Drug partnerships and global practices

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ABSTRACT

Tuberculosis poses one of the biggest threats to individuals living with HIV in most low-income regions of the world, and the increase of multi-drug resistant tuberculosis (MDR-TB) in South Africa, Eastern Europe, and elsewhere makes this threat that much more critical. Despite the extent of the problem, new drugs for tuberculosis have not been developed for over four decades, largely because tuberculosis occurs primarily among the poor in low-income regions and the market for tuberculosis drugs is not lucrative enough to warrant time and resource commitments by pharmaceutical companies. In the wake of sustained global criticism of pharmaceutical-state practices, however, new partnerships for drug development (PDPs) are forming to address critical shortages of drugs for diseases like tuberculosis that have been termed ‘neglected’ precisely because they have not seen new treatments for so long. This paper examines some of these partnerships, tracing some of the dynamic developments as well as challenges in forging alternative pathways to new drug and vaccine production.

1. Introduction

Tuberculosis poses one of the biggest threats to individuals living with HIV in most low-income regions of the world, and the increase of multi-drug resistant tuberculosis (MDR-TB) in South Africa, Eastern Europe, and elsewhere makes this threat that much more critical. As of 2007, 1.37 million cases of tuberculosis occurred among HIV-positive individuals, and cases of MDR-TB reached at least 500,000 (Donald and van Helden, 2009). Despite the extent of the problem, new drugs for tuberculosis have not been developed for over four decades, largely because tuberculosis occurs primarily among the poor in low-income regions and the market for tuberculosis drugs is not lucrative enough to warrant time and resource commitments by pharmaceutical companies.

The dearth of research and resources in the recent past for a disease like tuberculosis exemplifies the very spatialized convergences of capital and state discussed by Kearns and Reid-Henry (2009) which result in geographically uneven chances of disease and survival. In the wake of sustained global criticism of pharmaceutical-state practices, however, new partnerships for drug development (PDPs) are forming to address critical shortages of drugs for diseases like tuberculosis that have been termed ‘neglected’ precisely because they have not seen new treatments for so long. These partnerships differ widely in their constitution and focus, but typically involve nonprofit agencies, university researchers, and pharmaceutical companies or their offshoots collaborating to produce new therapies in ways that are sustainable and affordable. In the case of tuberculosis, several collaborations have developed and will constitute the focus of this paper.

These new assemblages of scientists, intellectual property, laboratories, and bacteria deserve examination in their own right for their potential to address in part the persistent problems of global health. I include the cautionary caveat ‘in part’ in recognition of persistent debates within global health literatures of what constitutes best approaches for intervening in problems of disease and poverty—in this case, whether spending millions to find technical fixes for a small handful of diseases is the best path for ameliorating broader issues of entrenched poverty. It is a question that I will not be addressing directly, but my interest in PDPs and their ability to produce effective and readily available drugs for infectious diseases such as tuberculosis indicates that I think the millions already suffering from burdens of infection deserve therapeutic intervention. In no way should these efforts, however, substitute for critical insights into historical and current global economic practices keeping millions of individuals in poverty and at continued risk of multiple infectious diseases (cf. Lee, 2003). PDPs as a whole do not address the question of

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1 Whether tuberculosis is included within the rubric of ‘neglected infectious diseases’ depends upon who you talk to. The WHO, for example, does not include tuberculosis on its list of neglected infectious diseases in part this is because

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(footnote continued) relative to many infectious diseases such as onchocerciasis or schistosomiasis, tuberculosis has recently gained greater visibility and much more funding. Yet for those researching new drug treatments, funding remains frustratingly inadequate and still only a small fraction of that funneled to other diseases—around 2% of total US development assistance for health from 2003 to 2007 went to tuberculosis research versus over 36% for HIV/AIDS (Liese et al., 2010).
why millions continue to suffer from a preventable disease; they take this as a given. But at their best, some PDPs open up the possibility not only of countering the kinds of market failures that have shaped particular patterns of disease and their persistence, but of countering the ‘prepackaged’ and formulaic recommendations for improving public health that too often emerge from high-level public health reports and that center on national government interventions (Sparks, 2009), or on the curtailment of particular kinds of population and pathogenic circulations (Hinchliffe and Bingham, 2008; Craddock, 2008a).

But partnerships forming around tuberculosis drug development potentially constitute as well an example of science and biomedicine – in this instance in the form of new chemotherapies – deriving primarily from western countries and being deployed in low-income regions, thereby illustrating the kinds of questions raised by Latour (2005), Jasanoff (2006) and many others in science studies and history of medicine of how technologies produce new structures of social practice and organizations of space, create new values inhering around biotechnological understanding and consumption, and constitute or reconstitute transnational relations. Though this paper adds to a growing body of literature inside and out of geography that explores the role of biotechnology in for example reconfiguring a politics of life (Rose, 2007; Grenough and Roe, 2006), therapeutic access (Nguyen et al., 2006), and tissue economies (Waldbly and Mitchell, 2006; Schepher-Hughes, 2003), the focus here is necessarily more on the interconnections of bodies, technologies, and places in the development – not deployment – of new therapies. As Rose in particular has pointed out (2007), new biotechnologies also present possibilities for community building and enhanced political visibility of populations galvanizing around points of disease treatment. I specifically draw in this paper as well from Hinchliffe and Bingham (2008), Latour (2005), Mol (2002) and others in seeing networks such as these partnerships and their attendant contexts of research – namely bacteria, immune systems, ecological and political environments, regulatory structures, market forces, and funding priorities to name a few – as dynamically creating particular realities as they play out, not just responding to particular realities or converging upon particular and static solutions.

