

# Open Development: Is the "Open Source" Analogy Relevant to Biotechnology?

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## Abstract

IP controversies are an increasing part of biotechnology policy discussions. Those concerned that strong IP regimes may limit innovation have considered patent thickets, fragmented rights, and transaction costs. Those concerned that strong IP regimes may adversely affect developing countries have considered the limited access of the poor to much needed biotechnologies (including pharmaceuticals and food crops) and to the resources needed to generate new IP claims. This chapter explores and critiques an approach to stimulating innovation and diffusion that has drawn increasing attention: open development. In the process, it examines some of the analogies that have been made to free and open source software manufacturing, where remarkable innovation and value creation have taken place outside of traditional IP regimes.

We consider open development broadly, including open licensing schemes, open innovation communities, open standards, and even open business models at the product market end. We address specific questions. Are these approaches conformant with recognized needs in the biotechnology industry and in developing countries? What might we expect to be the economic effects of open development on innovation and economic development? The current state of knowledge renders answers to such questions highly speculative, so we also suggest research strategies that might lead to more definitive answers.

# Introduction

During the past quarter century, innovation and growth have characterized the biotechnology industries. At the same time, multinational agreements have strengthened and harmonized global intellectual property standards. The link between these two developments is the subject of much controversy. Did economic growth occur because of the growth of IPRs? Did economic growth occur despite the growth of IPRs? Or was the growth of IPRs an institutional manifestation of the economic interests concomitant to economic growth?

Academic research and public policy discussions during the 1990s explored many concerns about the increased scope and global reach of IPRs, including IPRs in biotechnology. A spectre is haunting the biotech industry---the critics seem to say---the spectre of IPRs. Despite the rapid growth of the biotechnology industries, one common concern is that the proliferation of IPRs may raise the costs of innovation and thereby slow technological progress. A second concern is distributional: the increasing global scope of IPRs appears to disadvantage developing countries, who accede to a regime of global IPR harmonization without possessing the IPR riches of the developed countries. A related concern is that the assertion of IPRs over the genetic resources of developing countries may constitute a kind of "biopiracy" by developed countries. Such concerns are entangled with a concern that proprietary rights (such as patents) may be inappropriate in the field of biotechnology, where innovations may be mere discoveries and where substantial public-sector research funding can make it difficult to determine the substantial contributions of private agents.

Claims to biotechnological innovations are currently asserted as patent rights, plant

breeder's rights, trade secrecy, trademarks, and to a lesser extent copyrights. It is practically axiomatic that the present system has many defenders. However it also has vocal critics who call for reform. Proposals for reform include shifting the mix of proprietary instruments (e.g. emphasizing plant breeder's rights instead of patents) and creating new specialized forms of protection (e.g., "sui generis" provisions). Such responses leave largely unquestioned the traditional proprietary model of innovation. In this chapter, we explore an alternative: we consider a non-proprietary mode of innovation, known as 'open development'. While open development relies on contemporary legal institutions and does assert some limited IPRs, the open development approach to innovation is distinct.

An open development movement recently has emerged in biotechnology. We call this the OpenBio movement. (In some circles, it is known as "open source biotech".) Some participants in this movement have consciously emulated the free and open source software (FOSS) movement. This emulation often appears quite natural: both software and biotechnology are emerging fields of study, and there are some important parallels between the two fields.<sup>1</sup> Indeed, the open development movement in some areas of biotechnology, such as computational biology, is largely an extension of the FOSS movement. Our goal in the present chapter is to expand interest and encourage further inquiry into the OpenBio approach to biotech research and innovation.

Both the OpenBio and FOSS movements are in large part a reaction to the proliferation of IPRs and to concerns that IPRs may restrict research and access to new innovations. These concerns stem from a similar basis: both software and biotechnological innovation are often cumulative and sequential, and innovations in both areas often constitute

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<sup>1</sup> As Dawkins (2004) writes "genes are software subroutines that perform cellular operations."

research tools. Moreover, in both areas some observers have claimed that IPRs are too often granted for inappropriate subject matter: pre-existing art, or pure science, or even pure mathematics. For example, in software, certain innovations appear to be essentially mathematical algorithms, and in biotech, certain innovations appear to be essentially scientific discoveries. In both fields, it is sometimes difficult to differentiate between basic R&D and applied R&D (Stokes 1997).

There are also important differences between the two industries. These differences determine the extent to which lessons from the FOSS movement are applicable to the OpenBio movement. In particular, we are interested in differences that matter for research, innovation, and economic development.

This chapter is organized as follows. First we provide a very brief review of the IP framework relevant to biotech research and development. In the process, we briefly introduce some controversies related to IPRs in biotechnology. We then discuss the open development alternative and provide examples of open development in the biotech industries. Along the way, we review some economic principles underlying open development and innovation. Finally, we explore some implications of the OpenBio movement for developing countries.

## **Biotechnology and Intellectual Property**

This chapter allows for a broad definition of 'biotechnology'. Following the UN Convention on Biological Diversity (CBD), we use 'biotechnology' to mean "any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use." Ambiguities in this definition (for example, in the meaning of "technological application") will not be important

for our purposes. We wish to explore the role of intellectual property institutions in supporting or restraining biotechnological innovation and developing country access to such innovation.

The Green Revolution typifies early agricultural biotechnology innovation in an important way: the public sector and non-governmental organizations were heavily involved in its development. In contrast, industrial biotechnology consistently has been centered in the private sector. This distinction was never absolute and may no longer be tenable: large multinational firms are heavily involved in agricultural biotechnology, and in the fast evolving area of genetically modified organisms there have been complaints that public sector participation is largely missing in some important negotiations (such as the Cartagena Protocol on Biosafety).

