already reached the point where it is a net contributor of official development assistance.

A solid scientific base

Alongside its growing economy, India has at its disposal a relatively strong scientific base, built on the foundation of an expanding and increasingly well-educated science and technology (S&T) workforce. Every year, 2.5 million Indian university students graduate with science and engineering degrees – double the number produced by China on a per capita basis – and the country has a number of long-established research institutes with a proud history of achievement. Although some concerns exist about the quality and quantity of S&T education and the adequacy of the innovation ecosystem in the country – see for example those expressed in a 2010 report by the Science Advisory Council to the Prime Minister – a combination of current demographic trends and an increased focus on scientific excellence from the national government mean that India’s scientific base and S&T workforce is likely to only grow stronger.

An emerging pharmaceutical sector

In addition to its economic and human capital, the third element underpinning India’s contribution to global health R&D efforts is its large (and growing) pharmaceutical sector. With an annual revenue of more than $20 billion, the sector is an important element of the Indian economy, representing 2% of India’s GDP. More than half of this market is export-focused, and India is the sixth largest exporter of pharmaceuticals globally, exporting to more than 200 countries.

The sheer number of companies is also impressive. India has more than 300 US FDA-approved firms – the highest number of FDA-approved firms outside of the United States. Yet these represent less than 3% of the over 10,500 pharmaceutical and biotechnology companies in India – reflecting the hugely competitive and fragmented nature of the sector, as well as its size.
Very little of the Indian pharmaceutical sector’s efforts are focused on start-to-finish innovative R&D. The sector’s key strengths are in four main areas:

**Manufacture of generic drugs and APIs (and increasingly biosimilars):** The Indian drug manufacturing sector generates between $10 and $15 billion per year, making up half to two-thirds of India’s pharmaceutical industry – largely from the manufacture of generic drugs and active pharmaceutical ingredients (APIs).\(^{12}\)

**Contract research and manufacturing services:** There are at least 100 contract research organisations (CROs) in India performing R&D on a fee-for-service basis, largely focused on late-stage discovery and pre-clinical drug development services. Driven by India’s comparative advantages in manufacturing costs, skilled manpower and strong technical capabilities, the sector is estimated to be growing between 48% and 65% a year (more than triple the global rate), and is expected to be worth $8 billion per year by 2015.\(^{13,14}\)

**Process innovation and adaptive research into new vaccines:** The Indian vaccine market is much smaller than the drug market, with annual revenues of $500 million. Although they have never produced a completely innovative new vaccine, Indian vaccine producers have relied on their strengths in process innovation and formulation technology to develop low-cost versions of existing vaccines, supplying these to global health procurement agencies like UNICEF, the Pan American Health Organization and the GAVI Alliance.\(^7\)

**Development of new diagnostic technologies:** India’s diagnostics market is similar in size to its vaccine market, and grew by 22% in 2012 alone.\(^7\) It is also one of the areas in which Indian firms have proven their ability to deliver innovative products all the way from conception to registration – with promising products in the pipeline like a nucleic acid-amplifying device that can test for multidrug-resistant tuberculosis (MDR-TB) in remote settings.

The purpose of this report is to examine how India is using its key strengths to contribute to the global neglected disease R&D effort. How much is the Indian government investing in neglected disease R&D? What contribution are Indian organisations making to the development of new products? And what policies, programmes and partnerships exist to support this effort? By answering these questions, the report will show that India – through its funding, its policies and its partnerships – is moving beyond a ‘Team India’ approach, to establish itself as a vital partner in this global effort.

India is home to the highest number of FDA-approved firms outside of the US.
As befits its position as both an emerging economic power in an emerging region and a country with a significant domestic burden of neglected diseases, the Indian government is one of the top global funders of neglected disease R&D. Total public sector funding in India for neglected disease R&D in 2013 was $50 million, making it the world’s fifth largest government funder behind the US, the United Kingdom (UK), the European Commission, and France.

