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<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>List of Abbreviations</td>
<td>ii</td>
</tr>
<tr>
<td>Acknowledgments</td>
<td>iii</td>
</tr>
<tr>
<td>Executive Summary</td>
<td>iv</td>
</tr>
<tr>
<td>1. Understanding the context</td>
<td>1</td>
</tr>
<tr>
<td>Challenges for neglected tropical diseases and drug development</td>
<td>1</td>
</tr>
<tr>
<td>Open source: from software to neglected diseases?</td>
<td>2</td>
</tr>
<tr>
<td>2. Open source for neglected tropical disease research and development</td>
<td>5</td>
</tr>
<tr>
<td>in practice</td>
<td></td>
</tr>
<tr>
<td>What has been tried?</td>
<td>5</td>
</tr>
<tr>
<td>What have we learned?</td>
<td>8</td>
</tr>
<tr>
<td>The intellectual property challenge</td>
<td>10</td>
</tr>
<tr>
<td>3. How can open source advance neglected</td>
<td>13</td>
</tr>
<tr>
<td>tropical disease research and development?</td>
<td></td>
</tr>
<tr>
<td>Incentives and applications</td>
<td>13</td>
</tr>
<tr>
<td>The size of the prize</td>
<td>15</td>
</tr>
<tr>
<td>Looking ahead</td>
<td>16</td>
</tr>
<tr>
<td>Appendices</td>
<td></td>
</tr>
<tr>
<td>Appendix A. Participants in interviews</td>
<td>20</td>
</tr>
<tr>
<td>Appendix B. Profiles of open source neglected tropical disease research</td>
<td>21</td>
</tr>
<tr>
<td>Appendix C. Suggestions from expert interviewees</td>
<td>23</td>
</tr>
<tr>
<td>Notes</td>
<td>25</td>
</tr>
</tbody>
</table>
**List of Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDD</td>
<td>Collaborative Drug Discovery</td>
</tr>
<tr>
<td>DNA</td>
<td>deoxyribonucleic acid</td>
</tr>
<tr>
<td>GSK</td>
<td>GlaxoSmithKline</td>
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<td>IOI</td>
<td>Initiative for Open Innovation</td>
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<tr>
<td>IP</td>
<td>intellectual property</td>
</tr>
<tr>
<td>IT</td>
<td>information technology</td>
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<tr>
<td>NTD</td>
<td>neglected tropical disease</td>
</tr>
<tr>
<td>OS</td>
<td>open source</td>
</tr>
<tr>
<td>OSDD</td>
<td>Open Source Drug Discovery</td>
</tr>
<tr>
<td>PDP</td>
<td>product-development partnerships</td>
</tr>
<tr>
<td>R&amp;D</td>
<td>research &amp; development</td>
</tr>
<tr>
<td>SGC</td>
<td>Structural Genomics Consortium</td>
</tr>
<tr>
<td>TB</td>
<td>tuberculosis</td>
</tr>
<tr>
<td>TDI</td>
<td>Tropical Diseases Initiative</td>
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<tr>
<td>TDR</td>
<td>Special Programme for Research and Training in Tropical Diseases</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
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Open source approaches have had remarkable success in creating high-quality and low-cost software and enabling mass collaboration online; they have been responsible for much of the technology that powers the Internet. This landscaping paper discusses open source approaches for research and development (R&D) for neglected diseases and their potential to lower costs and R&D time frames, increase collaboration, and build a knowledge commons. The paper describes existing initiatives and debates and suggests how readers and the global health community might better make use of open source approaches.

After setting the stage, we consider initiatives that have actually used open source for neglected disease research, and how. We discuss several significant applications partially or wholly utilizing the open source approach, like India’s Open Source Drug Discovery project, the Patent Lens project and Initiative for Open Innovation, Collaborative Drug Discovery, and TDR Targets. While most have demonstrated potential, hard evidence of impact is limited thus far.

From the applications and literature to date, we suggest that the open source approach as applied to neglected-disease R&D comprises several linked but distinct functionalities: open access, open collaboration, and “open rules.” We diagram several open source initiatives against these functionalities and a simplified drug development pipeline and suggest that while open source is already showing value in the discovery and preclinical stages, its application in later stages, such as clinical trials and filing, is unclear.

The next part of the paper discusses challenges, incentives, and potential applications in applying open source. The importance of estimating the value of the open source approach is emphasized; tracking this value empirically may yield dividends.

We close with suggestions for short- and longer-term initiatives to better apply open source for neglected-disease research. In the short term, three next steps are suggested. First, develop detailed profiles of open source initiatives for neglected-disease R&D, incorporating purpose-developed evaluations and metrics. Second, develop and prioritize value propositions for more substantial and long-term investments in the area; value propositions such as those discussed in the next paragraph might be developed collaboratively with informed stakeholders. Third, start a demand-driven website incorporating a group weblog that will act as a focal point for disparate threads of discussion, as well as for seeding connections and a sense of community.

We propose three main longer-term initiatives (a number of other possibilities are discussed in the text and appendices). First, implement metrics and models for measuring accomplishments and potential cost savings across open source initiatives and for providing social and professional value for individual research contributions to open source initiatives. Second, develop a horizontal initiative—a platform that enables sharing of data and pooling of interests—for scientific and other communities currently working in different disease areas and organizations. Third, invest in better tools that move the whole field ahead, such as computational models or an open source clinical trials or epidemiology database. High-profile leaders and institutional buy-in will be essential in implementing any of these initiatives successfully.

The debate as to how best to use open source approaches for neglected-disease R&D is still open. However, we have identified specific areas where the approach seems to have value, as well as corresponding follow-on activities. Clarifying concepts and coalescing a community in this area would be worthwhile. By gaining a deeper and more realistic understanding of the potential and challenges of open source for neglected-disease R&D, the approach could evolve and become important for creating a healthier world.
Challenges for neglected tropical diseases and drug development

Neglected tropical diseases (NTDs) constitute a large fraction of the world’s disease burden, yet they receive only a small fraction of global R&D spending. This occurs because private and public purchasers in the developing world have limited ability to pay for treatments, and government and donor financial support for neglected diseases is limited. While the amount spent on NTD R&D has increased over the past decade and has involved new actors, certain events, such as GAVI’s difficulty in gaining follow-on financing after a decade in which it saved an estimated 5 million lives through childhood immunizations, suggest limits to simply increasing funding.

From the perspective of those doing the R&D, especially those motivated by commercial success, the “business model” for creating new drugs is in trouble. The creation of new drugs has flatlined, despite increased expenditure on drug development, while pressure to control drug prices is increasing. It can take over a decade to get a new treatment onto the market, with clinical trials being expensive and time-consuming. It has been argued that intellectual property (IP) issues, such as patent costs, complexity, and breadth, increase the cost and uncertainty of innovation. The pharmaceutical industry as a whole is facing serious financial difficulties, and the search is on for new models that deliver new health solutions with greater speed and less cost.

From the perspective of those concerned with reducing global disease burden, there is a lack of R&D focus on diseases that matter rather than diseases that pay. Commercial entities doing R&D might acknowledge this fact, while pointing out that the cause lies in a lack of incentives to innovate in this area. Globally, there is much duplication of effort in the current model, through not sharing clinically relevant knowledge and scientific progress. All this leads to high costs, waste, and delays in progress for NTD R&D.

Open source (OS) is a way of sharing data, expertise, and resources to increase collaboration, transparency, and cumulative public knowledge. It has been used in the software field since its infancy half a century ago and has been tried in the biopharmaceutical field for the last decade. In the long run, it may help minimize duplication of effort and create a “commons” of knowledge and data from which future innovation can grow. Based on its demonstrated success in the software field, and the remarkable growth of open innovation and Web 2.0 resources in the first decade of the 21st century, there has been speculation on what open source might provide for health R&D in general and for NTDs in particular. This paper discusses the modest efforts in this area to date; outlines the key debates on its potential to stimulate more innovation in NTD R&D; and suggests barriers, enablers, and recommendations for making use of this approach.
Open source: from software to neglected diseases?