PDPs make a particularly interesting case study for examining these points because they encompass several forms of transnational technological interaction. Typically within literatures on intellectual property rights (IPR) and antiretroviral access, debate has focused on the global regulatory mechanisms such as TRIPS (Trade Related Aspects of Intellectual Property, more on that below), and the recognition of patents on particular pharmaceuticals, as patents are arguably key in keeping prices of new drugs such as antiretrovirals too high to be affordable to the majority who need them. Transfers of intellectual property rights also confer the ability to manufacture and distribute new drugs internally, circumventing reliance upon other countries for drug imports and opening channels for developing scientific and manufacturing capabilities.

While the question of IPR is still critical to how PDPs are going to develop new pharmaceutical compounds for diseases overwhelmingly affecting poor individuals in low-income regions, these collaborations also suggest ways for moving beyond IPR in the qualitative evaluation of how new technologies impact particular communities. In addition to their scientific collaborations over chemical compound development, PDPs also encompass the design and implementation of clinical trials, and the manufacture, distribution, and consumption of successful compounds. In addition to how new technologies change social practice, PDPs thus also raise questions about the quality and nature of community involvement in technological development, variable understandings of infectious disease and technological consumption, and the particular interactions and spatial mobilizations of national, private, nonprofit, and transnational entities in the process of new drug development and distribution. The question might productively be raised as well of whether PDPs can create meaningful new forms of pharmaceutical and biomedical production driven as much by public health need as market potential, or whether they simply constitute a minor divergence from what has become the conventional norm of corporatized pharmaceutical research and development.

Using interviews, agency reports, industry announcements, and existing scholarship on pharmaceutical research and PDPs, I will address the questions above of how PDPs focusing on tuberculosis are approaching the process of researching and developing new drugs intended for low-income regions, and whether they are breaking the mold often criticized in science studies literatures of western technologies deployed in non-western countries with inadequate forethought to consequences or meaningful consultation. Given the initial state of many of these collaborations and their attendant new compounds, some of my discussions will necessarily be based on potential or stated intention rather than what is already in place. And some points will remain in the form of questions heading in particular directions given indications from other studies. I do not intend this particular paper to add to the literature critiquing pharmaceutical industry practices (cf. Pollock, 2011). It is not simply – as one anonymous reviewer suggested – a matter of obtaining and maintaining access to those within the industry while this project is ongoing; it is also a matter of locating politics in regulatory, scientific, logistical, financial, and social realms, and not just within the contradictions of pharmaceutical practices. It is undeniable that many pharmaceutical companies display differential ethics in maintaining a competitive edge in mainstream drug development, corporate merging, and marketing while simultaneously channeling resources into humanitarian projects such as drugs for neglected diseases. The question of what kinds of questions to raise about these differential and seemingly irreconcilable ethics remains for the ongoing research project of which this paper is a part.

2. The emergence of partnerships for drug production

The reasons why new treatments for diseases like tuberculosis have not emerged in recent decades involves, among other things, national and international policies and regulatory mechanisms that have entrenched pharmaceutical research and development largely in the private corporate sector. The United States' Bayh-Dole Act of 1980 opened the way for federally funded university discoveries to be licensed exclusively to private companies such as biotechnology or pharmaceutical firms. Before 1980, scientific or other discoveries made by researchers using federal funds automatically reverted to federal control. Yet inefficiencies in federal-level efforts to channel new products to the public meant that many new technologies either were never utilized or they met with long lag times before reaching the market. The Bayh-Dole Act was passed with the intention to improve efficiencies of product development by joining academia's scientific capabilities with the private sector's manufacturing and marketing resources. There is no absolute equivalent in Europe of the Bayh-Dole Act, but in 1988 the EU passed a Directive on biotechnologies to "harmonize and strengthen biotech patent law" (Schneider, 2009). Seeing greater public–private
coordination of scientific research as a means to strengthen economic competitiveness, the EU’s Directive was intended to accommodate new arenas of research, to attract more investment capital, and to more strongly link university and industry (Schneider, 2009).

A secondary result of inextricably linking scientific research with commercial production, however, is that university research in the sciences and technology has increasingly been directed towards discoveries with market potential and direct pipelines to pharmaceutical and biotechnology companies rather than towards areas with the greatest public health need. An oft-cited statistic emerging from this trend is that currently less than 10% of global drug research and development funding goes towards diseases affecting 90% of the world’s population (cf. www.msf.org).

At the global level, the 2001 Trade-Related Aspects of Intellectual Property (TRIPS) Agreement of the World Trade Organization has had a similarly critical role in shaping production, pricing, and distribution of new technologies. Main provisions of TRIPS are an extension of intellectual property rights to broader areas including pharmaceuticals, the extension of patent rights to 20 years, and the requirement that member countries recognize patents on new pharmaceutical products by 2005. Low-income countries gained a 10-year extension to the patent recognition clause, yet the conditions under which they are allowed to import or manufacture generic treatments in the meantime are stringent. The main result of TRIPS for pharmaceutical companies is thus the ability to charge higher prices for drugs in more areas of the world. TRIPS has also arguably thwarted incentives to research new compounds for diseases primarily affecting low-income regions, and it has to a certain extent prevented middle-income countries such as India and Thailand from manufacturing cheaper generic versions of new technologies.