The predominance of the developed-world private sector, and also its assertion of private intellectual property rights in innovations based on developing country resources and knowledge, has generated substantial international conflict. Developing countries have been seen as "gene-rich" in their biodiversity, and even rich in traditional knowledge of potential therapeutic agents, but firms from developed countries possess the technological know-how and financial resources needed to bring innovations to market and to establish contemporary intellectual property rights in these innovations.

## **IP Background**

The past century has seen radical shifts in intellectual property institutions, and the creation of new kinds of property rights has been particularly striking in biotechnology. The U.S. led the way to biotech patents with the United States Plant Patent Act of 1930. Another major shift occurred in 1980, when the U.S. Supreme Court narrowly ruled that living

organisms can be patented (in *Diamond vs. Chakrabarty*). Patent filings in biotechnology began a steady rise. Europe has been slower to allow patenting life,<sup>2</sup> but since the late 1990s European biotech filings have also risen steadily.

Until 1980, academe had little patent presence in biotechnology despite having a large research presence. Academe contributed to the common pool of knowledge through publication in peer reviewed journals. In the U.S. this was partly, perhaps largely, due to issues surrounding the ownership and control of patents generated by federally funded research: in particular, universities had little ability to offer exclusive licensing of government funded innovations. The Bayh-Dole Act (Public Law 96-517) changed that: signed in 1980 and subsequently amended to encourage university patenting and exclusive licensing, it has led to an increase in university biotechnology patents.<sup>3</sup> Some observers now express concern that journals are being supplanted by patents as vehicles of knowledge dissemination in the area of biotechnology (NRC 2003). The implications for researchers are profound. As an example, consider Cornell University's particle delivery system ("gene gun"), developed in the 1980s and then exclusively licensed to DuPont. Despite its academic origins, it is not a freely available tool of research. American Cyanamid claims that lack of

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<sup>2</sup> TRIPS has accommodated only part of the European reluctance to patent life. (See below.) In June 1999, the EPO decided to implement the European Union Biotech Patents Directive (98/44/EC), which allows patents on life, but still forbids plant and animal patents. This decision was controversial in Europe, and some have argued that it conflicts with provision of the European Patent Convention, Article 53, which forbids patents on plant or animal varieties.

<sup>3</sup> History suggests an irony in the timing. The 1980 Cohen-Boyer patent on "gene-splicing", often cited as an fundamental innovation that proved essential for the biotech industries, was licensed non-exclusively (to more than 300 licensees).

access to this tool substantially delayed their development of herbicide tolerant crops (Pray and Naseem 2005). The swell of patenting in the biotech industry has raised fears that such stories of delayed development will become increasingly frequent.

### **Proprietary Lifeforms**

International agreements and organizations have established the mechanisms by which rights to biotechnological inventions are protected, including trade secrets, plant breeder's rights (PBRs) or plant variety protection (PVP), and patents. We briefly discuss the relationship between PBRs and patents, and then discuss patents in more detail.

The WTO's Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) was negotiated in the 1986-94 Uruguay Round. TRIPS was a far-reaching agreement on various aspects of IPRs (including copyrights, patents, trademarks, geographical indications, trade secrets, industrial designs, and semi-conductor layouts). It was an effort to harmonize and internationalize intellectual property rules. The TRIPS agreement allows countries to exclude plants and animals from patenting, but then obliges them in that case to offer some other form of protection (essentially PBRs of some kind, possibly country specific). TRIPS did not formalize protections of traditional knowledge and indigenous genetic material: how to ensure these remain available to the country of origin has not been resolved. Currently the core international understanding of PBRs is governed by the International Union For The Protection Of New Varieties Of Plants (UPOV).<sup>4</sup> Like patents

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<sup>4</sup> The UPOV is a intergovernmental organization established by the International Convention for the Protection of New Varieties of Plants (UPOV Convention). This convention restricts farmers rights, including for example the right to save seed from protected crops for reuse.

under TRIPS, PBRs under the UPOV convention generate proprietary rights (to exclude others) for at least 20 years (25 years for trees and vines).

Patents are generally more expensive to obtain (to file, translate, and litigate) than PBRs. Even so, the cost to obtain a UPOV authorized Breeders' Right certificate in developing countries is expected by some observers to exclude all but the largest seed companies (Sahai 1999).<sup>5</sup>

The most economically important differences between patents and PBRs are the criteria for grant. Patents are granted if inventions are judged to be novel, non-obvious, and industrially applicable (i.e., the invention has utility). PBRs are granted if the protected organism is distinct (compared to previous varieties) and has never before been commercialized. Note that patents are not supposed to be granted for discoveries of substances found in nature, but PBRs may be granted for discoveries (of things in the wild).

Another crucial distinction is that patent grants (in principle, at least) have an enablement requirement. The patent application must allow someone ordinarily skilled in the art to replicate the invention. Enablement with biotechnology can be tricky: replication may not be ensured (e.g., with mutation). It may also be that, lacking a specimen, third parties are not able replicate an invention. Hence, often it is necessary to deposit biological materials with a designated center. The 1977/1980 Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure governs rules on depositing of materials. The deposited materials are open to the public. In contrast, PBRs do

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<sup>5</sup> Stiglitz (2004) argues that developing economies have a big disadvantage in playing the patent game against the patent players of the North (whether it's in claiming priority to a discovery or in challenging the validity of a patent grant).



not require that a third party be able to "repeat the invention." All that is required is that there be uniformity and stability in reproduction. Moreover, there is no public deposit requirement: the seeds or samples are held in confidence.

PBRs may provide for breeder's and farmer's exemption. For example, under the UPOV Convention, a country may elect to leave farmers free to use the saved seeds of a protected plant for his own use, so long as he doesn't sell them. More generally, a protected variety can generally be used without permission or royalties as a starting point for breeding other distinct varieties. Under patents, such actions may constitute infringement.<sup>6</sup>

Article 27.3b of TRIPS does allow countries to exclude from patentability "plants and animals", as well as essentially biological processes other than microorganisms and microbiological processes. Here "essentially biological" means rooted in processes occurring naturally nature (not implemented by the scientist). The term "microorganism" is ambiguous: it could mean any microscopic organism, or only a unicellular organism. While Article 27.3b allows countries the right to exclude plants and animals from patentability, it does not prohibit them from allowing it, as for example the US and Japan have chosen to do.