Indian public sector investment in global health R&D has also generally been trending upwards since the G-FINDER survey first started collecting data there in 2008, setting it apart from most major governments (especially in the wake of the global economic crisis).

The $50 million of Indian public sector funding in 2013 was the largest yet reported by the country, and represented an increase of $7.9 million (up 18%) over 2012 and $12.6 million (up 33%) compared to 2008, the first year in which data was collected. Some of this increase was related to better reporting from the Indian Council of Medical Research (ICMR), but it chiefly reflects the steady increase in Indian public sector funding over the last half-decade.

As well as being in the top five government funders globally, India is the most prominent developing country funder of neglected disease R&D by a significant margin, contributing just under half (44%) of all low- and middle-income country (LMIC) government investment for the period from 2008 to 2013.

However, despite this solid funding base and its outsize role among LMIC government funders of neglected disease R&D, India’s contribution represents just 2% of total global government investment. When India’s investment is calculated as a proportion of GDP, it drops from fifth to eighth largest funder, falling behind its fellow high-burden LMICs, South Africa. For a country that sits in the ten largest economies in the world, India could be contributing more.

India provided nearly half of all investment by low- and middle-income country governments in neglected disease R&D.
Key public funding agencies

Indian funding for neglected disease R&D is very concentrated. Between 2008 and 2013, 96% of government funding came from three agencies: the Indian Council of Medical Research (ICMR) provided 59%, the Department of Biotechnology (DBT) – one of the key departments within the Ministry of Science and Technology – gave 24%, and the Council of Scientific Research (CSIR) the remaining 13%. The remainder came largely from the Department of Science and Technology (DST, another department under the Ministry of Science and Technology) which gave 3.8%, while all other Indian government agencies reported providing less than 1% of total Indian government funding for the entire period.

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<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>Average annual funding</th>
<th>Share of total</th>
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<td>21</td>
<td>22</td>
<td>34</td>
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<td>Department of Biotechnology, Ministry of Science and Technology (DBT)</td>
<td>6</td>
<td>4</td>
<td>12</td>
<td>15</td>
<td>11</td>
<td>10</td>
<td>9</td>
<td>24%</td>
</tr>
<tr>
<td>Council of Scientific and Industrial Research (CSIR)</td>
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<td>5</td>
<td>7</td>
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<td>Department of Science and Technology (DST)</td>
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<td>All other Indian government funders</td>
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<td>0.1</td>
<td>-</td>
<td>0.6</td>
<td>0.1</td>
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<tr>
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<td>39</td>
<td>43</td>
<td>43</td>
<td>50</td>
<td>40</td>
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</table>

Where does funding go?

The vast bulk of Indian government investment is directed towards basic and early-stage research. Nearly two-thirds (64%) of all allocable funding from 2008 to 2013 was directed towards pure basic research, and a further fifth (20%) went to early-stage (discovery and pre-clinical) research. Just 16% was invested in the clinical stages of product development, a figure that includes the translational (pre-proof of concept) stages of early clinical research.

More than half (54%) of all Indian government funding went to the two highest-burden neglected diseases, tuberculosis and malaria, each of which received 27% of total government funding from 2008 to 2013. A further third was divided between the next four highest-burden diseases: diarrhoeal diseases (10%), which include rotavirus and cholera (two major causes of under-five mortality in India); the kinetoplastid diseases (10%), including leishmaniasis or ‘kala-azar’; HIV/AIDS (6%); and leprosy (6%). The remaining diseases, including dengue and the helminth (worm and fluke) infections, made up the remaining 19% of Indian government investment in neglected diseases.

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* Allocable funding includes all funding for which a research stage could be ascribed. Core-funding and unspecified funding which could not be attributed to a specific research stage have been excluded from the calculation.
The international effort to deliver new tools to prevent, diagnose and treat neglected infectious diseases has expanded enormously since the start of the twenty-first century, with more than $3 billion per year currently being invested into R&D for new neglected disease products. This increased attention and funding has helped deliver the 61 new neglected disease products approved since 2000, and as of 2013 was supporting a pipeline of over 360 product candidates.