Open source is a term derived from the software world, where it describes software whose source code is publicly available and freely redistributable. The source code is the “recipe” that programmers write to specify the desired operations of a computer or other programmable entity—a step-by-step description that defines what the software does.

The Open Source Initiative describes open source as “a development method for software that harnesses the power of distributed peer review and transparency of process”; it details an Open Source Definition that includes access to source code, the right to redistribute without charge, permission to create derived works, no discrimination against users or fields of application, and several other clauses.9 Open source licenses (of which there are many types) often have a “viral” quality, which specifies that users must be allowed to modify the source code and that such modified versions of the original program must be distributable under the same license terms as the original software. (We nuance this definition for neglected-disease R&D near the end of this section. Note that proprietary platforms can access open source components.)

Originally, open source in software grew out of the frustration of researchers who saw their creations being privatized by commercial entities, which both made it more difficult for researchers to innovate and limited the social benefit and ethos of sharing that they held dear.10 Later, various forms of open source were adopted by commercial and government enterprises and formed the basis for entirely new business models.11 Applications of open source (in both software and R&D) also draw from the open science movement and culture, which began centuries ago and is reinventing the process of discovery today.12

Four advantages that open source approaches provide are verification, collaboration, cost reduction, and the creation of a commons. Since the source code is open, it can be verified against errors and undesired features by a larger community, in a sort of “distributed transparent peer review”; the process of production itself can also be more transparent. Collaboration can easily take place across organizational boundaries and attract contributors with differing monetary and nonmonetary motivations; this is often enabled by splitting up large projects into numerous subprojects that can be tackled relatively independently. Open source software is usually much cheaper to acquire than proprietary software (though this comes with strong caveats: there may be a cost-based charge for access; fee-based products and services can sometimes be created from an initially low-cost open source base, and the total cost of ownership can rise dramatically when customization and support time are factored in). Over time, a commons of knowledge and capability can be created, since each piece of OS software is forever open for others to use, learn from, build on, and adapt for local contexts—the risks of vendor lock-in and barriers to knowledge access are reduced.

The success of open source has been attributed to various factors, including tapping a range of commercial and noncommercial motives, reducing transaction costs, functioning as a loss leader for add-on services, making contributions and error corrections easier, and taking advantage of the low cost of replicating software.13 However, skeptics in the software field point to the many open source projects that do not succeed and the requirement for commercial revenues to fund large-scale software investment and quality testing. Even open source enthusiasts advocate a realistic understanding of the skills and experience required to apply the approach successfully: “An open source license does not guarantee that hordes of active developers will suddenly volunteer their time to your project, nor does open-sourcing a troubled project automatically cure its ills.”14

Successful and well-known open source projects include the following:

• The Linux operating system, started as a student project in 1991 and now globally used by researchers, enterprises, and governments
• Apache and the “LAMP stack,” a set of open source tools that collectively power much of the Internet
• The Firefox web browser, managed by the non-profit Mozilla Foundation, with a market share approaching 25%
• Wikipedia, for which the source code and content is freely available
• The Android mobile operating system, based upon a modified version of Linux

While notable benefits have been achieved in the software field and many large companies like IBM use open source, proprietary models are still widespread; many enterprises combine open source with closed source and patents. To take a well-known example, Google uses Linux and other open source tools extensively in its software infrastructure, while having proprietary layers of code that operate on top of this infrastructure. Open source will almost certainly play a large and growing role in the evolution of software and the Internet; it is less clear how the relative mix of open, proprietary, and hybrid business models will evolve.

When translating open source ideas to global health R&D, similarities are evident. Software and biotechnology/pharmaceutical R&D are both knowledge-intensive fields with global communities of practice. Like software development, health R&D has a large virtual element, including software, biodata, and genomics and structural information; this facilitates Internet-enabled collaboration, which is a core feature of most open source applications. Both fields display a rapid pace of innovation that draws from a large commons of basic R&D; both fields have a diverse set of actors, from small start-ups to giant multinationals.

However, there are very significant differences. Most obviously, lab equipment and clinical trials are much more expensive than the capital equipment required for software development. Safety and regulatory issues play a larger role in health R&D and increase time, risk, and cost. Some researchers have found a greater reliance on patents for IP protection among biotechnology and medical device start-ups, as compared to software and Internet start-ups. Patents themselves are expensive and complex to prepare, register, and maintain; software receives copyright protection at minimal expense and often uses relatively simple licensing schemes. Smaller (and even solo) software enterprises are viable in the marketplace and are often accustomed to online, open collaboration. The modular nature of modern software engineering makes it easier to partition and distribute the tasks involved in software innovation. The R&D time frame and risk is arguably larger for a typical drug as compared to a typical software project—sometimes much larger, especially when testing and manufacturing stages are taken into account.

There is one other key difference, which lies in the very definition of “open source” itself when translated between fields: what is the “source code” at each stage of neglected-disease research? While some working in synthetic biology make the analogy of DNA as source code, the situation is actually more complex. In software, the source code is the product, while in biology, there are many relevant levels of description and analysis, from DNA to structural genomics, protein interactions, metabolism, and so forth—all interacting in complex ways and requiring a long and expensive process to go from description to approved product.

With this difference in mind, and drawing from applications and literature to date as discussed later in this paper, we suggest that the open source approach for neglected-disease R&D can be seen as comprising three functionalities: open access (to data), open collaboration (across organizational and geographical boundaries), and “open rules” (that enable or mandate various forms of openness). The term open source has been used in all these three senses in the context of application to neglected-disease R&D; clarifying the three functionalities helps to distinguish different aspects of the open source approach. This paper may use the terms open source or open source approach in all three senses, distinguishing them by context as appropriate. Ambiguity
remains in the use of this term in biomedical R&D, and developing consensus around terminology (or developing new and more specific terms) may be helpful as the field develops.

Given these similarities and differences between open source in software and neglected-disease R&D, the applicability of open source to biotechnology and neglected-disease R&D has been hotly contested, and many questions arise. How applicable is the model to neglected-disease R&D, and can it help address key gaps in the field? What are the key points of difference? Is the model only useful for unblocking knowledge gaps, or does it also have a role in bringing new health solutions to market? To what extent could it ameliorate cost constraints—for example, by reducing duplication of effort due to ignorance of work going on elsewhere, and hence putting fewer drugs into costly trials that others already have reason to believe won’t work?

The remainder of this paper addresses these questions. We first discuss examples of open source for NTD research, and then analyze the merits and drawbacks of the open source model in this field. We close by highlighting why open source is important for NTDs, and what readers may consider doing about it.
What has been tried?

A number of initiatives drawing from open source approaches have been tried for NTD R&D. Some of these explicitly draw from open source experiences in the software world, while others grew organically out of research needs and may not use the term open source at all.

What initiatives have been launched, how have they worked, and what can be learned? The remainder of this section describes a range of initiatives, selected for their perceived relevance, achievements, novelty, and momentum. (Additional detail is included in appendix B and in the references cited.)

We emphasize that these descriptions rely on public information and that due to time and resource limitations, evaluating the relative success of these initiatives was outside the scope of this paper, as was producing a comprehensive list of all potentially relevant initiatives and platforms. More detailed profiles, with an added evaluation component, are one of the short-term recommendations made at the end of this paper.

While reading through the initiatives, it may be useful to keep in mind three related functionalities of the open source approach as applied to neglected-disease R&D: open access (to data), open collaboration (across organizational and geographical boundaries), and open rules (that enable or mandate various forms of openness). These functionalities are discussed further and diagrammed with respect to the initiatives later in the section.

Open Source Drug Discovery

Year started: 2008

Funding: the Government of India has committed $35 million towards the project, of which $12 million has been released to date (according to the project’s public website).

India’s Open Source Drug Discovery (OSDD) project aims to build a collaborative online platform where contributors can collectively discover new therapies for neglected diseases. It is currently focused on tuberculosis (TB) research. With thousands of contributors, an active community, and high-profile scientific leaders, it has garnered significant attention globally. Indeed, interviewee Stephen M. Maurer of the University of California, Berkeley commented, “One possibility would be to invest in expanding OSDD. They already have more money and visibility than anyone else, and splitting the open source effort in two can only weaken both halves. As always, the investment will have to be made shrewdly . . .”