## **Functions of Patents and PBRs**

We have seen that patents and PBRs share many characteristics. We turn now to some of the anticipated economic effects of such IPRs.

Patents and PBRs are designed to transform a public good into a club good. Since my

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<sup>6</sup> These important exemptions may have been undermined in 1991, when UPOV was modified so that IP holders can simultaneously obtain a patent and PBR.

use of your invention does not reduce your ability to use it, we say that knowledge is non-rivalrous in consumption. If in addition you cannot exclude me from using your invention, we say that the knowledge is non-excludable. Public goods are characterized by non-rivalry and non-exclusion, so in this sense knowledge can be a public good. But in a society that creates intellectual property rights, knowledge may become excludable. Club goods are characterized by non-rivalry and exclusion, so in this sense knowledge can become a club good. From a public policy perspective, exclusion may mean that a club good is underutilized. Since knowledge is so ideally non-rivalrous, it is natural to explore the relative merits of creating excludability. The conventional view is that there are tradeoffs between the dynamic benefits and static costs.

### **Fostering Innovation**

Biotech firms make extensive use of IPRs, especially patents. This suggests that these firms find it profitable to claim IPRs, but it does not imply that this activity is socially beneficial. Public justifications of strong IPRs generally presume that the creation of such rights will promote innovation and commercialization. Ideally, the dynamic public benefit of bringing additional innovation to market will outweigh the static costs of granting rights of excludability. Theoretical and applied work by economists indicates that this ideal need not always be achieved, offering important qualifications to the standard understanding of innovation.

From a public policy perspective, intellectual property regimes are an effort to make sure that socially profitable activities are commercially profitable, so that private individuals will pursue them. Trade secrets, patents, and PBRs increase the economic reward to innovation by limiting the free access of competitors to the fruits of invention. Patents and

PBRs accomplish this by granting temporary rights of exclusion. Since patent applications are public documents, patents may additionally speed knowledge diffusion to the extent that the innovation is truly novel and the patent application truly enables others to understand and implement the innovation. (Such benefits clearly depend on the quality of patent institutions.)

Polanyi (1944) famously argues that "pioneer enterprises should in general be protected against free competition", and certainly many research activities of biotech firms qualify as pioneer enterprises. The basic intuition is simple when large sunk costs are required to realize important innovations that might easily be copied ex post. Additionally, Polanyi refers to a "strong presumption" that patent protection is required to secure profitability adequate to justify both the research investment and venture capital, especially when we consider innovation occurring outside of established firms.

In other circumstances, such justifications of IP protection fail. When innovations and their commercialization require small sunk costs to achieve, involve little novelty, and are likely to be independently produced in the absence of IP protection, then IP protection may work against the public purpose. Modern IP regimes, especially patent regimes, have been heavily criticized by some as failing to protect the public interest. Some observers believe that extensive IPRs are being granted for innovations that are not novel or are obvious to anyone skilled in the relevant arts. Such critics have been especially vocal in software manufacturing, where prominent computer scientists (notably Donald Knuth and Richard Stallman) have claimed that patents have been granted on programming techniques comparable to undergraduate homework assignments. Similar criticisms are now being raised concerning biotech patents.

## **Constraining Innovation**

The tale of the mid-19th century dyestuff industry appears as a cautionary tale in the discussion of patents and innovation: vigorous patent enforcement in Britain, home to the initial innovations, appears to have stifled the industry, which in contrast grew explosively and prospered under Germany's looser IP laws (Murmman 2003). Some studies of the contemporary software industry sound a similar cautionary note. In an empirical examination of software manufacturing, Bessen and Hunt (2003) find that software patenting activity can substitute for firm innovation effort. They argue that the predominant use of software patents appears related to strategic "patent thicket" behavior, rather than being a means to protect R&D investments. Naturally such results call into question the role of software patents in bioinformatics. More generally, these results raise serious questions about the role of strong IPRs in any industry that shares key characteristics with software manufacturing. For example, Bessen and Maskin (2000) show that strong patent protection can reduce innovation in industries where innovation is sequential and complementary. (That is, later innovations rely on earlier innovations to be practiced.) While Bessen and Maskin focused on IT related industries, sequential and complementary innovation appears characteristic of many biotech research efforts. Indeed, survey evidence finds that many industry researchers in the biological sciences have delayed, changed, or abandoned research projects due to complex licensing negotiations over necessary technologies (Hansen, Brewster, and Asher 2005).

## **Patent Thickets**

Rai (2004) observes that "large pharmaceutical firms---once vertically integrated engines of innovation---must now negotiate a complex array of university and small firm proprietary claims on research inputs", some of which are subject to exclusive licenses.

Economists refer to the need for such negotiations under the general rubric of "transactions costs". When the transactions costs associated with overlapping and dispersed IPRs begin to constrain innovation, we refer to a "thicket" of IPRs. The literature on such constraints has focused on patent thickets.

More generally, when innovation is cumulative and sequential, multiple parties may hold overlapping and/or fragmented IPRs to the different components necessary to constitute a larger innovation. The resulting transactions costs are potentially innovation reducing (Isaac and Park, 2004). Inventors reduce their level of effort, knowing that in the future that they will face these costs. These effects are worse when the extent of the patent thicket is unknown, since an inventor who sinks costs into innovation will be in a weaker negotiating position with the possessors of relevant IPRs. Indeed, "blocking" may occur if the IP holder refuses to license or demands a high royalty.