Pharmaceutical companies’ financial gain from WTO regulations, or their capacity to ‘put profits before people’, eventually generated the opprobrium of constituencies including transnational NGOs, grassroots movements, actors, university students, and politicians. Large international nonprofit organizations such as Doctors Without Borders have made visible the devastating effects of infectious diseases when treatments are inadequate, ineffective or toxic, thereby turning what had become normative corporate practices in the pharmaceutical sector into human rights and global health issues. Pharmaceutical companies’ struggle to maintain strict control of antiretroviral pricing and distribution in the midst of a growing AIDS pandemic in the 1990s and early 2000s evidenced even more starkly the privileging of corporate profit over global health and brought the contradictions of a market-driven system of pharmaceutical development to the forefront (Craddock, 2008b).

In part as a result of these contradictions, several pharmaceutical companies have turned their attention in recent years toward addressing the gap in treatments for infectious diseases, while nonprofit organizations have emerged with the mission of developing new compounds for neglected diseases that will remain affordable and available to those who need them. How the development of non-lucrative drugs happens varies by organization and disease, but it does not occur entirely outside of market concerns and resource constraints. As most of my informants were quick to suggest, pharmaceutical companies cannot

fund research and development of new drugs by themselves when these drugs will not secure profits, but nonprofit partners by default do not have consistent financial resources to support especially late-stage expenses of drug research. Agencies such as the Gates Foundation have been essential thus far, but even they do not cover all issues related more to the distribution and consumption of new drugs rather than their production. Such issues in the case of drugs for neglected diseases include sustainable distribution among low-income populations and resource-strapped governments, cumbersome regulatory mechanisms, and local research and clinical capacity.

For these reasons as well as the complexity of any kind of drug development, work on new compounds for neglected diseases is almost invariably characterized by collaboration across private, nonprofit, and academic sectors and across a multiplicity of scientific disciplines and research venues—hence the emergence of Public–Private Partnerships, or Partnerships for Drug Development. Virtually every informant from both the private and nonprofit sectors emphasize that neglected disease drug development would not happen without the other sector. Informants from the nonprofit sector point out the critical role of pharmaceutical company resources, their facilities and chemical compound libraries, and their greater access to scientists across the spectrum of disciplines needed for new drug discovery and development. Those from the pharmaceutical industry readily admit that nonprofit agencies are invaluable in gaining community trust, developing clinical trial sites, ascertaining regional variations in technological adoption, and working with transnational agencies such as the WHO in negotiating regulatory approval or purchasing plans.

2.1. PDPs in tuberculosis

Within the insular politics of neglected disease research and funding, tuberculosis has greater visibility than some diseases, but also an enormous burden of suffering: an estimated 14 million individuals with tuberculosis as of 2007, and close to two million deaths including almost 500,000 HIV+ individuals (World Health Organization, 2009). Perhaps for this reason there are a number of PDPs focusing on new treatments for tuberculosis, and in this paper I will not attempt to be comprehensive but rather will highlight a few key players and the different relationships that characterize them.

One of the main nonprofit actors in developing new treatments is TB Alliance (TBA). Started in 2000, TBA is a nonprofit that hires academic scientists, rents facilities from pharmaceutical companies, and partners with both biotech and pharmaceutical partners for developing new treatments for drug-susceptible tuberculosis. One advantage in developing treatments for TB, unlike many infectious diseases, is that tuberculosis is caused by a bacterium. The first approach TBA took upon its inception, then, was to approach pharmaceutical companies for permission to test already existing antibiotics to ascertain whether these would be effective for tuberculosis. A potentially successful example of this approach is Moxifloxacin, an antibiotic owned by Bayer Pharmaceuticals of Germany and already on the market to treat acute respiratory infections. Since the drug is already patented and FDA-approved, TBA could move past some of the early and time-consuming studies to establish safety data, and since 2008 has been testing Moxifloxacin in final or Phase III clinical trials in various sites in Africa (Ambrosino, 2009; TB
Alliance, 2009). Should it prove successful (more on that below), Bayer will retain its property rights on Moxifloxacin in high-income areas for non-tuberculosis indications, and TBA will retain control over sale and distribution for TB treatment in low-income regions (Ambrosino, 2009).

As one TBA representative, Derek Ambrosino, (2009), points out, the problem with current tuberculosis drugs is not that they are ineffective—for drug-susceptible individuals, current drug regimens are 95% efficacious. However, these regimens typically take 6 months to complete, leading to high default rates before cure. To prove successful by the standards of the FDA, TBA must demonstrate in clinical trials that Moxifloxacin in combination with other drugs reduces drug treatment from 6 to 4 months, thereby improving the likelihood of treatment adherence and completion (TB Alliance, 2009). Moxifloxacin also does not interact with antiretroviral drugs, thus offering to people with AIDS an advantage over one of the main first-line tuberculosis drugs, rifampicin (TB Alliance, 2009). TBA is paying for the clinical trials, a prospect that is always expensive given the necessary number of participants (thousands) and number of sites, which are expanding from South Africa, Kenya, Zambia, Tanzania, and other countries in Africa to high-burden areas of Asia (Ambrosino, 2009). Bayer's understandable unwillingness to pay for clinical trials for drug applications they will not benefit from points to the parameters of pharmaceutical involvement in this case, but also the necessity for nonprofits such as TBA to spend considerable time and effort raising money to support their mission of affordable treatments. In the case of TBA, these funds have come from both government sources such as USAID, as well as private philanthropic sources like the Gates Foundation.

