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Medicines in Health Systems: Advancing access, affordability and appropriate use

Chapter 4 – Annex 1

Innovation Tackling Antibiotic Resistance
Open Source Drug Discovery Initiative in India

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Innovation Tackling Antibiotic Resistance

The challenge of growing antibiotic resistance has placed the effectiveness of antibiotics in treating infections in jeopardy. In so doing, the benefits of modern day medicine, from surgical prophylaxis to chemotherapy, have been compromised. There exists, however, a paradox between patients receiving unnecessary antibiotic treatment and those who go without such access. Across the pharmaceutical value chain, the challenge of ensuring access to needed antibiotics might be characterized by therapeutic, financial and structural barriers. Overcoming each of these barriers, this paper describes innovative approaches to tackling antibiotic resistance.

Therapeutic access most directly relates to the R&D of new antibiotics. The dearth of novel antibiotics over the past few decades is symptomatic of a stalled pharmaceutical pipeline, which could be improved by the sharing of resources, risks, and rewards. India’s Open Source Drug Discovery Initiative (OSDD) is one example of these three “Rs” in action, and this initiative has built a network of online and wet-lab collaborators to innovate treatment by crowdsourcing contributions that advance pre-clinical research, publicly funding clinical trials for diseases such as tuberculosis and malaria, and eventually licensing scale-up at close-to-marginal cost pricing. Financial access requires not only ensuring the affordability of needed antibiotics, but also a price point that enables the sustainability of that treatment’s supply. A solution that delinks the return on investment from volume-based sales is crucial to addressing both the supply- and demand-side barriers to financial access. Finally, structural access is linked to the delivery system of antibiotics and involves the relationships among prescriber, dispenser and consumer. Innovations seeking to improve structural access can improve the rational use of antibiotics by targeting the consumer, but must not neglect the need to examine the patterns, incentives, and guidelines that influence the behavior of health providers. The Antibiotic Smart Use (ASU) Project in Thailand is an example of such a multi-pronged approach. Working through a staged implementation process, ASU has seen impressive declines in inappropriate antibiotics use by substituting culturally appropriate herbal remedies for viral or self-limited infections when antibiotic use is unnecessary, improving diagnostic capabilities by providing illuminators, and introducing a more robust discussion of the rational use of medications among local health providers. The case studies throughout this paper examine the issues of therapeutic, financial, and structural access along the pharmaceutical value chain and illustrate innovative approaches that work towards tackling antibiotic resistance.
Open Source Drug Discovery Initiative

Generic production of medicines has played an important role in ensuring affordable access to those in need. Much concern has arisen in India’s transition in 2005 to implementing the World Trade Organization’s Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement under which the country recognized patents on pharmaceutical products.

Prior to this transition, India’s Council on Scientific and Industrial Research (CSIR) had developed alternative and less costly processes for manufacturing triple-drug therapy for AIDS and transferred this technology to Cipla, an Indian generic drug firm (1). In 2001, Cipla’s offer of triple-drug therapy for AIDS at $350 per patient per year ushered in generic competition with multinational companies that had failed to provide affordable pricing on these drugs (2). By 2008, Indian generic firms accounted for nearly 90% of the purchase volumes of antiretroviral drugs globally (3). The world’s reliance on sourcing life-saving medicines from Indian generic companies has prompted much attention not only to how TRIPS flexibilities might apply to India’s treatment of intellectual property rights, but also to what alternative pathways for bringing needed medicines into health markets might work.

Starting in 2008, CSIR piloted the Open Source Drug Discovery Initiative (OSDD) to innovate for neglected diseases, first targeting tuberculosis and later broadening its scope to projects on malaria, filariasis and leishmaniasis. OSDD ambitiously seeks to change the way knowledge is produced, owned and harnessed in order to reduce global health inequities and provide affordable healthcare for all. Through a model of open source innovation and collaboration, OSDD is reengineering the means of bringing a new drug to market by sharing resources, risks and rewards (4).