Given its growing economic weight, significant burden of neglected diseases and emerging pharmaceutical industry, what part has India played in this global effort?

**Indian involvement in neglected disease product development**

Despite India accounting for just 2% of all global government funding for neglected disease R&D, Indian organisations have played a role in developing one-quarter (15) of the 61 new neglected disease products that have been successfully registered since 2000. Their role has been particularly prominent in developing new drugs and vaccines, with nearly two-thirds (6 of 10) of new neglected disease vaccines and one-third (6 of 18) of the new neglected disease drugs registered since 2000 having Indian involvement.

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### 15 of the 61 new neglected disease products registered since 2000

- **60%** of all new vaccines
- **33%** of all new drugs
- **9%** of all new diagnostics

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The relative contribution of Indian organisations to diagnostics development was much less significant; the three new diagnostics developed by Indian organisations (one of which was a diagnostic platform to diagnose multiple diseases, including tuberculosis, *P. falciparum* malaria, dengue and typhoid) represented only 9% of all new diagnostics registered globally since 2000.iii

India’s involvement in the global neglected disease product pipeline – that is, the pipeline of candidates currently in development – is proportionally less than for newly registered products, reflecting the fact that Indian organisations are often brought in by international partners late in the product development process. Indian organisations were involved in 12% of the more than 360 product candidates in development in 2013, with 42 either involving an Indian partner or being solely developed by Indian organisations.

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iii To see which disease and product areas are included under the definition of ‘neglected diseases’, please refer to the G-FINDER R&D matrix, available at https://gfinder.policycures.org/staticContent/pdf/G-FINDER-disease-product-matrix.pdf. Some product areas are restricted; for example, R&D for standard adult antiretroviral drugs for HIV is excluded, as there is a strong private sector market to stimulate for-profit R&D.

iv We have not counted the many serological diagnostic tests for tuberculosis developed and marketed by Indian organisations, as these tests are inaccurate and ineffective, and their manufacture and distribution has been banned by the Indian government.
Work to develop new vaccines dominates the Indian neglected disease R&D effort, with vaccine candidates accounting for nearly two-thirds of the 42 Indian product candidates in the pipeline in 2013. New drug candidates make up a further quarter (26%), and diagnostics the remaining 12%.

**What role do Indian organisations play?**

A range of Indian sectors partner internationally on neglected disease product development, including academic institutions, government research groups and pharmaceutical companies, although pharmaceutical companies are by far the most common partners. Companies predominantly play one of two roles – late-stage product development and commercialisation, or contract research and manufacturing – reflecting their areas of comparative advantage. Innovative research is less common and, when it does occur, it is often early-stage research conducted by government agencies and research institutes, who also have a major role as research facilitators, including through helping to conduct and coordinate clinical trials.

<table>
<thead>
<tr>
<th>Type of involvement</th>
<th>Small pharmaceutical and biotechnology companies</th>
<th>Government agencies and research institutions</th>
<th>Academic and other research institutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product development / Commercialisation</td>
<td>24</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Contract research and manufacture</td>
<td>19</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Innovation</td>
<td>4</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Facilitation/Trial support</td>
<td>0</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total number of registered products and pipeline candidates</strong></td>
<td><strong>47</strong></td>
<td><strong>18</strong></td>
<td><strong>9</strong></td>
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**Late-stage product development and commercialisation**

Late-stage product development and commercialisation are almost entirely carried out by Indian pharmaceutical companies, with the sole exception being the Hilleman Laboratories, a public-private partnership of Merck & Co (MSD) and the Wellcome Trust, based in Delhi.