The project’s online hub organizes contributors who do small pieces of work to collectively complete larger tasks—a classic open source strategy. It has succeeded in producing a browser and an annotated map of the TB genome, though not without controversy regarding validation of the results. While the approach has a sophisticated IT infrastructure and seems to have the potential for significant achievement, this is not yet proven. The standardized way data gets deposited is promising, as is the energy to create networks and potential products. Two intriguing features are the grouping of small tasks into a set
of stages that parallel a traditional drug development pipeline and a reputation system that ranks contributions based on peer review and gives higher-ranked contributors more privileges in the OSDD process.\textsuperscript{18}

OSDD illustrates several factors that can make an open source collaboration work; the data lends itself to standardization, the project lends itself to granular decomposition so people can work on small pieces and collectively contribute to a larger goal, there is a culture among the researchers that responds to reputation-based incentives, and individual contributions can be validated in a cost-effective way. Finally, much of the “product” on which members work can be effectively described, shared, and collaborated on through online platforms.

**Collaborative Drug Discovery**  
*Year started: 2004*  
**Funding:** N/A (though in 2008 announced a $1.9 million grant “from the Bill & Melinda Gates Foundation to develop a collaborative database that will enable scientists to archive, mine, and selectively collaborate around their research data to discover new cures for tuberculosis (TB)”).

Collaborative Drug Discovery (CDD), a California-based company, has created a platform for selective sharing of collaborative drug discovery data. It allows preclinical biological and chemical drug discovery data to be securely stored, shared, analyzed, and collaborated upon through a web interface. It can be used to build private, semiprivate, or public virtual drug discovery networks, thus allowing for both open source and closed source approaches and providing tools and a platform that are useful for both.

This platform has been used in, for example, tuberculosis research, with outcomes including “novel insights into the key 1D molecular descriptors, 2D chemical substructures and 3D pharmacophores related to Mtb activity based on public data.”\textsuperscript{20} The platform’s choices for how public to make data (public, semiprivate, or private) suggest that, as an empirical experiment, it may be worth analyzing what kinds of projects and data are made public and which kept private. Interviewee Barry Bunin of CDD points out, “Not to be self-serving, but doing open drug discovery for neglected diseases in a practical way (that respects IP when it is sensitive, but makes it open when it should be) is not trivial and not something others are doing.”

**Cambia’s Patent Lens and Initiative for Open Innovation**  
*Year started: 1991 (Cambia), 1999 (Patent Lens), 2009 (Initiative for Open Innovation [IOI]*)

**Funding:** sources include several government and granting agencies, including the Bill and Melinda Gates Foundation ($3 million in 2008) and the Lemelson and Rockefeller Foundations.\textsuperscript{21}

Cambia is a nonprofit institute based in Australia with a mission “to democratize innovation: to create a more equitable and inclusive capability to solve problems using science and technology.” One of its older projects is Patent Lens, an open access, free full-text patent informatics resource, which made searching biotech patents easier when released.\textsuperscript{22}

A newer project is IOI, which aims to “create, test, validate and support new modes of collaborative problem solving” in the life sciences, with a focus on navigating complex IP landscapes. (A previous project, BiOS, attempted to popularize open source licenses for biotechnology projects, in a manner similar to existing open source licenses for software. The project has faced challenges, such as motivating usage of the licenses,\textsuperscript{23} and uptake has been low to date.)

Patent Lens and IOI can be viewed as “innovation cartography tools” that provide maps to understand patents and their uses. They support risk assessment and avoidance and decrease information asymmetry for small players (as does another project, the freely available IP Handbook). As such, they may have a quasi–public-good character as tools that make innovation easier for all players. They focus on the IP aspects of developing new health solutions and, as such, are complementary to initiatives like OSDD and CDD, which are more focused on drug discovery and development.
**Tropical Diseases Initiative**

*Year started: 2004*

**Funding:** N/A (appears to have little initiative-specific funding).

The Tropical Diseases Initiative (TDI) modeled itself explicitly on open source approaches as early as 2004 and produced a set of potential drug targets from pathogen genomes that have been released under a Creative Commons license for further work.24,25 Thus far, participation in TDI’s approach appears to be low relative to the other initiatives discussed in this section. As TDI itself notes in discussing its incentives to create a set of potential drug targets, “... a major stumbling block for open source drug discovery has been the absence of a critical mass of preexisting work that volunteers can build on incrementally.” Investigating why TDI does not yet appear to have achieved a critical mass of participation and support might provide lessons for future initiative design. On a promising note, many of the people from TDI are listed as advisors for the Synaptic Leap project,26 which has received modest funding for open source research into schistosomiasis.27

**Structural Genomics Consortium**

*Year started: 2003*

**Funding:** the Structural Genomics Consortium (SGC) states funding of roughly $30 million per year from many partners, including several Canadian and Swedish research organizations, GlaxoSmithKline (GSK), Merck, Novartis, the Knut and Alice Wallenberg Foundation, and the Wellcome Trust. SGC is a public-private partnership doing basic science for drug-relevant proteins and placing all information, reagents, and know-how into the public domain. While not an open source approach in its research operations, it is a productive research consortium that is open source in its products and IP policies. As such, it may have lessons on practical ways to balance between open and closed approaches and deal with potential rivalries, as may other consortia such as the Human Genome, SNP Consortium, and HapMap Projects. The open consortium approach might be built on for precompetitive NTD R&D.33

The SGC’s main goal is to determine 3D structures of proteins cost-effectively on a large scale; NTD-related proteins are one of many areas of focus.34 It targets proteins of medical relevance and human parasite proteins and is responsible for, respectively, over 25% and 50% of structures in these areas deposited into the Protein Data Bank each year. SGC has argued for more open access tools and public-private partnerships, and itself uses...
OPEN SOURCE FOR NTD R&D IN PRACTICE

open access and interactive publication of 3D structures.\textsuperscript{35,36} It has a policy to not file for patent protection on any research outputs and seeks the same commitment from research collaborators. However, it leaves open the possibility of proprietary drug discovery and development building on its research outputs.

**Related initiatives**
A number of other initiatives with aspects of the open source approach have occurred over the last few years:

- The release of neglected-disease drug information by pharmaceutical companies such as GSK and the development of patent pools.\textsuperscript{37,38}
- Collaborative tool and community development (e.g., Sage Bionetworks, Bioinformatics.Org, and ChemSpider). Other open source platforms with commercial linkages are under development, such as OpenClinica for clinical trials.
- Programs by basic science organizations, such as the National Institutes of Health’s (NIH’s) Molecular Libraries Program for large-scale screening of potential chemical probes. University-based initiatives other than those mentioned previously also exist, such as the Distributed Drug Discovery project.\textsuperscript{39}
- Innovative licensing approaches such as humanitarian licensing schemes, Cambia’s BiOS license, and the Science Commons Biological Materials Transfer Project,\textsuperscript{40} all of which aim to provide alternative IP arrangements—balancing direct rewards for R&D with long-term social value and development of a commons of R&D, which can seed future biomedical innovation.
- Product-development partnerships (PDPs) such as DNDi (Drugs for Neglected Diseases initiative), a neglected-disease R&D organization that has advocated for an open model to development and has used many developing-world networks in its R&D. Its IP policy includes the objective “. . . to develop drugs as public goods when possible,” while being pragmatic and negotiating with the best interests of patients in mind.\textsuperscript{41} While not an open source approach itself, it represents an existing model extending through the clinical stage that may work well in partnership with open source approaches.

There is significant scope for further investigation of open source approaches that have (and have not) worked in practice. Interviewee Claire Driscoll of the NIH believes that “credible success stories would help convince companies, public-private consortia, academics, etc., to consider open innovation approaches for drug development projects, including ones aimed at commercializing new therapeutics for neglected diseases.”