OSDD shares resources through an online collaboration platform---a semantic, web-based, wiki portal built with donated support from InfoSys---to which participants agree through a click-wrap license not to remove for proprietary gain knowledge generated from the online commons. Crowdsourcing their collective talents, this platform brings together a network of scientists, students and universities across different countries and disciplines. To date, this includes over 7600 registered participants from 130 countries; 10 engaged CSIR labs, 39 academic institutions and 14 industry partners; and signed partnerships with product development partnerships, from the Drugs for Neglected Diseases Initiative to the TB Alliance and Medicines for Malaria Venture. Presently OSDD hosts over 240 projects, led by over 180 principal investigators.
The network infrastructure bridges work both on-line in virtual collaboration and offline in wet labs. On-line, well-defined and coordinated “work packages” reframe large complex problems into more discretely manageable tasks. These collaborations range from projects on the experimental gene expression of targets and the optimization of successful hits to pre-clinical toxicity catalogs and profiles of an experimental drug. OSDD also maintains publicly accessible databases, including an integrative genomics map of *Mycobacterium tuberculosis*.5 Engaging its on-line community, OSDD recently conducted a YouTube Video competition on “The Need for New Drugs for TB.” One product from the OSDD network has already involved network volunteers, who re-annotated the entire *M. tuberculosis* genome, telescoping 300 person-years of effort into four months (6).

Off-line OSDD has sought to line up the infrastructure to translate early stage discoveries into first-in-human trials, facilitating the transfer from basic research scientists to those who might translate this work into a druggable compound. Biological resources are available through such collections as a plant-derived, anti-infective library of compounds for screening and an open access repository of *Mycobacterium tuberculosis* clones. The Open Source Drug Discovery Initiative has also assembled a diverse small molecule repository, synthesized by a community of synthetic chemists, numbering about 80 from 35 institutions.

Risk is shared through OSDD with US $12 million in Indian government funding and private sector donations from in-kind IT support from Infosys to grants from foundations like the Sir Dorabji Tata Trust. Funding is, in turn, released to projects, both as awards to principal investigators or as projects commissioned and coordinated by OSDD itself. OSDD uses the online portal to accept and process applications through an open peer review format. The Tata Trust grant has supported students and early career researchers to participate in crowdsourcing their efforts in the open source discovery of drugs for neglected diseases.

The OSDD initiative also shares rewards, both at the individual and collective levels. Individual rewards have ranged from activities encouraging women scientists to small prizes in the form of credit for phone usage and Internet access. Largely supported by the Indian government, scientists and students alike contribute voluntarily to the network’s activities. The collaboration platform tracks the contributions of individuals through a micro-attribution system that is peer reviewed and awarded through defined credit points. Those contributing more than 1% to the online community project receive authorship and acknowledgement in subsequent publications. Moreover, the best performers in the OSDD community
have leveraged their participation into competitive applications for fellowship training in programs abroad.

By publicly financing the R&D of novel antibiotics, OSDD seeks fair returns from this investment by keeping drug costs affordable through generic licensing. Along these lines, OSDD has secured a non-exclusive right to PA-824 from the TB Alliance for testing this drug in a new combination regimen (pyrazinamide + moxifloxacin + PA-824) in Phase IIB clinical trials. This has the potential of shortening TB treatment from six to two months. To advance its virtual R&D pipeline, OSDD engages partners in such undertakings in two ways: 1) it contracts service providers on a “work for hire” basis, and 2) it collaborates with partners that donate their services, with the resulting intellectual property belonging to the OSDD community.

OSDD's non-hierarchical structure carries over to its governance. A Science Support Group, comprised of seven core members and people drawn from the OSDD community, guides the direction of the OSDD initiative and makes decisions on policies governing its open access repositories.

Though the vision and mission of OSDD is to improve innovation for neglected diseases and provide affordable healthcare to all, its efforts have also inspired a generation of young minds. By sharing resources, risks and rewards, not only is OSDD developing a publicly owned R&D pipeline for bringing new health technologies to market, but it is also building a pipeline for training its future scientists.

References

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