Potrykus and Beyer's "golden rice" is a well known example. A biotech innovation of the mid-1990s, golden rice produces beta-carotene, and thus could potentially mitigate deadly vitamin-A deficiency in millions of children in rice-consuming developing countries. Striving to bring this product to the developing world, Potrykus learned that more than two dozen different biotech companies claimed patents on the technologies used to create golden rice (Piore 2003). In this case the thicket was successfully penetrated, and eventually the primary patent holder agreed to offer golden rice seed freely to small farmers in developing countries. Unfortunately, the mechanism for cutting through the patent thicket may not be replicable: it appears to reflect a pressing need felt by green biotech firms to garner some favorable press.

## **Research Tools**

IPRs on core research tools may be particularly problematic. In the commercial

sector, they may increase transactions costs on a wide range of innovators. Academic researchers may also be affected, as discussed below.

Heller and Eisenberg (1998) explore how the patenting of research tools can be innovation reducing. They consider ESTs (expressed sequence tags), an important tool in genome research. (We discuss their work in more detail below.) In contrast, Walsh et al. (2003) find in survey evidence that an increase in patents on research tools important for drug discovery has generally not slowed innovation in existing projects. (Projects that failed to emerge due to research tool patents are of course not in their sample, potentially biasing their results.) They note an important exception to their core finding: patented genetic diagnostics appear to be constraining university research efforts.

Overall, Walsh et al. find that transactions costs have usually been manageable rather than prohibitive. But some cost-reducing factors may decline in effectiveness. For example, some firms offshored, where proprietary rights could not be claimed. Increasing international homogenization of IPRs will reduce the effectiveness of this strategy. Additionally, academic researchers sometimes claimed a "research exemption" and used proprietary tools without seeking licenses. In the U.S., a successful 2003 patent infringement lawsuit against Duke University (*Madey v. Duke*) suggests that the "research exemption" strategy will see declining use in the U.S. However European and Japanese patent law is more inclined to protect the unrestricted access of academic researchers to patented tools of research (Eisenberg 2003).

### **The Anti-Commons**

If IPR holders are blocking one another, their technologies may be underutilized. This blocking may be intentional, or it may simply represent the high transactions costs of

negotiating with diverse IP holders. In either circumstance, useful technology may never be developed, and extant innovations may remain unexploited. The term ‘anti-commons’ is meant to capture the role of strong property rights in producing an underuse of knowledge when IPRs transform it into a club good by creating rights of exclusion. The term is chosen to contrast with the theory that real property held in common (the commons) will be overused in the presence of inadequate property rights.<sup>7</sup>

Murray and Stern (2005) broke new ground by offering modest empirical support for the anti-commons thesis: they look for citation frequency declines for scientific publications (in one journal, *Nature Biotechnology*) after patents are granted in the innovations described in the publications. They find a decline relative to other papers, whether or not the patented knowledge involves a research tool. Unfortunately citation rates are an extremely indirect measure of knowledge diffusion, and the authors consider only scientific citations, not patent citations. They also did not address lags in scientific publications (e.g., due to the refereeing process), which might be rectified by adding working papers to their analysis. Nevertheless, their results are suggestive.

Heller and Eisenberg (1998) wrote what is probably the most widely cited paper on the anti-commons in biotechnology. They discuss the implications of expressed sequence tag (EST) patenting. ESTs are considered an important research tool in gene discovery and sequence identification. In 1991, a group of NIH researchers attempted to patent a large collection of ESTs, but they abandoned this attempted after encountering resistance from the USPTO. Many human ESTs are now contained in the freely accessible 100 gigabase

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<sup>7</sup> Common goods are rivalrous but non-excludable, whereas club goods are non-rivalrous but excludable.

GenBank database of sequence data. Many scientists opposed allowing EST patents (HUGO 2000). Industry however has tended to support EST patents,<sup>8</sup> and the USPTO has taken a series of positions that appear in principle to allow EST patents. Nevertheless in 2005, Monsanto's assertion (making analogy to the microscope) that ESTs should be patentable as a research tool was rejected for failure to identify the specific utility of individual ESTs. If we accept the arguments of Heller and Eisenberg, this decision appears to erect an extremely thin barrier against the anti-commons in this area of biotech research and development.

## Varieties of Openness

A recent movement in biotechnology is that of open development, which explicitly borrows ideas from the free and open source software movement. We call this the OpenBio movement. This section considers a variety of open development possibilities, relates them to the free and open source software movement, and explores the relevance to modern biotech enterprises. We consider open standards, open development, and open source.

### Open Standards

Standards are pervasive in any complex industry, and biotech is no exception. Commercial and government standards can affect every aspect of biotech research, production, and sale. These standards may be regulatory requirements, commercial contractual requirements, or simply industry practices. We illustrate with a few quick examples.

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<sup>8</sup> For example, the International Association for the Protection of Intellectual Property (AIPPI) urged that "ESTs, SNPs and entire genomes must be considered as patentable subject matter".



A multitude of government agencies and intergovernmental organizations are heavily involved in standards setting. At the international level, the Codex Alimentarius Commission (CAC, the UN's food standards agency) promulgates food safety standards affecting genetically modified (GM) food. The World Organization for Animal Health (OIE) has a biological standards commission, which like the CAC is involved in antimicrobial resistance testing standards. The International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) provides internationally harmonized guidance for the stability testing of new biotech veterinary medicinal products.

In the present paper, however, we are primarily interested in standards that directly facilitate the coordination of innovation efforts. Technology standards promote interoperability, even in the absence of direct contact between developers. For example, Standard Reference Materials (such as those purveyed by the NIST) support efforts to achieve accurate, reliable DNA devices in pharmaceutical and forensic labs.