The Indian company is generally engaged late in the development process – once a candidate has been developed and taken to ‘proof of concept’ stage and beyond – to undertake further process development and scale-up for production, and to pursue product registration in India. This generally involves the company in-licensing a compound or vaccine candidate previously developed by another organisation, and often involves technology transfer from the licensor.
**Contract research and/or manufacture**

The second most common role played by Indian organisations is in contract research and manufacture. In this case, Indian organisations are either contracted early in the development process to provide discovery and pre-clinical services (medicinal chemistry, pharmacokinetics, toxicology, formulation development and chemical synthesis) and to manufacture products for clinical trials; or they are contracted solely as a manufacturing partner for end-stage development.

Early-stage contract research is also largely the preserve of pharmaceutical companies, however two government research institutes have begun to take on this work in collaboration with international product development partnerships (PDPs). The Drugs for Neglected Diseases Initiative (DNDi) has engaged the Central Drug Research Institute to help with early development of drugs against leishmaniasis and tuberculosis, and the International AIDS Vaccine Initiative (IAVI) and Translational Health Sciences and Technology Institute (THSTI) – an autonomous institute of DBT – have recently established the HIV Vaccine Translational Research Laboratory to develop new HIV vaccine approaches.  

**Innovation**

Despite a long-standing expectation that Indian organisations would become increasingly involved in the development of innovative products, this has proven to be elusive. Indian organisations have rarely acted as originators of new products. This is particularly true for vaccine research, where it is still the case that no Indian firm has developed a truly new, first-in-class vaccine. Although some firms have registered new vaccines without the involvement of international partners – and have begun to develop expertise in areas such as recombinant technology – all registered vaccines and the majority of candidates in the pipeline are based to varying degrees on existing licensed vaccines.

There are also very few instances where Indian organisations have delivered innovative new drugs. Four of the six registered drugs developed with Indian involvement were developed wholly by Indian organisations. However, in all four cases these drugs were either derivatives of existing product classes or new formulations of an existing product. None of these drugs has been registered outside of India, and one (Ablaquine) is no longer in production.

Another drug often held up as an example of indigenous Indian innovation is Synriam, a combination of artemolane and piperaquine developed and manufactured by Ranbaxy. But this drug was discovered and initially developed by researchers at the University of Nebraska in the US, and was transferred to Ranbaxy for clinical development by the Medicines for Malaria Venture (MMV), a malaria PDP, which invested $20 million in the drug’s development. When initial clinical results were disappointing, MMV dropped the candidate, but Ranbaxy proceeded to registration.

Indian organisations have had more success in truly innovative R&D in the field of diagnostics, where there have been success stories with indigenously developed technologies, including the micro-PCR diagnostic platform from Molbio Diagnostics, and the Dengue Day 1 rapid diagnostic test developed by the International Centre for Genetic Engineering and Biotechnology (ICGEB) and J. Mitra. All of the three newly registered diagnostic technologies from Indian firms have been developed without any input from international organisations.

**Facilitation and clinical trial support**

Aside from conducting early-stage research, Indian government agencies and research institutes also commonly play a role as research facilitators, for example through coordinating technology transfers, or by helping to support and coordinate clinical trials of prospective products for neglected diseases, including those being developed by Indian pharmaceutical companies. Many of the institutes under the umbrella of the ICMR, for example, play a particularly important role in conducting clinical trials for drug and vaccine development, and for the evaluation of new diagnostic technologies.

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\* Ablaquine, developed by the Central Drug Research Institute and licensed to Nicholas Piramal, is a derivative of primaquine; E-Mal, also developed by the Central Drug Research Institute and licensed to Themis Chemicals is a derivative of artemesinin; and Amphomul and Fungisome are reformulations of amphotericin B.
**Disease focus**

Over 90% of the products and product candidates in which Indian organisations are involved are targeted at one of six major disease areas: malaria; kinetoplastids; salmonella infections; tuberculosis; bacterial pneumonia and meningitis; and diarrhoeal diseases.