**What have we learned?**

What can we learn from the examples above? First, they cover a range of activities. While the term open source has been used for many activities, making distinctions is helpful.

As mentioned earlier, one way of categorizing the examples is to think of “three kinds of open”: open access, open collaboration, and open rules.\textsuperscript{42}

- **Open access:** free and open access to data. Examples include the release of data by pharmaceutical companies (e.g., GSK) and the tuberculosis-related output of OSDD—but not the process OSDD used to generate this output. (The TDR Targets database, while open access, also has elements of open collaboration in its process.)
- **Open collaboration:** collaborative workflow across organizational boundaries, often harnessing many volunteers through online systems. OSDD is a prime example; its core workflow includes thousands of collaborators from a range of institutions.
- **Open rules:** a set of rules (contractual, IP, licenses, etc.) that mandate various forms of openness. Examples include Cambia’s BiOS license, the Creative Commons license used by TDI, and SGC’s foundational agreement that outputs will be made public. Cambia’s Patent Lens and IOI can be seen as *enabling tools for open rules.*
These categories are diagrammed in figure 1, along with several open source initiatives. Each initiative’s vertical position suggests the category with which it is most associated. The horizontal extent of each initiative indicates its area(s) of focus along a simplified drug development pipeline. (Italicized initiatives, while not explicitly open source, have aspects of the open source approach as discussed above.)

To create R&D solutions, open access is not enough. Open collaboration can bring in the additional resources required to understand and make use of raw information. Open rules serve to keep enabling tools for follow-on innovation open, and to provide a set of customs and legal practices that ensure a project can harness open collaboration, while maintaining focus and capturing value to recoup original investments.

Each of these open approaches can have gradations; for example, for open access, Creative Commons and Science Commons define a spectrum of rights in a “some rights reserved” approach, from which a user of the rules can tailor a rule set to their preference.

(We note that approaches like InnoCentive that present challenges for interested parties worldwide to respond to—often referred to as “crowdsourcing”—can be viewed as a limited type of open collaboration for scientific problem solving.43 One might call such systems “open input,” as their key goal is to harness innovators worldwide to solve specific challenges, in many cases without releasing IP or contributing to public knowledge development. The term open innovation, as publicized by Henry Chesbrough and others, is a more general approach that argues that organizations should bring in more external ideas and make underused internal ideas more available externally, and evolve business models and collaborations accordingly.44)
A second observation is that the open source activity for neglected-disease R&D to date has been heavily weighted toward the discovery (or precompetitive) stage of R&D, with little activity in the development stage and none in the delivery stage (e.g., clinical trials and filing). This is largely a consequence of the greater investment required and reduced reward for collaboration in later stages of drug development, as well as incentives to hold exclusive IP rights at later stages in order to obtain a higher return on investment.

Figure 1 illustrates this preponderance of open source activity in earlier stages; note that the initiatives plotted fall mostly in the left half of the diagram, representing discovery and preclinical work. The right half of the diagram is the more controversial half, where it is not clear whether and how open source approaches can be used to take new treatments through clinical trials and to market.

Thirdly, looking at the diagram and the variety of projects discussed above suggests that there is, at present, no single model of an integrated open source alternative to proprietary R&D. Rather, several different initiatives have been tried, each of which implements some aspect of the open source approach. A skeptic might contend that these form a hodge-podge of ideas and initiatives, from open databases to data-sharing rules to web collaboration platforms, that have only some kind of “openness” in common. The reality may lie in between: a variety of initiatives to date suggest methods and platforms that could affect different parts of the traditional R&D model, and implementing open source ideas will likely be an evolutionary process.

Lastly, most of these initiatives relied on donor and government funding. CDD is an interesting partial exception, though its success remains to be gauged—it seems to have succeeded in providing a virtual collaborative platform that can be used for open source R&D, aided by the lower costs to operate a purely virtual platform. The question of where private sector capital is required has direct bearing on where open source models can be applied: unlike many software applications, there are significant manufacturing, regulatory, and distribution costs after the R&D phase. As such, there is a correlation between neglected-disease R&D funding mechanisms from private, public, and foundation entities at particular R&D stages and the viability of open source applications at those R&D stages.

In concluding this section, it is important to consider what we have not learned. We don’t know whether viable models can be developed to apply open source methods to later-stage drug development and delivery, and how such models would combine private and public funding (though some tentative suggestions are provided later in this paper). It is not yet clear how much these methods can push down the cost and time involved in new drug development, nor what the best way is to subdivide complex scientific problems into manageable subproblems that can be tackled in parallel by a collaborating team. Robust simulations remain to be developed to allow exploration of the effects of different open, proprietary, and hybrid regimes on health R&D investment and progress.

Notwithstanding these challenges, several interviewees saw significant opportunities. Interviewee Jody Ranck of the mHealth Alliance and InSTEDD urged, “Let’s build collaborative, open science platforms that can pool intellectual property and human resources in areas where the economics of neglected-disease research don’t make sense at the moment.” Scoping out such a platform could be one point of collaboration among the diverse parties that have considered open source approaches for neglected-disease R&D. Other potential opportunities are discussed later in this paper.

The intellectual property challenge

Looking at what has been tried suggests that a core challenge for scaling up open source models is ensuring that follow-on and collaborative innovation is not hindered, while also assuring investors that they will receive value for their money for the large investments required to take new treatments to market.
Patents and IP rights figure prominently in discussions about open source. (Some commentators make the distinction that patents in the pharmaceutical industry have a clearer social-benefit case than those in biotechnology, and indeed, than in many other industries.45) At the risk of oversimplifying, those advocating for stronger and broader application of patents argue that only with patents or similar protections can their investments in costly late-stage R&D, trials, and distribution be recouped. Those advocating for keeping outputs of R&D less encumbered argue that only by doing so can future innovation be assured, and that this is particularly true for R&D outputs that are themselves necessary to do follow-on innovation.

Before addressing this dilemma, it is worth noting that there is considerable debate about whether “patent thickets” need to be addressed. Arguments can be found for the view that patent thickets are more a theoretical problem than one that has blocked serious health R&D to date, and for the contrasting view that patents are a barrier to health innovation.46–49 The latter view draws from arguments that patents are given for inventions that are not truly novel, deter innovation by smaller players due to their cost and complexity, and prevent researchers from accessing patented materials or methods they need for their studies.

Interviewee Harry Thangaraj of St. George’s University, London, observed, “Until the patent quagmire can be resolved, no amount of investment can solve health (patent) problems through open source initiatives. Software engineers can provide usable solutions and knowledge for IT solutions, but patents in health are a different beast altogether.” (Though patents in the software industry have generated a good deal of controversy and even calls for abolition, arguably they have had less impact to date on the actual practice of software development than of health R&D, perhaps partly because they can be “invented around” more easily.)

If patent thickets and IP rights are considered to be a real problem, open source might help in understanding the IP landscape (e.g., Cambia’s Patent Lens and IOI). It might also help in incentivizing innovation without patents, to the extent that projects such as OSDD can tap into a distributed community to do neglected-disease R&D in small chunks, following the model shown to work by Wikipedia, Linux, and many other online examples. However, this latter avenue may only work for the virtual elements of R&D; it is much less clear how it would work for massive collaboration on lab-based work, let alone clinical trials. (A “fair reward principle” has been proposed that may be relevant, though thus far it appears not to have been applied; it targets “specifying the process for allocation rather than the allocation itself,” so that parties might contractually agree in advance to share future rewards by some fair division process.50)

Researchers have suggested that patents serve another function in commercializing earlier-stage R&D: they act as a signal to investors that an invention has value and is worth developing for downstream applications. The extensive 2008 Berkeley Patent Survey found empirically that start-up firms in all industries (and especially the biotechnology and medical-device sectors) use patents for such signaling, as well as for other strategic reasons like gaining leverage in cross-licensing negotiations.51 Although it is unclear how such functions would work in practice in open source situations, the same survey found that many entrepreneurs do not patent their inventions because the cost of doing so is too high; open R&D efforts might be aided in signaling their value by being able to publicly display collaborative processes and interim outputs.