Corporations and non-profits are involved in standards development, sometimes with government funding. Many biotech standards efforts focus on various kinds of data exchange. For example, the Clinical Data Interchange Standards Consortium (CDISC) develops industry standards to promote medical and biopharmaceutical product development. CDISC has dozens of corporate sponsors. A smaller but interesting example is the Open Bioinformatics Foundation (OBF), a volunteer organization focused on supporting open source programming projects in bioinformatics. Supported project includes BioMOBY and BioDAS. BioMOBY is a small, grant-funded open source project dedicated to the creation of standards and tools for the registration and exchange of biological data stored on multiple hosts. BioDAS supports the development of an open source distributed annotation system

(DAS) for exchanging and collating annotations on genomic sequence data.

Technology standards committed to transparent and reasonable licensing terms can reduce patent thicket problems. Unfortunately, as Shapiro (2000) stresses, ex ante price setting may attract the attention of anti-trust enforcement, so standards setting bodies may need accommodation from the anti-trust institutions. Such anti-trust concerns are diminished when standards are free and open.

Whether standards emerge via formal or informal industry processes, the intellectual property implications are immediate: industry adoption of a standard valorizes patents essential to implementation of the standard. A patent holder may profit directly through increased licensing fees or indirectly by refusing to license competitors. It is natural that industry groups in standards development organizations (SDOs) will struggle to reconcile the interests of intellectual property owners with the interests of others who wish to practice the standard. This suggests that SDOs should require participants to disclose any patent interests in the standard. It also seems natural that SDO participants should agree as well to license all patents essential to compliance with the standard on "fair, reasonable, and non-discriminatory" terms. In the absence of such safeguard, an SDO risks that its standards will be "captured" by a strategic member.

Free and open standards diminish the risk of such capture. A standard is called "free and open" when any party is licensed to read and implement it without payment. This is usually understood to imply an open standards setting process, structured to circumscribe the market power of specific vendors or groups. Free and open (FO) standards are clearly nondiscriminatory and also clearly set ex ante price limitations.

Such open standards can benefit all industry participants, but the benefits appear especially great for new entrants with small or nonexistent IP portfolios. The incentives of

established firms with substantial IP portfolios to actively participate in open standards bodies are less clear, and economic analyses remain incomplete.

From an economist's perspective, SDOs appear to be involved in the private provision of a public good. This raises the concern that standards will be undersupplied. Offsetting this may be a snowball effect of accepted standards: when biotech firms participate in an SDO in order to align their development process with emerging standards, these standards movements may become dominant as the number of participants reaches a 'critical mass'.

In any case, it is clear that open standards at times garner widespread industry support. We consider one example from the software industry, and one from the biotech industry.

The World Wide Web Consortium (W3C) is the preeminent open standards body for the internet. The focus of these standards is data exchange and display. Hundreds of organizations participate in the development of interoperable technologies (specifications, guidelines, software, and tools). The W3C has struggled to remain independent of specific vendors, who face incentives to co-opt an open standard through 'embrace and extend' tactics or to patent standards-related technologies. The W3C has worried publicly about "the growing challenge that patent claims pose to the development of open standards for the Web". To ensure the continuing openness of both the standards and their implementations, the W3C adopted a patent policy that its specifications must be implementable on a royalty free basis. Adoption of W3C standards has been extremely widespread, and this has ensured a remarkable level of interoperability on the internet. This in turn has supported tremendous innovation, manifested as a multitude of competing, standards compliant technologies.

Biotechnology does not have a single SDO that plays a comparable role to the W3C. However there are number efforts to promote open standards, especially in the areas of data

exchange and interoperability. Consider for example the standards developed by CDISC, which reflect its mission of improved data quality and accelerated innovation in medicine and biopharmaceuticals. CDISC explicitly commits to vendor-neutral, platform independent standards. A variety of pharmaceutical companies, biotech companies, and researchers participate in developing these standards. Companies that practice these standards can evade capture by single vendors while increasing their ability to interoperate (e.g., through reliable data exchange) with the rest of the industry.

### **Free and Open Development**

A development process where innovations are shared freely rather than fenced off with IP claims are called 'free and open development'. (Distribution of modified technology may be restricted to ensure that the modification also remains free and open.) Enabling disclosure is public. While IP recognition may be sought and granted, the licensing to use, redistribute, and modify the technology is provided gratis by the developer. So while enabled technology in the public domain is obviously free and open, patented or copyrighted technology may be as well.

Free and open (FO) development accompanying rapid innovation has been noted in many industries. This seems to challenge the presumptions of many intellectual property arguments. Rosenberg (1976) documents FO development in the machine tool industry, von Hippel (1988) in the scientific instrument industry, and Allen (1983) in the iron industry. It appears typical of FO development that users of technologies are actively involved in the innovation process. Motivations for participation are diverse. Some consider it essential to preserve core research tools in the public domain. Others are concerned about data exchange and interoperability. Generally there is no intent to preclude commercial development,

although some licenses constrain actions that would render proprietary a modified version of an open development tool.

Free and open source software (FOSS) is the most famous contemporary example of FO development. Software development is considered to be free and open only if the source code is readily available and freely redistributable. There are no legal restrictions on the redistribution of the unmodified open source software to others, and in practice FOSS software has generally been available for download without charge. FO development practices in biotechnology have often been deliberately modeled on the FOSS example. This is most evident in bioinformatics, where many FO development efforts *are* FOSS development efforts. For example, computational biologists make heavy use of a public domain sequence search tool (BLAST). In addition, well known FOSS software tools from the Linux operating system to the Python scripting language often play a supportive role in bioinformatics.

Database projects have also been heavily influenced by open development paradigms. An example is the International HAP MAP project, an open collaborative database project among scientists from various countries. This project aims to map common patterns of variations in the genome. The goal is to put the completed data in the public domain. Data access policy imposes minimal constraints: "users agree not to reduce other's access to the data, and to share the data only with others who have made the same agreement." Patenting of subsequent discoveries are allowed "as long as [patentees] do not prevent others from obtaining access to the project's data."