There is some alignment between this neglected disease product development activity and Indian government R&D investment priorities – malaria is still the most prominent focus, for example, and kinetoplastids (in particular leishmaniasis), tuberculosis and diarrhoeal diseases are in the top six most active areas. But the impact of other factors is also clear: products against salmonella infections (largely for typhoid fever), and bacterial pneumonia and meningitis collectively make up more than one-quarter (28%) of all Indian pipeline and registered products, despite receiving less than 1% of reported Indian government funding between 2008 and 2013. This is partly due to the impact of international partnerships (such as for MenAfriVac), but largely reflects the semi-commercial nature of a lot of Indian neglected disease R&D – three-quarters of these vaccines are being developed by small Indian pharmaceutical firms without any international collaboration.
For a country that is often characterised as overly bureaucratic, India has been a keen student of innovative policy solutions from around the world that might be used to improve its global health R&D outputs.

From open source, early-stage research initiatives to public-private partnership models and international partnerships, India has proven willing to experiment with new and innovative policy solutions to stimulate the development of new health technologies, particularly in the field of neglected infectious diseases.

**Partnering and the Department of Biotechnology**

Among a sometimes complicated web of collaborations, DBT is undoubtedly the key player in the wide range of new institutes, programmes and initiatives, many established in the last decade.

The DBT spends 70% of its budget on external research, with the remainder invested internally through DBT research centres. DBT’s efforts are heavily focused on partnership initiatives, and 30% of DBT’s total budget is set aside specifically for public-private partnerships. The majority of its partnerships are within India, although around 4% of DBT’s budget goes to international collaborations. Perhaps more than any other Indian government organisation, DBT looks internationally for ideas and models, with a primary emphasis on accelerating product development.

At the apex of DBT initiatives relevant to neglected disease R&D sits the Biotechnology Industry Research Assistance Council (BIRAC). BIRAC was established in 2012 as a not-for-profit organisation, and acts as DBT’s interface agency to “stimulate, foster and enhance the strategic research and innovation capabilities of the Indian biotech industry.”

Among other things, BIRAC is responsible for administering two distinct programmes that support the development of new products for neglected diseases:

- The **Small Business Innovation Research Initiative (SBIRI)**, which supports early-stage, high-risk research by companies with less than 500 employees. SBIRI funded Lifecare Innovations’ development of India’s first liposomal treatment for visceral leishmaniasis. Around 5% of SBIRI funded projects in 2011 were neglected disease-specific.

- The **Biotechnology Industry Partnership Program (BIPP)**, a cost-sharing programme that also focuses on high-risk research, targeting diseases of national importance. The BIPP is currently supporting Tergene Biotech’s efforts to develop an affordable, Asia-specific 15-valent pneumococcal conjugate vaccine.

The **Centre for Cellular and Molecular Platforms (C-CAMP)** is another organisation under DBT’s umbrella that is working at the interface of academia and industry. Designed as an ‘incubator’ for early-stage research, C-CAMP provides scientific infrastructure for a nominal fee, offering a flexible environment for representatives from the private sector and academia to collaborate. It specialises in the development of technology platforms, and is currently involved in high-throughput screening of drug targets for leishmaniasis.
DBT is also involved in a wide array of international partnerships with various countries, and at multiple levels. One of the longest standing collaborations is the **Indo-US Vaccine Action Program**. First established in 1987, it provides support to key vaccine development projects in India including those for rotavirus, malaria and dengue, in partnership with DBT and ICMR.\(^{18}\) Perhaps its most prominent success story is ROTAVAC©, advertised by its manufacturer Bharat Biotech as “India’s first indigenously developed rotavirus vaccine.”\(^{16}\)

DBT and the Wellcome Trust co-run the **The Wellcome Trust/DBT India Alliance**, which provides post-doctoral fellowship funding for biomedical research. The programme is co-funded by the Wellcome Trust and DBT, with a current funding commitment of £8 million per year.\(^{19}\)