TBA has a very different partnership with Tibotec, an offshoot of Johnson and Johnson dedicated to developing novel treatments for infectious diseases such as HIV, Hepatitis C and tuberculosis. Tibotec developed a compound, TMC207, which inhibits a synthase (ATP) needed by the tuberculosis bacterium to reproduce. After Phase II trials it is showing promise in active and latent forms of both drug-susceptible and multi-drug resistant forms of tuberculosis, and is enrolling in larger Phase IIIb trials over multiple sites in Thailand, Latvia, Peru, South Africa, and Brazil—all areas with high MDR-TB burdens. TBA has formed a partnership with Tibotec, testing TMC207 for efficacy in drug-susceptible tuberculosis while Tibotec focuses on MDR-TB. As stated by David McNeely, the former Director of Global Clinical Development and Medical Leader of TMC207 for Tibotec, "Tibotec does not get direct benefit from the relationship [with TBA], but TMC207 does" (McNeely, 2009). In other words, it is faster to prove efficacy of a new compound in individuals with MDR-TB, so it is in Tubotec's interest to focus on MDR-TB and thus gain regulatory approval to begin making the drug available more quickly. TBA, by agreeing to conduct clinical trials for TMC207 among drug-susceptible TB populations, shoulders the financial burden of larger and longer trials but in so doing, creates the possibility of adding a new and potentially more efficient TB drug to currently available regimens. McNeely also pointed out that TBA is critical in working with the WHO to navigate regulatory agencies and purchasing regimens for governments with high TB and MDR-TB burdens (McNeely, 2009).

A major pharmaceutical (Johnson and Johnson) supporting an offshoot focused on infectious disease drug development does not fit the stereotype of pharmaceutical companies embracing profit as their primary objective. Though Tibotec also researches ARVs, which constitute a ‘crossover’ class of drugs (i.e., there is a lucrative ARV market in high-income regions even though the majority of HIV positive individuals live in low-income regions), they are able to pursue tuberculosis drug treatments largely because Johnson and Johnson channels them money from the sale of their more lucrative drugs. In this case TBA cofinances particular aspects of the drug development process such as toxicity studies, but otherwise TBA and Tibotec independently pay for their respective trials. TBA however also expedites multinational availability of new drugs through their negotiations with the WHO, and with donors who might eventually subsidize large-scale purchases for distribution in low-income regions.

Otsuka is another example of a major pharmaceutical company with a longstanding record of tuberculosis drug development. They also have a promising compound they are developing, OPC-68683, which inhibits the production of mycolic acid, a component of Mycobacterium tuberculosis’ cell wall (Matsumoto et al., 2006). Though the details have yet to be arranged, Otsuka also has intentions to make their compound affordable should it prove successful.

Clinical trials also represent an obvious site of community contact, knowledge production, and capacity building. Recent scholarship has pointed more often to the potential in clinical trials for abuse of human subjects. The point at which all new drugs need to be tested in large numbers of individuals to scientifically confirm effectiveness – Phase III trials – inherently creates vulnerabilities for trial subjects in the course of knowledge production if new drugs prove ineffective, if there are side effects not found in earlier phases of testing, or if trial designs are flawed. Currently compounding the vulnerability are increasing tendencies to conduct trials on nonwestern, low-income populations of new drugs intended for western markets; the corporatization of trial management; and a financial incentive to focus more on producing the ‘right’ data than on participant safety (cf. Petryna, 2009; Petryna et al., 2006). While this work is critical and relevant, it also can obscure the potential for clinical trials to make positive interventions in participating communities as well as the necessity of conducting trials of tuberculosis and other neglected disease treatments in regions where they are needed. For both TBA and its tuberculosis vaccine counterpart, Aeras, developing clinical trial sites represents a challenge as well as an opportunity for outreach and capacity building. Until trial sites have been redeveloped from decades-long dormancy, it also represents a stumbling block to getting potentially effective drugs FDA-approved (Ambrosino, 2009). The bottom line is that new TB drugs or vaccines have to be tested in areas where there are enough individuals with tuberculosis to enroll in later-phase clinical trials, and where consequently the drugs and vaccines will be needed the most; these areas are also low-income regions, however, that do not possess resources to maintain clinics, laboratories, and trained personnel.

What ‘redeveloped’ means is obviously key, but for TBA, Aeras, and organizations like the South African Tuberculosis Vaccine Initiative (SATVI), the strategic necessity of getting new drugs or vaccines tested for approval and subsequent distribution as part of their basic missions means comprehensive approaches to site development. In other words, clinical trials happen in the same areas as the marketing of successful drug treatments, thus inextricably tying together financial commitment, participant welfare, and community trust. Trial design thus goes well beyond optimal data procurement. For Aeras and SATVI, training not just health personnel but everyone working within the larger vaccine trial apparatus, including drivers and cleaners, is critically important to successful recruitment of participants in clinical trials, and for imparting better understanding to community members of

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9 Moxifloxacin in the meantime is already being used for tuberculosis treatment since it is already FDA-approved as an antibiotic (cf. www.msf.org). Also, treatment adherence depends not just on length of drug regimen, but on a host of other, typically localized factors (cf. Das and Das, 2006). Thanks to Beth Greenough for pointing this out.
what trials are about and why they are important to engage with (Willingham, 2010; SATVI website). Training courses at SATVI have also become a means of educational access and development of local expertise (Willingham, 2010), with individuals gaining skills in lab management, statistics, health care, good laboratory and good clinical practices. At the same time, staff at SATVI take care to present vaccine trials, and even tuberculosis, in language and images that will be more readily understood by local communities, and meet regularly with a Community Advisory Board constituted by members representing various constituencies and their potential concerns (SATVI website). Evident here is the place-specific context in which scientific research happens and the localized dynamics that make field sites variable domains of knowledge production despite increasing standardization of laboratory equipment, assays, and data generation.