The SNP Consortium (TSC) makes an interesting case study of the effort to cut through patent thickets. Several large pharmaceutical and technology companies joined with Wellcome Trust and academic researchers to file patent applications on single nucleotide

polymorphisms (SNPs) that will be freely accessible to all. (They will not allow the patents to issue.) The SNP Consortium characterizes a SNP map as "an important, but essentially pre-competitive, research tool". TSC has already characterized about 2 million SNPs, so the potential for fragmented patent rights with associated high transactions costs for SNP dependent research was obviously high. The SNP Consortium is a successful example of open development providing tools to advance industry goals. Apparently the prospect of large transactions costs motivated private firms that normally seek proprietary rights to turn instead to free and open development.

The success of the SNP Consortium appears surprising. Each individual firm seems likely to face substantial incentives to "defect" and patent its SNP discoveries. This will provide bargaining chips if the other firms patent, and it will gain a competitive advantage if the other firms do not patent. Explaining this success is beyond the scope of the current paper. However our brief analysis suggests that the SNP Consortium would not be a Nash equilibrium outcome in a "one-shot" game without precommitment, so that to understand its existence we would need to consider the roles of precommitment and of the diachronic relationships among the consortium members.

### **Incentives**

Open development is often considered a puzzle. Why do individuals select an open development model? Is it a viable business model? What are the effects on research and innovation? These are large issues that transcend the scope of this paper, but we briefly point to a few possibilities: inducing complementary innovation, collective invention, and strategic revelation by users.

A producer may find that open development in one area can stimulate product

demand or lower production costs in another area. Open development may raise the rate of innovation in product complementary to a firm's commercial enterprises: it may pay to freely reveal innovations in razors if this stimulates additional razor innovations that increase the demand for blades. Or a firm may freely reveal an innovation in order to stimulate the development of a research tool it needs in a separate commercial endeavor. The issue is one of opportunity cost: such induced innovation may prove the least cost route to the desired innovation.

Under a collective invention process, researchers freely exchange information about new techniques. They share innovations and participate in experimental and developmental projects, working on different modules and/or revising one another's contributions. Famous examples include the development of the Cleveland blast furnace for iron production and Cornish pumping engine for mines (both during the 19th century U.K.). These important innovations were not the result of explicit research and development programs. Rather, innovations emerged gradually as a by-product of capital investment and experimentation (what some economists term "exogenous innovation"). An engineer who freely revealed his design innovations was more likely to see them implemented and thereby tested in real world conditions. This is economically similar to the case of induced research tool development. Owners may encourage their engineers to freely reveal knowledge that might lower the costs of competitors in anticipation both of their own lower cost and of a capital gain on complementary assets (e.g., the value of mines). Additionally, if the industry is oligopolistic, prices may not be viewed as tightly tied to costs of production.

Traditional theories of innovation tend to be manufacturer-centric (von Hippel, 2005). Yet users also contribute to innovation. Users may freely reveal information to producers in hopes of having an innovation implemented. Users may know their needs better than

manufacturers. Rather than be passive, they may actively participate in innovative activity and develop solutions customized to their needs. Users of research tools often propose improvements in functionality or interface. They may rely on open revelation to encourage the adoption of innovations that might otherwise be ignored.

Open revelation is easy to imagine, and easy to find, when users are skilled professionals desiring innovation in a heavily used research tool. It is more difficult to imagine how consumers of pharmaceutical products might contribute innovations to the pharmaceutical industry. And yet a recent example suggests that even in apparently unlikely circumstances, motivated users may invent new ways to foster innovation. People suffering from orphan diseases (like cystic fibrosis) found no existing drugs or treatments perfectly matched to their needs (because the market is too small). Using the Internet to lower the cost of coordination, groups offered themselves as test subjects (Economist 2005). They now participate in creating clinical trials and developing databases (i.e., tissue banks).

### **Concerns**

Might open development actually reduce innovation? Consider the impact of OpenBio on innovation in research tools. OpenBio certainly promotes access to certain research tools, and it encourages user innovation that might be absent from a different development process, but it may also reduce the profits from commercial R&D in the area of research tools. The effect on innovation will depend on conflicting influences: an open innovation process may lower the cost of research tool innovation by eliminating the transactions costs of license negotiations, but the potential benefits of inventive activity may no longer include possible profits from licensing the innovation. This may be because the open innovation process uses licensing that restricts a developer's ability to commercialize



improvements or modifications of an open research tool, or it may simply be that a useful innovation cannot successfully compete with free research-tool substitutes. Such effects could lower development effort in the production of research tools, which could have a net negative effect on innovation in an entire field of research.

The extremely difficult project of anticipating the impact of OpenBio on private incentives is therefore critical. Recall that the core public policy justification of patents is that they stimulate innovation and diffusion by raising the private return to research, development, and commercialization. If open development lowers this private return, growth might suffer. In a simple endogenous growth model, Saint-Paul (2003) shows that philanthropic innovation can reduce long run growth by crowding out proprietary innovation. In his model, the philanthropic innovator offers a substitute for the proprietary good, which reduces the sales and profits of the proprietor, and additionally uses up human capital that could otherwise work in the proprietary sector. However growth reduction is only one possible outcome: it depends on the parameters of the model. If philanthropic innovation lowers the cost of private innovation, private innovation may be "crowded in" even if the proprietary sector will face a lower price.

## **Is the Open Source Analogy Relevant to Biotech?**

Attempts to harness the communitarian, licensing, and organizational innovations of the free and open source software (FOSS) movement to promote biotech innovation and diffusion have been spreading. For example, the BIOS Initiative explicitly speaks of trying to "extend the metaphor and concepts of open source software" to biotech innovation.

Analysis of these attempts has been somewhat contentious. Like Maurer et al. (2004),

some have seen in open development a hope that underserved populations will be more effectively targeted. Like Saint-Paul (2003), others have worried that open source practices will reduce the overall rate of innovation.