The **International Centre for Genetic Engineering and Biotechnology (ICGEB; New Delhi)** started its life as one of two research centres making up the ICGEB, the other being in Trieste (Italy). The Delhi component was jointly funded by the Italian and Indian governments, with the dual purpose of carrying out high quality scientific research addressing the needs of the developing world, and training manpower in biotechnology. When the Italian government withdrew its partial financial support of the New Delhi centre in 2012, the Indian government announced that it would take over responsibility, and ICGEB has now been moved under the umbrella of DBT. Among other programmes, ICGEB has an international collaboration with the Emory Global Vaccine Centre to develop vaccines for tuberculosis and malaria, as well as a research collaboration with Genzyme India for malaria drug development.\(^{20}\)

### Other partnership initiatives

One of the few initiatives not to sit under the aegis of DBT is the **New Millennium Indian Technology Leadership Initiative (NMITLI)**. Established in 2000, NMITLI is India’s largest public-private partnership effort within the health R&D space, and is coordinated by CSIR. It aims to provide investment “in areas where India has a sustainable comparative advantage”;\(^{21}\) and is positioning itself to promote upstream (high-risk) R&D in areas of low market certainty. Like the (also CSIR-led) **Open Source Drug Discovery (OSDD)** initiative, one of NMITLI’s initial focus areas is the development of new targets, delivery systems and drug candidates for tuberculosis.

The **Drugs and Pharmaceutical Research Programme (DPRP)** is a programme funded by the Department of Science and Technology (DST), which like DBT also reports to the Ministry of Science and Technology. It is focused on supporting product development through public-private partnerships and soft loans to industry, with a particular emphasis on diseases of national relevance.\(^{22}\) Around 16% of funding between 2004 and 2009 was for neglected diseases, and a grant-in-aid from the DPRP supported the development of Fungisome, a single-dose reformulation of an existing drug (amphotericin B) now registered in India for the treatment of visceral leishmaniasis.
The Open Source Drug Discovery initiative

Established in 2008, the Open Source Drug Discovery (OSDD) initiative is a global consortium led by the CSIR, which aims to “provide a platform for collaboration where the best researchers from around the world can work together to discover affordable & novel therapies for NTDs [neglected tropical diseases] such as malaria, leishmaniasis and tuberculosis.”

The primary focus of the unit is on early-stage research and translation, which lend themselves to open source approaches. The OSDD aims to use crowd sourcing and social networking methods for drug discovery, “bringing together students, scientists, researchers, academicians, institutions, and corporations from across the globe”, and currently reports having over 7,900 participants from more than 130 countries. The unit has established a number of public-private partnerships with Indian pharmaceutical and biotechnology companies, and is collaborating with around 30 universities and colleges across India, as well as with international organisations. For instance, the unit has generated an annotated genome of *Mycobacterium tuberculosis* through a collaborative platform called Connect2Decode.

However, the OSDD’s proposed scope of activities goes well beyond drug discovery, with plans to progress its open source molecules into clinical trials (these will be conducted in the usual way, since clinical trials do not lend themselves to open-sourcing). To date, no compounds developed by the OSDD have advanced to the clinical trial stage.

The OSDD also plans to conduct trials of drug candidates developed by other organisations in order to hasten the delivery of new therapies to Indian patients. In such cases, the OSDD will in-license molecules under OSDD principles, so that registered products are made available to the generic industry on a non-exclusive basis. The first such example is PaMZ, a TB Alliance product, which will be the first Phase II trial for MDR-TB to be conducted in India (see text box).

The Phase IIb trial will be conducted in collaboration with the National Institute for Tuberculosis and Respiratory Diseases, an institute of ICMR.

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**PA-824 + moxifloxacin + pyrazinamide (PaMZ)**

Although established as an open source drug discovery initiative, the OSDD is moving outside this remit by conducting clinical trials of its own and others’ candidates – one of these external candidates is the new tuberculosis drug candidate PaMZ.