Aeras attempts as well to work in places that have research histories, or at sites that have experience conducting trials in other areas such as nutrition, malaria, or HIV and thus have facilities that can be adapted for tuberculosis diagnosis and testing. As Peg Willingham, former Senior Director of External Affairs at Aeras explained, on the technological side the necessity of creating trial sites that meet international standards of scientific and clinical practice means building hospitals or clinics often better equipped than those in the US. It also means producing new professions where none existed before, and creating regional capabilities in scientific research, data management, diagnostics, laboratory technologies, and biostatistics that can be continued beyond Aeras' involvement and in other areas of biomedical research (personal communication, 2010). To that extent, Aeras always employs local staff wherever they develop trial sites, maintaining a minimal American or European presence; they also partner when possible with regional organizations such as the South African TB Vaccine Initiative, which according to a recent Aeras report runs “the most advanced clinical field site for TB vaccine development in the world” (Aeras Global TB Vaccine Foundation, 2009:9).

Collaborating with regional organizations and employing local staff is especially important in gaining the trust necessary for successful vaccine trials. As pointed out by Willingham, drug trials potentially enable participants to see the diminution or disappearance of symptoms, whereas in vaccine trials there is never a “feel good moment” (2009), only the abstract hope of prevention. There is also often stigma attached to tuberculosis, an issue potentially compounded in an efficacy trial Aeras is conducting with The Aurum Institute of South Africa6 for a vaccine to prevent tuberculosis among people with HIV. Since all of their vaccine candidates will be tested for safety in people living with HIV (Aeras Global TB Vaccine Foundation, 2009), community outreach and trust are critical, another reason Aeras joins research sites that have had community presence over a long period of time. One example of this is a joint Kenyan/CDC-run site in western Kenya that has done malaria research for the last 30 years and AIDS research for the last 5 years. When Aeras recently joined them, the local staff’s buildup of trust among community members slowly over time helped expedite TB vaccine research (Willingham, 2010). The long-term investments of government and nonprofit organizations in developing clinical trial sites attests to the recognition that area residents have the choice not to enroll in clinical trials, to refuse participation in experimental phases of new technology production. Though trials such as Aeras' and SATVI's Phase III trial of a tuberculosis vaccine are enrolling well,

it was apparent from my interviews that this fact is never taken for granted. Though poverty and limited access to health care still almost certainly play roles in determining whether or not to participate in a clinical trial, the greater availability of health care as a result of trial site development – with or without trial participation – creates more complicated relationships among researchers, research subjects, research sites, and drug development.

Aeras's partnerships also include large pharmaceuticals, and in some respects these partnerships contradict usual patterns. GlaxoSmithKline is actively working on a tuberculosis vaccine, but Aeras currently is expediting its development using funding from the Gates Foundation. As Willingham put it, Aeras is able to further vaccines developed by major pharmaceutical companies when company shareholders are not willing to support such non-novel projects. In return, Glaxo is agreeing to make the vaccine available at low cost should it prove effective (2010). Sanofi Pasteur, another major vaccine manufacturer, is also partnering with Aeras in developing a tuberculosis vaccine. As indicated by Willingham, European pharmaceutical companies still have a model of maintaining vaccine production for diseases of poverty that US companies do not, yet Aeras makes production less risky by subsidizing costs of clinical trials and other costly vaccine development processes (2010). As she implies, the relationships between Aeras and GSK or Sanofi represent a dynamic balance between a newly articulated corporate social responsibility on the part of major pharmaceutical companies in response to global criticisms of their practices, and a profit motive retained by shareholders and company executives. Tapping the expertise, community presence, and financial help of nonprofits like Aeras enables companies to attain both goals when these would otherwise remain in irreconcilable opposition.

A final example of the various arrangements found among PDPs focused on tuberculosis is Eli Lilly's Drug Discovery Initiative (DDI), a public–private partnership with the agenda of filling the early-stage pipeline with new compounds for MDR-TB. With support from the NIH, the DDI's objective, as stated in one of its press releases, is “bringing together specialists from around the world for the systematic exploration of vast, private molecular libraries in search of new TB treatments” (2008). The primary library referred to is Eli Lilly's chemical library of over 500,000 compounds, to which the DDI will bring “microbiologists, molecular biologists, synthetic chemists, medicinal chemists, pharmacologists, toxicologists, and process chemists” to systematically screen these compounds for their possible efficacy in treating tuberculosis (Lilly, 2008). In addition to Lilly's library compound, the DDI takes on compounds other companies say they cannot (do not want to) develop alone, as well as academics needing resources and facilities to pursue promising leads that their own universities cannot support (Lilly, 2008). DDI and the larger operation of which they are a part, the Lilly MDR-TB Partnership, collaborate with biotech firms pursuing various areas of tuberculosis research but who need financial or other resources to bring their endeavors to fruition. The Microbial Chemistry Research Foundation of Tokyo, for example, recently donated to DDI a new candidate for treatment of TB, CPZEN-45, for further development (Lilly Drug Discovery Initiative, www.thedrugdiscovery.org). Recognizing the multiple approaches beyond drug development needed for effective intervention into MDR-TB, Lilly's MDR-TB Partnership has also joined the Red Cross and Red Crescent and the Infectious Diseases Research Institute, among

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6 The Aurum Institute is a South African-based nonprofit medical research organization dedicated to researching and treating infectious diseases like TB and HIV.