Licensing is a parallel dimension of the IP challenge. Exclusive licensing to a single entity can lead to waste of knowledge if that entity doesn’t advance important projects; this lesson from past experience has resulted in the addition of “march-in rights” and similar clauses to ensure that a non-delivering licensee cannot hold up a technology’s implementation.52 (Indeed, the US Bayh-Dole Act allows march-in rights to force patent holders to license their inventions under limited circumstances; that authority had not been exercised up to the time of a survey in 2009, though several petitions to do so have been
received by the NIH over the years. A number of universities have implemented “humanitarian licensing” practices, and their practical experiences to date are valuable for any parties considering specific licensing schemes.

A number of questions remain:

- Can licensing arrangements be devised to enable open source drug development, and move beyond Cambia’s BiOS license which has had limited appeal? Yann Joly argues the need for more effective licenses for OS biotechnology, facilitated by places “where researchers interested in open biotechnology licensing could discuss common problems and harmonize their efforts.” Humanitarian licensing may have relevant lessons, as might IP management for collaborative innovation in patentable fields.

- Is protecting the commons a model worth pursuing, using open source licenses and practices combined with IP informatics systems like Cambia? How can the value of the commons be estimated? Can more empirical data and better models be researched in the case of drug and biotech R&D?

- How much value comes from tools like the IP Handbook and Patent Lens, which aim to make the IP process itself more accessible? What tools could be devised specifically to assist open source initiatives?

- There are debates about how the IP system should link to the international development agenda. Are there specific provisions that might be adopted similar to compulsory licensing, such as mandating that key enabling technologies be kept open source?

PDPs, such as the Medicines for Malaria Venture (MMV), aim to operate all the way from early-stage R&D to clinical trials. Such PDPs have learned a good deal about coordinating diverse stakeholders toward common goals, and about making use of open databases and processes along with the IP system. Might PDPs grow to include open source initiatives similar to OSDD, or is a more natural evolution to have a range of independent and “modularized” actors? This choice echoes a design choice in open source projects between monolithic all-in-one projects and diverse ecosystems of small independent projects that collectively solve some large challenge. The diverse-ecosystem approach often uses alternatives to the IP system to coordinate work and protect investments, including standards, first-mover advantage, branding, and platform lock-in.

As noted earlier, there are many differences between open source approaches in software and those in drug discovery, let alone in later-stage drug development: greater regulatory, safety, cost, and modularity barriers all play a role. Innovative software businesses often find speed of innovation to be more important competitively than patent protection. In contrast, a drug development organization may be required to freeze innovation on a new treatment for years during the regulatory and clinical trials process. Advances in personalized medicine, synthetic biology, and emerging-economy capabilities may make discovery and development significantly faster and cheaper, which might in turn shift the funding landscape—and, therefore, the viability of collaborative and open source approaches. This suggests the value of modeling potential cost savings via open source and related approaches, which might be linked with models of innovative funding mechanisms. However, until the cost of getting an approved new drug through the development and regulatory process drops enough to be covered by public and philanthropic funds (i.e., by an order or two of magnitude), open source approaches would seem to require some degree of “interoperability” with commercial licensing and development approaches to deliver new therapies and drugs for neglected diseases.
Incentives and applications

There have been a number of insightful commentaries on the potential of open source for biomedical and neglected-disease research, such as those by Bernard Munos, Janet Hope, Yann Joly, Tatum Anderson, Sara Boettiger, Arti Rai, and Emily Marden. Insights from such informed commentaries help navigate a debate where points of view range from mass skepticism to religious zeal. In this subsection, we draw from the literature and our interviewees and findings to address common concerns about incentives and applications for the open source approach.

Incentives. Why would anyone take part in an open source initiative? The question has received significant attention in the software field, and motivations in neglected-disease R&D have some overlap, as discussed in, for example, the Hope and Joly commentaries mentioned above.

Costs of drug or biotechnology R&D still need to be covered in an open source model. One method is grant funding and the concomitant rules and cooperation imposed by funders. As discussed earlier, many of the initiatives to date have relied on grants to fund their operations. Given the large fraction of neglected-disease R&D funded by granting agencies, there is substantial scope for expanding this funding avenue.

A second method to cover costs of drug or biotechnology R&D is to develop open source business models that could drive substantial participation by skilled and well-resourced entities in the absence of grant funding. The degree to which this can be done is very much an open question; below, we offer some thoughts.

To help develop business models, it is useful to separate incentives for participating in R&D into personal and organizational ones. At a personal level, reasons include financial gain, intellectual curiosity, intrinsic task enjoyment, personal brand and reputation development, academic or institutional credit, customization of a solution to a personal problem, and altruism. Note that these cover a range of common motivations, and that they are linked to a characteristic of many open source efforts of being voluntary meritocracies of distributed problem solvers.

At an organizational level, incentives relevant to open source business models can include the following:

- To collaborate precompetitively (e.g., in discovery phases or in creating open source tools of sector-wide value that can be used to better develop proprietary products)
- To compete for grant or foundation funding by showing innovative value creation
- To support services sold by the same entity (e.g., customizing an open source product for a customer) or to support hardware sales by the same entity
- To make money through innovative business models
- To undermine a competitor (e.g., by creating an open source alternative to a competitor’s revenue-generating product)
HOW CAN OPEN SOURCE ADVANCE NTD R&D?

• To market oneself to employees, policy makers, governments, and the public (e.g., as an innovative organization with a social conscience)

Open source should be viewed through a wide lens, including a range of motivations and even cultural perspectives. Initiatives should consider how they can appeal to the diverse incentives of their target audiences, and structure their workflow to match these diverse incentives where possible.

Applications. Where does open source actually work, and have potential to work, in neglected-disease R&D? We offer some thoughts, while cautioning the reader that this is still very much an open question whose answers will evolve as our ingenuity, incentives, and resources do.

The landscape of personal and organizational incentives for open source R&D naturally links to the kinds of applications that are feasible. Indeed, the question of potential applications for open source health R&D has been touched on by the Munos, Hope, Joly, and Rai commentaries mentioned above, and by other researchers.68,69

In exploring potential applications, it may be useful to look to other fields. For example, Anderson lists 50 business models for “free” goods or services;70 many are targeted toward retail offerings, but others may be applicable to larger-scale goods and services, like implementing tiered pricing with basic services offered free. It may also be of value to consider lessons and potential collaborations with open source approaches to rare diseases, including genetic diseases that occur in both rich and poor countries but have a prevalence too small to attract large amounts of funding.

The discussion in the previous section suggests that the strengths of the open source approach lie in the preclinical phase, particularly the discovery phase. Several initiatives have demonstrated significant success in this area, as shown graphically in figure 1.

Clearly, where open access is desired by most relevant parties, an open source approach will be natural. An approach like Cambia’s Patent Lens/IOI, which seeks to clarify not only the innovation system’s raw data but also the implications of these data, is also a natural niche for an open approach—clarifying the innovation landscape for all parties should lower the cost of innovation, as well as making clear strengths and shortcomings of the innovation system for policy makers and funders.

Better tools could help move the whole field ahead, and be a precompetitive point of collaboration for academia, nonprofits, government labs, and pharma and biotech. Platforms like TDR Targets that make open chemical data public are one method.71 As another example, open source development of computational models for molecular properties such as ADME (absorption, distribution, metabolism, and elimination) and toxicity has been advocated based on early experiences as a win-win solution that can provide better models at lower cost to pharma and biotech, incentivize them to share their models and avoid unnecessary expense and duplication, and leverage pharma’s expertise in the area to help academic and nonprofit researchers at a precompetitive stage.72 According to Sean Ekins of CDD, “Free technologies on the web for this kind of thing are just as good as commercial software costing big companies millions of dollars in license fees. Therefore, they can do the same modeling at zero cost. If this is the case here, there may be other places they can cut costs using free tools that the companies have not explored aggressively . . .”