### **Analogies Between Biotech and Software**

Popular discussions of FOSS applications can leave the impression that enterprise quality software is being produced as a hobby by amateurs, perhaps even by teenage hackers. This would offer a substantial contrast to some biotech fields, where research can require a team of scientists with advanced degrees, and the credentials of scientists and engineers matter. Useful FOSS software is indeed written by individuals and small groups. However, writing enterprise quality software is generally not a trivial project, and substantial professional and corporate resources are also involved in the development of FOSS software.<sup>9</sup> Biotechnology projects like software projects vary in size and scope: some may need only the resources of a Luther Burbank or a Jonas Salk, while others may require the resources of Monsanto or Pfizer.

Some biotech research shares important characteristics with software development. For example, some research in computational biology focuses on algorithm development. It *is* software development. Other biotech related research focuses on facilitating data exchange, which bears analogy to the W3C efforts to develop standards for information exchange on the web.

Lessons drawn from the FOSS movement are most likely to be applicable to such

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<sup>9</sup> Consider the heavy involvement of large corporations in the Carrier Grade Linux working group of the Open Source Development Lab.

near neighbors. But in biotech considered more generally there are some important differences.

### **Disanalogies Between Biotech and Software**

Traditionally, software code has been protected by copyright, while biotech innovations have been protected by patents. (Obviously this is not a hard and fast distinction, given the large role of software in bioinformatics, and given the growing use of software patents.) Copyright grants rights of exclusion for a very long time (e.g., life of author plus 70 years) but protects only a particular expression of an innovative idea. Patents offer a shorter period of protection (e.g., 20 years, or even less if the rights holder chooses not to renew his patent right) but protect the innovation and not just a particular expression. Copyright is much cheaper to obtain than a patent. Copyright is automatic, while patents applications involve filing fees, lawyer fees, translation fees, and depositing of materials, and even then the application may be rejected.

Outside of bioinformatics, open development is generally not simply a matter of source code sharing. Hope (2004) notes that technical information often is not enough to convey an innovation. "Uncodified" knowledge may be needed to understand how to practice an invention. Once we move outside bioinformatics, "open source" is largely a metaphor for open development: sharing the underlying technological secrets or information and giving access. When a patent holder excludes, knowledge should still be disclosed (through the patent application), but permission to practice the innovation is restricted.

In particular, the "open source" metaphor is misleading if it is applied to the "code" in biochemical sequences, including ESTs, SNPs, or even genes. If these are patented, the "code" is fully disclosed. Indeed, the revelation of "code" in such cases goes far beyond the

standard applied in software patents, where software patents often do not have to reveal the underlying source code in order to satisfy the enablement requirement.

Another divergence of biotech from software manufacturing is that certain fields of biotechnology appear inherently capital intensive, requiring large labs and other physical capital. In addition, substantial sunk costs may derive from needs to comply with regulations (on health and safety) in order to get to market. Venture capitalists may have no incentive to fund biotech startups who cannot claim adequate proprietary rights in their innovations. This of course is just a contemporary application of the Polanyi (1944) argument that "pioneer enterprises" need protection from free competition.

Hope (2004) notes a subtlety in the capital intensity argument. While our first instinct may be that open development in software manufacturing has low capital intensity, this may be false. Of course the incremental project may be able to proceed with a low capital investment. But huge sunk costs support the current software industry: operating systems, fiber optic cables, DSL lines, wireless access points/towers, and modern computer hardware (including modern processors and memory) all reflect tremendous capital investments. Rather than presume that biotech has capital needs beyond those of the software industry, researchers need to explore the extent to which a similar supportive infrastructure may be emerging.

Finally, analogies between software manufacturing and biotechnology are most persuasive when the final products share the key characteristics of knowledge goods: an essential non-rivalry and non-excludability rooted in negligible costs of reproduction. (Of course, this non-excludability may be over-ridden by IPR institutions.) However the final products of biotech research are often not software or databases but rather physical substances or devices that must be produced and sold, and these products are essentially

rivalrous in consumption and excludable.

### **Innovation and Open Development: Where Can It Work In Biotech?**

Biomedical research appears increasingly proprietary and secretive, generating fears that future progress may be impeded by access and licensing difficulties. Some propose mitigating this by requiring researchers to offer easy access to certain types of data and research tools. Others propose that open development models, including what Rai (2004) calls "open and collaborative" science, promise relief from potential patent thickets or problems of hold up. Finally, there is of course the possibility, highlighted by Saint-Paul (2003) that open development may reduce innovation effort by reducing anticipated profits.

Any assessment of these possibilities must be extremely tentative. However at the moment it seems reasonable to say that open development is in use and is working in a number of areas, including bioinformatics, database development and data exchange, and "pre-competitive" sequencing efforts. Many research tools in bioinformatics are free and open software, including operating systems, scripting languages, and sequencing algorithms. Database development has illustrated additional possibilities for free and open development. From an economists perspective, one of the most fascinating developments in OpenBio is The SNP Consortium, where commercial interests were driven to open development in an effort to reduce future transactions costs.

While user innovation has been important for research tools in bioinformatics and computational biology, it is much less plausible that consumers of biopharmaceuticals will propose improvements, and perhaps scarcely conceivable that even the most sophisticated consumer will be implementing improvements. If OpenBio really has few prospects in biopharmaceutical development, many proponents will be disappointed. Yet end user

innovation appears rather unlikely, modularity looks low, and the costs of safety testing and regulatory compliance are high. Prospects for OpenBio look much better as we get closer to basic R&D, projects involving platforms, or enabling technologies.

## **Is OpenBio Good for Developing Countries?**

Might OpenBio promote economic development more favourably than existing proprietary modes of innovation? Might it at least reduce the costs developing countries face in licensing products and research tools from the developed world? These are extremely general questions, for which we highlight some specific considerations.