7 This statement was contradicted by Gail Cassell of Eli Lilly's Drug Discovery Initiative when she stated that US-based Lilly's policy was continuing to manufacture drugs even if they are selling less than $5 million if there is unmet medical need and if Lilly is the only one manufacturing them (Cassell, 2009).
other agencies, to train physicians and other health care workers, fund advocacy groups, build or bolster manufacturing capacity for tuberculosis drugs, and strengthen surveillance systems in high-burden countries including several in Eastern Europe, Russia, China, India, Kenya, and South Africa (Indianapolis Star, 2007; Lilly, 2008). Part of their agreement is to transfer to several high burden areas the blue-prints for manufacturing capreomycin and cycloserine, two second-line tuberculosis drugs patented by Lilly.

3. The promise of partnerships

Returning to Jasanoff’s question concerning the impact of new biotechnologies on the organization of space and social practice, the dedication of pharmaceutical companies, nonprofits, university researchers, government agencies, and philanthropies to finding drug treatments for infectious diseases such as tuberculosis is creating highly dynamic spaces of social, scientific, and political engagement, if not of political order. Moving away from conventional patterns of pharmaceutical practice and towards sharing of distribution rights, a focus on public health benefit instead of or in addition to profit, mediation of the WHO and other global entities in negotiations of government adoption, regulatory approval, and funding means a much more complex and multifaceted landscape of scientific and technological exchange at multiple scales. Surveys of community-level technology adoption in South Africa, for example, shape product and delivery method development at universities and pharmaceutical firms in the UK or US; global entities like the WHO meet with nonprofits and national government representatives to work out purchasing schemes eventually enabling new therapies to appear in even isolated rural clinics; and clinical trial sites are revitalized through European, American, and regional expertise while refracting highly localized social practices and preferences.

PDPs also provide incentives to university researchers discouraged by their departments from pursuing infectious disease research, and provide as well the possibility of expanded resources. Scientists in low-income countries have access to better laboratory and clinical facilities, bolstered training, and research opportunities where few existed even a decade ago. Down the line, health care workers and their patients in high-burden areas will have new treatments for a disease that has proven highly intractable and because of HIV, even more pervasive in many communities. Governments might see a decline of tuberculosis in their populations and – at least for one disease – the extraction of drug procurement from inequitable and highly burdensome intellectual property agreements and towards internal production capabilities. As one MSF representative said, the growth of PDPs has electrified the field of infectious disease research, opening the way for getting new compounds into the drug development pipeline for the first time in decades and creating more potential for treatment capacity down the road than existed even a decade ago (Casenghi, 2009). Enabling scientists across a wide spectrum of disciplines to get together within optimal conditions of laboratory and chemical library resources also presents the possibilities not just of speeding up scientific discovery, but of forging potential new arenas of research.

A departure from TRIPS-based regulations in the context of PDPs has not yet been replaced by another set of implicit or explicit rules, which means that there is a degree of creative unpredictability in how partnerships form and what agreements will look like should successful treatments result in the course of collaboration. Unpredictability shows in particular among the pharmaceutical companies involved in infectious disease research. Contrary to the stereotype of the pharmaceutical industry as undifferentially aggressive, profit-driven, and unmoved by global burdens of disease, several companies have shown not only a commitment to infectious disease research, but a track record (in the case of GSK and Otsuka, for example) of having pursued this kind of research and development long before global criticism made it advantageous to do so. This is not to suggest that the industry has experienced a complete morphing of principle objective; even those pharmaceutical companies supporting neglected disease research that could benefit millions of individuals rather than earn millions nevertheless continue to commit the vast majority of their resources to the status quo of TRIPS-governed, market-driven practices. It is to suggest, however, that even without a more radical reorganization of an entire industry and its regulatory apparatus, there is room for pharmaceutical companies to forefront humanitarianism in some of their R&D decisions or to redefine ‘market potential’ to one of high volume and low cost rather than the converse. Indeed, it is ironic that minus a global change in how all drugs get developed (that is, the dissolution of TRIPS and beyond) it is necessary for pharmaceutical companies to practice business as usual so that profits from blockbuster drugs earning millions in high-income countries can subsidize less lucrative lines of neglected disease research.

The negative side of unpredictability is that much of how collaboration between private and public entities will work in the long term, and how successful products of these collaborations will be distributed, has not been worked out. In the short term, as stated above, the complimentarity of public and private is clear and the need for collaboration understood by both. Similarly when the product in question is a compound with multiple markets and applications, distributional rights of the compound are relatively easy to secure. But for early stage compounds that will require more resources to develop, or which might not have applications beyond tuberculosis, ultimate production and distribution remain tenuous. Here, the expense of developing new drugs and the limits of how much pharmaceutical companies are willing or able to spend without a promise of ample return become evident. Global health entities like the WHO’s Stop TB program are actively working with various constituencies to address issues of distribution and purchase of new tuberculosis drugs and vaccines, but these areas are complicated and regionally specific. The point is not that the WHO’s Stop TB department needs to solve all of the myriad logistical problems confronting the advent of new tuberculosis compounds, but that in the new terrain of infectious disease drug development all sectors need to help figure out how final stages will happen even when new compounds are being developed by pharmaceutical companies.