As discussed earlier, the right half of figure 1 is the controversial half, where it is not clear whether open source approaches can be used in taking new treatments through clinical trials and to market. To our knowledge, no plausible model with a pure open source approach yet exists for taking a novel drug for a neglected disease all the way through the development and regulatory process and to market. However, later-stage open source applications have been suggested, such as better applications for managing and sharing clinical trial data. Interviewee Ted Bianco suggested that epidemiological data sharing could be another area for later-stage open source focus; epidemiological data naturally increase
HOW CAN OPEN SOURCE ADVANCE NTD R&D?

in value with the sample size, and data sharing between new treatment developers and health agencies and providers could have a broad range of benefits.

Utilizing search methods may help gauge the evolution of interest and applications in the area. One might be able to build on methods used by search engines and information analysis applications to develop an “open source activity index”—for example, by analyzing link, key phrase, and citation patterns in websites, scientific material, press releases, speech transcripts, articles, discussion forums, etc. Analyzing this index by geography, organization, and time could help map the flow of proposals, applications, and analysis for open source neglected-disease R&D. Particular niches might then be found through flagging unusual flows of interest and correlated search terms and categories.

We close with the thought that health technologies themselves are developing swiftly, and new advances like synthetic biology and personalized medicine may change the technological feasibility and cost of new-treatment development. Carlson discusses open source approaches in the context of R&D breakthroughs that synthetic biology might make possible.73 Maurer advocates for a collaboration in synthetic biology to implement “the idea of assembling standard biological parts into increasingly complex DNA blueprints.”74 The technologies of collaboration themselves are also advancing rapidly, and may enable new forms of mass collaboration on complex technological and scientific problems.75

The size of the prize

Is it possible to estimate the financial, social, or knowledge impact of a future successful open source model for neglected-disease research? This is vital, since otherwise it is difficult to argue for the benefits of open source and, consequently, for funding; interviewee Jackie Hunter of Pharmivation indicated that there is currently “...no clear articulation of the business and societal benefits.”

To give an analogy, the value of public libraries is clear today. However, they required substantial capital costs, their value was not widely acted upon until the 20th century, and the idea of “open books” might have been perceived by booksellers as a threat to their revenues.

Similarly, how much would be saved by not having compounds of interest to NTD research locked up in proprietary databases, not experiencing financial and complexity barriers with the IP system, and not missing R&D advances through lack of collaboration? The difficulty in estimating this “unrealized value” is that we have no counterfactuals—no “alternate universes” with which to compare.

Economic modeling might help to estimate the potential cost savings from open source approaches.76 For example, it could be possible to reduce duplication of effort due to ignorance of work going on elsewhere, to put fewer drugs into costly trials that others already have reason to believe won’t work, to collaboratively speed up regulatory processes, and to contribute to filling knowledge gaps in systems biology.77

One potential method to roughly estimate this might be “value tracking.” It might be possible to devise a scheme by which any use of an open source platform, technology, or data set would automatically be recorded in a common database, perhaps in an anonymized way. Cumulative actual uses would thus be recorded, and hence the value of these uses could be much more easily measured. It might even be possible to estimate instances in which researchers were stymied by cost or lack of access, by giving them a one-click way to record that into a real-time census of “unrealized value.”

Clear metrics of value will be essential when discussing the value of open source for NTDs—“the size of the prize.” This value comes in several forms: creating knowledge for future innovations, reducing disease burden, making money for investors, rewarding researchers, and achieving economic development in R&D industries. Metrics and indicators for such types of value have been suggested for health research.78 Estimates have been made for the
value of open source software, which may suggest approaches; for example, one study in 2006 found the value of the EU’s investment in free and open source software to be €22 billion.79 Business cases have also been made for neglected-disease vaccines, though they only cover direct financial revenues.80

The challenge with developing metrics (and indicators in general) is that open source initiatives span a range of functions and approaches. With this caveat in mind, some tentative possibilities are listed below as starting points for discussion adapted from suggestions by our interviewees (these are speculative and would need further review, discussion, and evolution before any consideration of use; all depend on being able to obtain suitable data):

• Number of open licenses granted to further develop compounds for NTDs (potentially disaggregated by stage of compound when license is granted)
• Number of public-private partnerships created with an explicit open source focus
• Number of compounds developed largely by open source methods that reach clinical trial stage; similarly, number of new drugs developed in large part via open source R&D that are actually delivered to populations in developing countries
• Avoidance of clinical trial duplication or of entering clinical trials (which constitute a major part of drug development expenses)

Looking ahead

As this paper draws to a close, two questions remain. What is the promise and potential of the open source approach? What might the reader do to help realize this potential?

The open source approach has undeniably had tremendous impact in the software world, and this shows no signs of slowing down. However, to date in neglected-disease R&D, the approach has shown more potential than impact; it has not answered major scientific questions, nor does it have a large amount of momentum behind it yet. It seems to be more valuable in the early and precompetitive stages of R&D; its value is less clear in later stages. It is worthy of further assessment and collaborative support, and needs time to ripen.

In the short term, three next steps might be considered. First, generate detailed profiles and evaluations of open source initiatives for neglected-disease R&D, incorporating metrics developed specifically for the area. Those who write these profiles might be independent of the initiatives; gain access to existing evaluations and audits of the initiatives; and speak with funders, the scientific community, and other third parties. This could help others to evaluate the achievements, shortcomings, and potential impact of a range of initiatives and suggest generalizable lessons. To facilitate this, funders might at a minimum require initiatives to make public annual summary reports.

Second, collaboratively develop and prioritize value propositions for substantial, long-term investments in the area, building on ideas such as those discussed below and in the appendix. These value propositions might be developed with a community of informed stakeholders to converge on a few tested initiatives worthy of substantial support. With engagement from academic, industry, and foundation stakeholders, it might be possible to draw together research, financial data, and practical lessons to evolve a schema or flowchart, to suggest where and how to apply open source approaches. This might be a practical approach to defining and applying the key determinants of where open source models might work (and where they might not) in neglected-disease R&D.

Third, start a demand-driven website to act as a focal point for threads of discussion currently occurring in many disparate forums, and to seed connections and a sense of community between experts and enthusiasts. It could incorporate a group weblog where the contributors are “insiders” in the community, as NextBillion, for example, has for social entrepreneurship and development. The paid support could initially be as simple as a single, part-time
editor who solicits and links to contributions and publicizes existing tools, initiatives, data sets, and case studies. It could grow into a collaborative web portal and community, and help to move the field ahead and synthesize lessons from initiatives already underway. Interviewee Yann Joly of McGill University argues that “… developing a common forum where policy makers, academic researchers, industry, and NGO representatives could meet on a regular basis to discuss the potential (and shortfall) of the OS model for developing drugs for neglected diseases could be a good strategic investment.”

Longer-term initiatives are more difficult to plan without collaborative, expert participation. We therefore mention several initiatives as possibilities to be improved and built on; other possibilities from interviewees are discussed in appendix C. Metrics and indicators could be implemented across open source initiatives, following on the value-tracking suggestions above; models drawing from pharmacoeconomics and other fields might use these metrics to estimate cost savings from further initiatives. Metrics could also provide social and professional value for individual contributions to open source initiatives—what if it were possible to aggregate contributions to an open source initiative, and use the cumulative “score” as a proof point with granting agencies and promotion committees, similar to how publication metrics are used today? Such individual metrics might go hand in hand with devising better ways of splitting up neglected-disease R&D into smaller contributions, to enable a mass-collaborative approach to doing neglected-disease R&D, learning from what has worked in many online systems.

Specific funding initiatives similar to the Grand Challenges Explorations grants (e.g., $50,000 and access to mentorship, with a possibility of larger follow-ups) might be tried to prototype a range of innovative approaches. As interviewee Zakir Thomas of OSDD put it, we need to “pump in more funds into open source research.” One area of focus might be investment in better tools that move the whole field ahead, such as the computational models and open source clinical trial and epidemiology databases discussed previously. Getting starry-eyed idealists in the same room with hard-nosed investors to agree on open source approaches would be a facilitation challenge, though not an impossible one—might some degree of agreement be reached on how to advance science without cutting off private investment?