PaMZ is a combination of an experimental compound (PA-824) with an existing anti-tuberculosis drug (pyrazinamide) and the antibiotic moxifloxacin. PA-824 was developed by the TB Alliance, a US-based product development partnership. The TB Alliance continues to hold the rights to the PaMZ regimen, but have licensed it to the OSDD for continued clinical development and commercialisation in India.

The Phase IIb trial will be conducted in collaboration with the National Institute for Tuberculosis and Respiratory Diseases, an institute of ICMR.
The role of product development partnerships

A significant proportion of India’s successfully registered and pipeline products have sprung from collaborations with product development partnerships (PDPs). PDPs are public health driven, not-for-profit organisations that typically use private sector management practices to drive product development in conjunction with external partners. They aim to develop products suitable for developing country use, and may focus on a single neglected disease (for example, malaria in the case of MMV, or HIV for IAVI) or on multiple diseases (as in the case of DNDi or the Foundation for Innovative New Diagnostics).

PDPs were involved in half of all successful new vaccines and a third of all new drugs developed with an Indian partner since 2000. In fact, PDPs were a partner on every registered product where Indian organisations collaborated with international partners (all the remaining products were developed solely by Indian organisations).

PDPs also feature heavily in the Indian product pipeline, and were involved in just under half (48%) of all product candidates under development with an Indian partner organisation in 2013. As was the case for registered products, these partnerships are only for drugs (73% of all Indian drug pipeline candidates) and vaccines (46% of all Indian vaccine pipeline candidates); there is no PDP involvement in any of the diagnostic tests currently under development by Indian organisations.

PDPs were a partner on every registered product where Indian organisations collaborated with international partners.
Upstream research and the Indian Council of Medical Research

Basic research remains the bedrock of Indian investment in R&D for neglected diseases, and the ICMR is its leading proponent.

The ICMR is one of the oldest medical research agencies in the world, having been established in 1911 as the Indian Research Fund Association and adopting its current name in 1949, shortly after Indian independence.

The ICMR is the largest public sector funder of neglected disease R&D in India, and contributed a hefty 59% of all public investment between 2008 and 2013. This is significantly higher than the share of public investment provided by an organisation like the UK Medical Research Council, at 42% of UK public funding; although lower than the outsize share of public funding contributed by its counterparts in North America and Australia – the US National Institutes of Health and the Australian National Health and Medical Research Council are responsible for 87% and 82% respectively of their country’s public investment across the same period.

As a result of its majority contribution, the ICMR’s funding decisions have a major impact on the face of neglected disease R&D funding in India. With nearly nine-tenths (86%) of the ICMR’s investment in neglected disease R&D being directed towards pure basic research, it is a major driver of the prominence of basic research investment in the Indian funding landscape.

The proportion of research that is conducted ‘in-house’ is one factor that sets ICMR apart from its counterpart agencies. More than 90% of all ICMR investment in neglected disease R&D is invested internally, going to research conducted within the 32 research institutes, centres and units that make up the ICMR. Although headquartered in New Delhi, ICMR’s research institutes are located across the country, with each focused on a specific research area. Many of these are relevant to or exclusively focused on neglected diseases, with centres existing specifically for the study of tuberculosis (NIRT), malaria (NIMR), leprosy (NJILOMD), and cholera and enteric diseases (NICED), among others. Collectively, these four disease areas account for almost three-quarters of ICMR’s total investment in neglected disease R&D. Along with the National AIDS Research Institute (NARI), these ICMR institutes also play an important role in the other important function of the ICMR: conducting clinical trials to evaluate new diagnostics and support drug and vaccine development.