The enormous expense involved in new drug development is an issue that not only remains unresolved, but that threatens the sustainability of PDPs perhaps more than any other factor. Nonprofits like TB Alliance and Aeras depend primarily on donations from government and philanthropic agencies to fund the work of hiring scientists, conducting clinical trials, etc. Yet this funding by nature is constantly precarious. In part this has to do with the larger politics of global health, wherein organizations dedicated to the many underfunded infectious diseases affecting large swaths of the globe battle over scarce resources from western governments that may or may not prioritize global health or that prefer to target prevention over treatment. Though tuberculosis garners more funding in this unfortunate struggle than many infectious diseases, financial resources remain grossly inadequate. While it helps to have tuberculosis listed by the US Department of State as a biodefense threat, it is down the list from higher priority diseases like smallpox and anthrax, and money in the area of biosecurity typically does not extend to large-scale drug manufacturing and distribution.
In a joint letter recently written by TB Alliance and Aeras, both organizations express their profound disappointment at the low level of funding designated by the Obama Administration in its new President’s Global Health Initiative. Citing the large funding allocations for diseases of ‘similar magnitude,’ TBA and Aeras protest that apparently ‘tuberculosis is a relatively low priority for the Administration, which is puzzling since TB is the world’s second-leading infectious killer and is the leading cause of death among people living with HIV/AIDS’ (Aeras Global TB Vaccine Foundation and TB Alliance, 2010:1). As Willingham succinctly put it, ‘what is it about two million deaths a year that doesn’t warrant funding?’ (2010).

In addition to the vagaries of government funding priorities are the parameters of philanthropic support. Again the politics of global health matter, as particular infectious diseases capture the attention of donor agencies as a result of a congey of factors. One of these is how easily diseases can be ameliorated, thereby effectively translating donor support into the most lives saved per dollar spent. Tuberculosis does not necessarily perform well against this rubric as it is an extraordinarily difficult disease to eliminate: the bacterium that causes it is tenacious, it is difficult to diagnose in low-income regions, current drug regimens can take the better part of a year to complete, and the only available vaccine is largely ineffective. This does not mean that philanthropies do not fund tuberculosis at all; the Gates Foundation in particular has generously supported tuberculosis research. It does mean that TB is not likely to become a priority funding arena within the politics of global health.

Supporting new drug or vaccine development for any disease is also not always a priority for philanthropic agencies because of a combination of high cost, high risk, and low visibility. The Gates Foundation is funding tuberculosis vaccine trials through Phase II because these are less expensive. Conducting Phase III trials involving numerous sites around the world, thousands of participants, clinical facilities, various health care personnel and scientists, and well-equipped laboratories will cost hundreds of millions of dollars, eventually straining the largesse of even the most generous donors (Willingham, 2010). Finding agencies willing to fund the development of clinical trial sites is also a struggle because the benefits to disease reduction in money spent on diagnostic tools or data management training could take 10 years to realize. The result then of constant flux in the level of donor support, and precariousness in long-term donor commitment, means a continuous search for ways to fund drug development. The primary mission of nonprofits to make new tuberculosis drugs available and affordable to all who need them, however, makes selling even at minimal profit levels something of a point of contention for some. Others see slight profit margins acceptable, or point to the large middle classes of India and China as potential large-volume, low-price markets to subsidize drugs to the very poor who cannot afford to pay anything. As it currently stands, however, no solid plan has been worked out to fund non-competitive drug production, and the conspicuous lack of investment from governments makes calls for less reliance on market factors and more on public sector funding (Buse and Harmer, 2007) difficult to achieve.

As the collective partners within PDPs are well aware, regulatory and distributional issues can also be exceptionally challenging to overcome. On the regulatory front, most local research approval boards are not used to seeing projects at such an early stage, and therefore find it difficult to assess the quality and validity of clinical development projects not yet approved by the FDA. The inability to employ full time scientists dedicated to reviewing proposals also means sometimes significant delays in receiving approvals to begin trials – in one case, a delay of 18 months (Geiter, 2009). One suggestion in amending this situation would be working with the WHO to develop regional capacities for reviewing high-priority projects, a sort of research approval board equivalent of regional trading blocs (Geiter, 2009). One concern, however, is that national sovereignty issues would prevent movement in this direction.

Another issue, as articulated by Michael Kimmerling (2010) of the Gates Foundation, is the training of health care personnel required when a new drug regimen for tuberculosis (or any other disease) is adopted in government-supported programs. Educating physicians and other health personnel about the new drugs, how to prescribe them, the potential side effects to look for, and whether they are safe for all populations including HIV positive patients takes careful training and resource allocations. Financially as well, governments can be faced with difficult decisions about how to allocate insufficient health budgets when high tuberculosis burdens typically mean high burdens of other diseases and other health complications. The rapid increase of MDR-TB cases in areas like South Africa make it more compelling for governments to purchase new treatments, but more expensive as well when MDR cases require several new compounds. However, according to TB Alliance, new MDR-TB drugs represent the potential to significantly reduce the cost of treatment because they are faster-acting and would be available at much lower prices than current second-line pharmaceuticals.

A further issue of access characterizing some new drugs but potentially not those produced through PDPs was highlighted by Kmat and Nyato (2010) in their recent study of pharmaceutical consumption patterns in Tanzania. They found that even after governments purchased new treatments for infectious diseases (in their case, for malaria) and made them available in local pharmacies, it did not mean they were getting to people because people often chose not to buy them. The newest drugs not produced through PDPs not only are more expensive, but getting them from municipal dispensaries at subsidized rates can mean standing in line for hours. Though long lines obviously means that some are gaining access to the newest treatments, many individuals either are unwilling or unable to endure the wait and instead go to local pharmacies. These continue to stock primarily the older, less expensive drugs because – as pharmacists told Kmat and Nyato – this is what their customers demand regardless of whether the older drugs are effective (Kmat and Nyato, 2010). Though most of these obstacles should be avoided with new drugs that will cost little to nothing, implicit in this study is the need to ensure that communities get information about new drugs when they appear so that patients will select new drugs over older, and potentially less effective ones—an aspect of access that PDPs are increasingly aware of.