Resources and some degree of active coordination of the area as a whole might be worthwhile, instead of hoping that success emerges solely through individual efforts. Interviewee Ted Bianco of the Wellcome Trust argues for “a small but entrepreneurial secretariat to provide high-quality curation of the open source resource, grow it over time, enrich its value by collating new information on the material as it arises, [and] provide an industry-experienced consultancy service to would-be innovators who were using the resource.”

Building on suggestions by several interviewees, a horizontal initiative might be developed—a platform that enables sharing of data and pooling of interests for scientific and other communities currently working in different disease areas and organizations. It might include metrics, collaborative access to and development of analytical tools, needs assessments, shared experiences, a collective raising of the profile of the area, and so forth.

Designing such an initiative would require considering incentives to engage in open source approaches for pharmaceutical and biotechnology companies, PDPs, research consortia, individual scientists, and other private and public sector participants. It might include capacity development in developing countries themselves, as advocated by interviewee Bernard Munos of InnoThink: “Build open source drug R&D capacity in the countries affected by neglected diseases...They have the patients and the motivation, are change-friendly, and have no legacy to restrict their creativity.” All this would depend upon the buy-in of high-profile leaders and institutions to be successful, as would many of the other initiatives and data-sharing projects discussed.

Is open source for neglected diseases a magic bullet or a mirage? We believe the correct answer is neither.
The opportunities identified above suggest that the concept is not without value. However, open source approaches will require well-informed and thoughtful initiatives, that successfully inspire and coordinate diverse partners. By gaining a realistic understanding of the potential and challenges of open source for neglected diseases, and considering options for better harnessing it, the approach can be evolved to help create a healthier world.
## APPENDIX A. PARTICIPANTS IN INTERVIEWS

### Participants in interviews

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<thead>
<tr>
<th>Name</th>
<th>Organization</th>
<th>Title</th>
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<tbody>
<tr>
<td>Aled Edwards</td>
<td>Structural Genomics Consortium</td>
<td>Director and Chief Executive Officer</td>
</tr>
<tr>
<td>Andrew Hessel</td>
<td>Pink Army Cooperative</td>
<td>Founder</td>
</tr>
<tr>
<td>Barry Bunin</td>
<td>Collaborative Drug Discovery</td>
<td>Chief Executive Officer and President</td>
</tr>
<tr>
<td>Bernard Munos</td>
<td>InnoThink</td>
<td>Founder</td>
</tr>
<tr>
<td>Chas Bountra</td>
<td>Structural Genomics Consortium</td>
<td>Chief Scientist</td>
</tr>
<tr>
<td>Claire E. Driscoll</td>
<td>National Human Genome Research Institute, National Institutes of Health</td>
<td>Director of Technology Transfer</td>
</tr>
<tr>
<td>Harry Thangaraj</td>
<td>Access to Pharmaceuticals Project, St. George’s University, London</td>
<td>Director</td>
</tr>
<tr>
<td>Jackie Hunter</td>
<td>Pharmivation Ltd</td>
<td>Chief Executive Officer</td>
</tr>
<tr>
<td>Jody Ranck</td>
<td>mHealth Alliance and InSTEDD</td>
<td>Executive Team Member (mHealth) and Senior Health Policy Advisor (InSTEDD)</td>
</tr>
<tr>
<td>Mark Wilson</td>
<td>GlaxoSmithKline</td>
<td>Director, Collaboration Management, Europe Pharmaceutical Development</td>
</tr>
<tr>
<td>Pascale Boulet</td>
<td>Drugs for Neglected Diseases Initiative</td>
<td>IP and Regulatory Advisor</td>
</tr>
<tr>
<td>Richard Jefferson</td>
<td>Cambia Patent Lens and Initiative for Open Innovation</td>
<td>Founder and Chief Executive Officer</td>
</tr>
<tr>
<td>Sara Boettiger</td>
<td>The Public Intellectual Property Resource for Agriculture</td>
<td>Director of Strategic Planning and Development</td>
</tr>
<tr>
<td>Sean Ekins</td>
<td>Collaborative Drug Discovery</td>
<td>Collaborations Director</td>
</tr>
<tr>
<td>Solomon Nwaka</td>
<td>Special Programme for Research and Training in Tropical Diseases (TDR), World Health Organization</td>
<td>Leader, Drug, Discovery and Innovation Research</td>
</tr>
<tr>
<td>Stephen M. Maurer</td>
<td>Information Technology and Homeland Security Project, University of California, Berkeley</td>
<td>Director</td>
</tr>
<tr>
<td>Ted Bianco</td>
<td>Wellcome Trust</td>
<td>Director of Technology Transfer</td>
</tr>
<tr>
<td>Wesley Van Hooris</td>
<td>School of Public Health, University of Washington</td>
<td>Professor, Department of Medicine</td>
</tr>
<tr>
<td>Yann Joly</td>
<td>Centre of Genomics and Policy, McGill University</td>
<td>Professor</td>
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<tr>
<td>Zakir Thomas</td>
<td>Open Source Drug Discovery</td>
<td>Project Director</td>
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Profiles of open source neglected tropical disease research and development projects

This appendix contains additional information on several open source projects discussed in the text. All the information in these profiles is taken from the projects’ publicly available information. (The authors suggest that a future area for work is to motivate such projects to publicly provide more detailed and verifiable information, including suitable metrics for project outcomes and impact.)

Open Source Drug Discovery

Head: Zakir Thomas, Project Director; Samir K. Brahmachari, Chief Mentor

Statement of purpose: “OSDD is a CSIR Team India Consortium with Global Partnership with a vision to provide affordable healthcare to the developing world by providing a global platform where the best minds can collaborate and collectively endeavor to solve the complex problems associated with discovering novel therapies for neglected tropical diseases like Malaria, Tuberculosis, Leishmaniasis, etc. It is a concept to collaboratively aggregate the biological and genetic information available to scientists in order to use it to hasten the discovery of drugs . . . The success of Open Source models in Information Technology (for e.g., Web Technology, The Linux Operating System) and Biotechnology (for e.g., Human Genome Sequencing) sectors highlights the urgent need to initiate a similar model in healthcare, i.e., an Open Source model for Drug Discovery.”

Notable claim(s): over 4,000 user accounts as of December 2010; re-annotating the Mycobacterium tuberculosis genome to link genes to their function.

Website: www.osdd.net

Collaborative Drug Discovery

Head: Barry A. Bunin, CEO

Statement of purpose: “CDD’s products enable scientists to archive, mine, and collaborate around pre-clinical chemical and biological drug discovery data through a web-based interface.”

Notable claim(s): hosts chemical data sets on malaria and TB from GSK and Novartis.

Website: www.collaborativedrug.com

Cambia’s Patent Lens and Initiative for Open Innovation

Head: Richard Jefferson, Founder and CEO

Statement of purpose: “The growth, opacity and misunderstanding of the world’s patent systems, and the fragmentation of scientific, technical, regulatory and business information makes navigation of the innovation system an expensive, uncertain and inefficient activity . . . IOI fosters evidence-based navigation and operation within the complex intellectual property landscapes that surround innovation in such critical areas as health, agriculture, environment and energy.”

Notable claim(s): created free global full-text patent search tool with Patent Lens; attracted follow-on funding from Gates and Lemelson Foundations for IOI.

Website: www.cambia.org
**Tropical Diseases Initiative**

**Head:** Initiated by a team of 5

**Statement of purpose:** “TDI was conceived as a decentralized and web-based open source drug discovery effort in which academic and corporate scientists volunteer to work together on discovering drugs for neglected diseases.”

**Notable claim(s):** published a “kernel” containing “... 143 and 297 protein targets from ten pathogen genomes that are predicted to bind a known drug or a molecule similar to a known drug, respectively.”

**Website:** www.tropicaldisease.org

**TDR Targets**

**Head:** N/A (network from several institutions)

**Statement of purpose:** “The open-access resource TDRtargets.org facilitates drug target prioritization for major tropical disease pathogens. The TDR Targets database functions both as a website where researchers can look for information on their targets of interest; and as a tool for prioritization of targets in whole genomes.”