The ICMR provides a minority of its funding to other organisations through a mix of investigator-driven grants and targeted research initiatives, often established in collaboration with other Indian agencies. Although primarily a domestically-focused organisation, the ICMR also has collaborations with 13 countries and organisations outside India and has started to become involved in more formal collaborations, in which multiple agencies work together on a particular disease or product, such as the HIV Vaccine Translational Research Laboratory collaboration.
It is clear that the Indian government has a strong commitment to developing new products for neglected diseases, and this will very likely remain the case so as long as India has a significant domestic burden of these diseases. The signs are also good for India to retain this focus in the future: India is a signatory to the 2012 London Declaration on Neglected Tropical Diseases, and joined other World Health Organization member nations at the World Health Assembly of that same year in adopting a resolution for controlling, eliminating and eradicating 17 identified neglected tropical diseases. The test will be whether or not India is able to maintain this focus as its national wealth increases and the country’s burden of disease tips predominantly towards non-communicable diseases.

Currently, Indian government funding for neglected disease R&D is relatively strong – albeit low if measured in terms of its GDP. It is also increasing, unlike that of many of the more developed nations.

However, Indian government funding is heavily skewed towards basic research, reflecting the high proportion of funding (59%) coming from the ICMR, and investments are too often driven by researcher priorities. Currently, the primary approach for neglected disease product development varies from agency to agency and programme to programme, with limited strategic direction: in the words of one key agency head, “we are funding what comes to us.” Improving research prioritisation would offer very significant benefits, as would a rapid transition to a combination of top-down and innovative investigator-driven proposals, rather than relying predominantly on the latter. The NMITLI is a promising step in this direction, with its focus on strategic rather than investigator-driven priorities.

The ‘delivery’ side of India’s neglected disease R&D funding is also increasingly segmented, characterised by an overlapping web of initiatives, institutes and programmes. In part this appears to be related to what should be considered a positive: the Indian government’s broader aim of making India a “Drug Discovery and Pharma Innovation hub” by 2020, and its strong push to improve the innovation ecosystem in the country, in particular through improved translation and better linkage of the public and private sectors. But while the intent is positive, the outcome can be duplication, with multiple disconnected initiatives each trying to achieve very similar goals.

Despite the introduction of a plethora of strategies and programmes for translational research, some of this also appears to be translation in name only. For example, the ICGEB recently commented publicly that, “while we have given an impression of being a product development institute, we are essentially a basic research institute... when you concentrate on the basic research, it automatically provides leads to the product development.”

In order to capitalise on its undoubted advantages, India would benefit from a coherent and unifying strategy for neglected disease R&D – it is therefore promising that the DBT reports that they will have such a strategy framework in place very soon. And efforts to improve India’s innovation ecosystem are likely to deliver the greatest benefit from rationalising existing structures and initiatives rather than adding to them – this will be critical.

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There is an understandable desire to demonstrate India’s ability to develop new products without the assistance of international partners, and to establish that India can not only produce generics, but also do innovative R&D. But India is not alone in the world, and the pharmaceutical industry is increasingly about outsourcing, buying in and partnering rather than on solely in-house R&D. In the increasingly interconnected and collaborative field of global health R&D, India’s most successful future strategies are likely to be those that are targeted towards capitalising on its key strengths and areas of comparative advantage. Leveraging India’s skills in process development and incremental innovation to turn the best late-stage drug and vaccine candidates from around the world into high-quality, low-cost products for neglected diseases; and capitalising on its growing contract research skills to help with the global effort to translate promising new leads into robust clinical candidates.

Effectively engaging with international partners will remain an important feature, and is not inconsistent with a ‘Team India’ approach. India has a long and successful history of international collaborations, some of which have delivered India’s highest impact new products for neglected diseases. This success should be celebrated and expanded upon – including through actively pursuing partnerships with PDPs, as is being done by the Vaccine and Infectious Disease Research Centre of the Translational Health Science and Technology Institute.

There are many reasons to be positive about India’s contribution to the research and development of new products for neglected diseases, as well as some areas for improvement. The next decade represents an opportunity for India to play an even larger role than it currently does. The global health community will undoubtedly be watching with interest.
REFERENCES