Finally, Jasanoﬀ raises the issue of whether new biotechnological developments offer the structural capabilities for local negotiation (2006). This question as it is couched is in large part not relevant yet for PDPs given that actual technologies have not yet been deployed. Indications would suggest, however, that PDPs are doing a good job in ensuring a certain degree of consistent local input. One form of community participation is in the kind of technology adoption surveys especially critical to TB Alliance’s

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8 The alarming rise of MDR-TB in many areas is in part a result of better reporting, but it is also becoming clear that the increase is also due to MDRI-strains of bacteria being transmitted from person to person, rather than MDR-TB resulting from nonadherence to drug regimens.

9 Hospital politics, government changeovers, Green Light Committee approvals (the GLC is a part of the WHO ensuring proper use of new tuberculosis drugs), stigma, and other issues also impede distribution and access, but I do not have room to deal with them all here. See Peris Jones (2009), for an excellent example of some of these issues at play for antiretrovirals in South Africa.
process of drug development. Well before new drugs are approaching the end of the research and development pipeline, communities have been canvassed for preferred delivery methods and other critical points for successful new technology adoption.

Another point of input is in the conduct of clinical trials. Even when carefully designed with multiple points of input, clinical trials still represent potential sites of vulnerability and tension. As Holden and Demeritt (2008) suggest in a recent study of biomedicine in Singapore, attempting to adhere to international scientific standards in medical research can create bioethical tensions between maintaining standards in order to ensure future regulatory approval, and protecting human subjects (81). In their estimation, "Science in Singapore requires the construction not only of an entrepreneurial subject [scientists] but also of an individuated biopolitical subject willing to offer itself as the raw material for scientific research" (76). In Singapore, the clinical trial participant was 'deafeningly silent' (81). Though the point could be carried too far, the excision of financial entrepreneurialism from the trials of new tuberculosis drugs suggests a different pattern of biomedical knowledge production. That is, the absence of financial incentive in these trials, the added community input, and the humanitarian nature of PDPs' objectives all point towards trial designs geared toward maximum benefit and minimum risk in the short as well as long term. A question so far unanswered is whether it also suggests a different biopolitical subject with a greater capacity and willingness to shape the experience of trial participation.10

4. Conclusion

In their recent critical overview of numerous public–private health collaborations, Buse and Harmer (2007) point out the 'seven bad habits' of many PDPs, one of which is not including sufficient local expertise within partnership advisory boards or scientific staff. When evaluating directions of scientific expertise and technological innovation in conventional terms, there is no question of relations being entirely equitable between the producers and recipients of new tuberculosis compounds. Though PDPs might hire local staff when conducting surveys and clinical trials in high burden regions, for instance, their base of scientific operations, most of their research scientists, and the majority of their board members are from Europe, the US, or Japan. Yet in one significant respect at least PDPs complicate conventional analyses of technological adoption because of course the technologies they are developing are targeted explicitly to low-income populations, not – as is typical – targeted toward prosperous markets with the possibility of eventually trickling out to everyone else. If the decoupling of biotechnological development with market incentives poses logistical problems, it also enables the creation of new research ecologies linking together infectious diseases, scientific advances, and financial resources. Should PDPs prove sustainable, these ecologies could solidify into production ontologies that redefine market, modes of production, and research targets and the relationships among these.

At their best, then, PDPs represent multiple articulations of scientific discovery, university research, pharmaceutical industry, global health organizations, and nonprofit agencies that together are creating new relations of research and production across multiple scales. Within recent literatures on local–global relations, the trend is often toward recognizing the multiple directions these relations flow, refract, and morph from communities to regions to the global. The complexity of PDPs makes it sometimes difficult to actually trace directions of influence or even their derivation, and this points to the need in discussions of circulations of exchange to acknowledge the often tenuous and distilled nature of relations that happen across geographic scales as well as across scientific disciplines, organizations, modes of production, and governments. Though global opprobrium in part fueled some pharmaceutical companies' decisions to fund neglected disease drug research, for example, it is unclear what propels it now or the degree to which market forces and regulatory changes played equal roles in launching more humanitarian research directions. The result of this turn is sometimes explicit, or potentially explicit, in the outcome and distribution of a new drug. Yet corporate influence on particular communities is just as often obfuscated by being embedded in a larger web of drug production involving so many other individuals and entities that by the time it gets to the community level – if it gets there at all – might have lost all trace of corporate input even if that input was initially critical. By the time a successful new compound becomes available to high-burden regions, the influence of community surveys in determining delivery methods will be largely forgotten, especially if logistical, financial or other factors mediated the final decision on packaging and delivery.

In the shorter term, PDPs are providing a few areas in Africa, Asia, Eastern Europe, and South America well-equipped laboratories, clinical facilities, scientific expertise, and drug production capabilities. The benefits of these clearly will extend beyond local communities as regional populations access medical facilities and scientific expertise is applied toward research on other infectious diseases and potentially, new treatments. In the long term, if new tuberculosis drugs ultimately become available and logistical hurdles of distribution and access are overcome, the benefits to communities of individuals living with tuberculosis and HIV are potentially profound.

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10 See Fairhead et al. (2006) for an ethnographic study of why parents in the Gambia did or did not choose to enroll their children in a pneumococcal vaccine trial. Factored into their decisions was not just the risk of the new therapy being tested, but the longer history of the particular organization running the trial and of past medical interventions more generally.