**Notable claim(s):** fourth version of database released; illustrative potential drug target listings generated for seven tropical disease pathogens.

**Website:** www.tdrtargets.org

**Structural Genomics Consortium**

**Head:** Aled Edwards, Chief Executive

**Statement of purpose:** “The SGC is a not-for-profit organization that aims to determine the three dimensional structures of proteins of medical relevance, and place them in the public domain without restriction. The SGC operates out of the Universities of Oxford and Toronto and Karolinska Institutet, Stockholm, and works on structures of proteins from its funder-created Target List of ~2,000 proteins, which comprises human proteins associated with diseases such as cancer, diabetes, inflammation, and genetic and epigenetic diseases, as well as proteins from human parasites such as those that cause malaria.”

**Notable claim(s):** “The core mandate of the SGC is to determine 3D structures on a large scale and cost-effectively—targeting human proteins of biomedical importance and proteins from human parasites that represent potential drug targets. In these two areas, the SGC is now responsible for >25% and >50% of all structures deposited into the Protein Data Bank each year. The SGC released its 450th structure in June 2007 and has passed the 1000th structure milestone in July 2010.”

**Website:** www.thesgc.org
Suggestions from expert interviewees

In preparing this document, a range of experts were interviewed. We subsequently asked each expert to write, in no more than 150 words, their answer to a common question. The answers from those experts who agreed to be quoted are given below.

“What single investment would maximize the impact of open source on developing new and affordable drugs for neglected diseases?”

If you ask what is the one single thing: it would be more funds! Pump in more funds into open source research.

— Zakir Thomas
Project Director, OSDD

Although there are a number of initiatives in neglected diseases ongoing, there is no mechanism for easily sharing data between initiatives and no clear articulation of the business and societal benefits which would drive such sharing and incentivise companies to invest more resources. So the one thing would be some initiative which would create a mega-data set from this data and use it to answer a ‘big’ question/project which would give some tangible output in the near term.

— Jackie Hunter
CEO, Pharmivation Ltd

There is no single investment that could dream of doing that.

— Aled Edwards
Director & CEO, SGC

More financial support from public sources would certainly help, but I [still] think the most important thing is to sell the OS development model to the private sector. With that in mind, developing a common forum where policy makers, academic researchers, industry, and NGO representatives could meet on a regular basis to discuss the potential (and shortfall) of the OS model for developing drugs for neglected diseases could be a good strategic investment.

— Yann Joly
Professor, Centre of Genomics and Policy, McGill University

Credible success stories would help convince companies, public-private consortia, academics, etc., to consider open innovation (OI) approaches for drug development projects, including ones aimed at commercializing new therapeutics for neglected diseases.

It would have a big impact if a “big player” such as the Wellcome Trust, the Gates Foundation, GSK and/or NIH adopted OI policies and funded the needed OI-supporting infrastructure in order to facilitate getting a new drug into the clinic and on to the market. Taking an OI approach doesn’t sound like it would cost very much especially as compared to R&D costs—however it will be essential to have IT systems that foster restriction-free sharing of ideas and data. In addition there should be dedicated OI collaboration managers who ensure that projects are well-managed, that thoughtful policies are developed and implemented, and that there is ongoing extensive communication among collaborators. Doing all this will require significant resources.

— Claire Driscoll
Director of Technology Transfer, NHGRI (National Human Genome Research Institute), NIH

The funding to support a small but entrepreneurial secretariat to

• provide high quality curation of the open source resource;
• grow it over time;
• enrich its value by collating new information on the material as it arises;
• provide an industry-experienced consultancy service to would-be innovators who were using the resource.

— Ted Bianco
Director of Technology Transfer, The Wellcome Trust
APPENDIX C. SUGGESTIONS FROM EXPERT INTERVIEWEES

One possibility would be to invest in expanding OSDD. They already have more money and visibility than anyone else, and splitting the open source effort in two can only weaken both halves.

As always, the investment will have to be made shrewdly. Nature News has suggested (9 June 2010) that OSDD is less efficient than claimed. If so, investors should find and fix the problem before contributing more funds. Alternatively, Nature News’ concerns may be overstated. In that case, investors should say so and add funds. The new money could be profitably spent on various projects including (a) expanding OSDD to include more Western students and commercial scientists, (b) setting up wikis to transparently collect evidence about why different drug ideas will or will not work, and (c) hiring paid scientist-curators to provide leadership and quality checks for volunteers.

– Stephen M. Maurer
Director, Information Technology and Homeland Security Project, University of California, Berkeley

Let’s build collaborative, open science platforms that can pool intellectual property and human resources in areas where the economics of neglected disease research don’t make sense at the moment. There’s a fundamental mismatch between the way the world works in biological terms, and the way the pharma industry works. The problem we’re trying to solve requires integrated thinking and systems biology. Can open source business models be transferred over?

There are spaces where people are not currently making money and the pipeline is dry. Downstream there could be a market. Why not open up the data? If you open it up and create a market, then all parties might eventually benefit. It would be an “open source strategy development exercise.” We can combine information about market sizes and purchasing power with scientific feasibility, to understand where a shared strategy that develops new products could yield revenues.

– Jody Ranck
Executive Team Member, mHealth Alliance; Senior Health Policy Advisor, InSTEDD

The creation of an end-to-end R&D pipeline that is transparent and community owned and operated, capable of supporting dozens of initiatives, and with funding pledged by individuals or groups on a project-by-project basis.

– Andrew Hessel
Founder, Pink Army Cooperative

Build open source drug R&D capacity in the countries affected by neglected diseases. Research tells us you need to shorten the feedback loop between the clinical observation and the therapeutic intervention. The problem must be solved by Africans, Indians, Brazilians, etc. They have the patients and the motivation, are change-friendly, and have no legacy to restrict their creativity.

They need help with education, a bit of infrastructure, and modest financial support. I emphasize the latter, because money numbs innovation. If there is too much of it, the costly and unproductive ways of the drug industry will simply be duplicated. PPPs [Public-Private Partnerships] are successful because they had to reinvent the model in order to do drug R&D within their budgets. Novel initiatives such as the African Network for Drug and Diagnostic Innovation (ANDI) aim at building such a local networked R&D capability, and should be encouraged.

– Bernard Munos
Founder, InnoThink

IMHO the answer is none. This is a hugely complex issue. Open source is supposed to solve problems but the industry in software and health are different beasts altogether. Until the patent quagmire can be resolved, no amount of investment can solve health (patent) problems through open source initiatives. Software engineers can provide usable solutions and knowledge for IT solutions, but patents in health are a different beast altogether.

– Harry Thangaraj
Director, Access to Pharmaceuticals Project, St. George’s University, London

Not to be self-serving, but doing open drug discovery for neglected diseases in a practical way (that respects IP when it is sensitive, but makes it open when it should be) is not trivial and not something others are doing. So from the bottom up Collaborative Drug Discovery has proven that it provides a large benefit for little cost, for many researchers. We think this method could be applied to all researchers. It would be highly leveraged, because novel capabilities for selectively sharing data, models, and supporting the community (as we’ve done for TB) would benefit all researchers in the space.

– Barry Bunin
CEO & President, CDD

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Founder, InnoThink


9 Open Source Definition from the Open Source Initiative (OSI; opensource.org).


26 “About the Synaptic Leap,” http://www.thesynapticleap.org/about (accessed December 27, 2010).


NOTES


62 See note 46 above.


64 See note 23 above.


75 Tovey M, ed., Collective Intelligence: Creating a Prosperous World at Peace (Oakton, VA: EIN Press, 2008).

76 Munos, B, “The Compelling Economics of Open-Source Drug R&D” (paper presented at the 240th meeting of the American Chemical Society, Boston, MA, 2010).


78 Panel on Return on Investment in Health Research, Making an Impact: A Preferred Framework and Indicators to Measure Returns on Investment in Health Research (Ottawa, Canada: Canadian Academy of Health Sciences, 2009).


80 BVGH business cases for neglected-disease treatments, at www.bvgh.org.