It is natural to suspect that developed and developing countries anticipate very different effects of an international harmonization of IPRs. Many observers expect a resulting wealth transfer from the IPR-poor South to the IPR-rich North. This transfer might be offset if stronger IP regimes stimulate increased innovation in developing countries, or perhaps even if adequately increased global innovation lowers the relative price of technology and improves the developing world's terms of trade. Currently, neither empirical nor theoretical work supports such hopes. Theoretical work suggests that stronger global IP regimes will reduce welfare in developing countries (Deardorff 1992). Recent empirical work suggests that stronger IP regimes do not stimulate technological innovation or diffusion in developing countries (Park and Lippoldt 2005).<sup>10</sup>

Since the innovation response to IPRs is not detectable in developing country data,

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<sup>10</sup> The same work, however, does claim to find positive effects on developed country innovation and diffusion.

these countries should be cautious about establishing stronger IPRs in their present environment. At the same time, it is difficult to pin down causality in such data. For example, perhaps the R&D response is low because IP enforcement is currently very weak. Or perhaps there is a vicious circle: the resources to create and maintain a vigorous IP regime (with an intellectual property office, specialized courts, enforcers, education and training for IP professionals) may be impractical given the level of development---even if necessary for development.

Development economists often characterize developing country innovation systems as relying on imitation and adaption (Evenson and Westphal 1997). In this case, premature enforcement of developed country IP claims could undermine the nation's chance for an indigenous biotech industry. IP enforcement may restrict opportunities to imitate and produce while simultaneously reducing access to IP inputs.

In fields where innovation is characterized by incremental, imitative, and adaptive innovation, OpenBio therefore may be a suitable mode of innovation for developing countries. OpenBio may offer developing countries opportunities to imitate, learn, and innovate without violating their IP agreements. In such fields, OpenBio effectively lowers the cost of entry into biotech research. Particularly in a world where there is mounting pressure for expansive IPRs asserted by the developed countries to be enforced in developing countries, open development may help foster the human capital accumulation of developing countries and thereby alleviate the problem of their shortage of resources complementary to innovation. These arguments closely parallel arguments that have been offered for developing countries to embrace free and open source software (UNCTAD 2004).

## **Neglected Diseases**

Love (2002) argues that the patent systems in many African countries are "relics of colonial regimes, and serve the interests of the former colonial powers better than they serve the people who live in Africa." As an example of this bias, he notes that as of 2002 not a single African country imposed compulsory licensing on any medicine patent, despite tremendous need, especially in the treatment of AIDS. Some researchers have proposed that the OpenBio movement may aid developing countries in getting needed medicines that current institutions have denied them.

Maurer, Rai, and Sali (2004) propose that open source software can provide a model for improving innovation in tropical medicine. Major tropical diseases affect large populations, but poverty offsets size in limiting market demand for new medicines. In these circumstances, the market power provided by patents may be inadequate to ensure the recovery of research costs. The result is "neglected diseases", where treatment innovation is slow despite the large size of the affected populations.

Maurer et al. hope that establishing a body of basic research that cannot be patented (at least in developing countries) can lower the costs of development to the point where the commercial sector can profit from R&D on neglected diseases. They seek an alternative to subsidizing third world purchases of first world medicines or attempting to have benevolent non-profits play a venture capitalist role. Their "Tropical Diseases Initiative" (TDI) raises the hope that the increasing reliance of biotech on computation implies that the open source model of software innovation can be transplanted into the arena of early-phase drug discovery. Since "open source" discoveries will not be patented, it is hoped that zero licensing fees and competitive pressures will conspire to keep prices low. Clearly the choice of license will be crucial. Maurer et al. wish for a key licensing restriction: "open source"



drugs cannot be patented in developing countries.

Advances in computational biology make it plausible that OpenBio can facilitate some aspects of early-phase drug discovery. However many difficulties remain in actually bringing a drug to market. Firms in developed countries face extraordinary regulatory costs in the introduction of new drugs. The rise of a generic drug industry in the largest developing countries may allow them to support late-phase drug discovery and even development and testing efforts. However we suspect that, for now at least, large sunk costs in drug development will continue to pose a substantial barrier to OpenBio drug development.

### **Biopiracy**

Some developing countries complain that foreign firms have been "pirating" their genetic resources and traditional knowledge. They claim that patents are granted for products derived from the genetic resources of the South without consent of the owners of the resources, and even without the knowledge of the owners. They also claim that patents are based on the traditional knowledge of the South, in which case the putative innovation is actually common knowledge (or prior art). This is the charge of "biopiracy".

Modern IP regimes do not deal easily with collective and traditional knowledge. Developing countries have been clamoring for international reform in this area, to require Northern firms to obtain consent and to share the distribution of the benefits from patents. This concern is reflected in the UN Convention on Biodiversity (CBD), which however has no enforcement power. It is also reflected in the efforts by India to pre-empt biopiracy by digitally placing traditional knowledge into the public domain. Central to this effort is the Traditional Knowledge Digital Library (TKDL), under the auspices of India's National Institute of Science, Communication, and Information Resources (NISCAIR).

It is natural to ask why the South has not simply used the global intellectual property rules to assert IPRs in their "genetic" resources, which would allow them to charge Northern firms for licenses. Part of the answer lies in the current rules of the game: these can require that traditional knowledge and crops be modified before they can be protected, and developed countries currently have an advantage in producing such innovations.

Stiglitz (2004) explores additional ways in which developed countries are disadvantaged in the IP race. Applying for IP protection is expensive. The process of obtaining international protection requires expertise that is more likely to be available to a large multinational firm. It is expensive to litigate or make invalidity challenges against developed country firms. In addition, the international system is based on first to file (not first to invent). This interacts with the need for IP-system expertise: it takes time and expertise to properly draft an application, giving an advantage to a rich experienced inventor (e.g., a multinational pharmaceutical firm). So even if a developing country inventor is first to invent, he may not be first to file. Such considerations raise concerns that the North will continue to amass massive patent portfolios and property claims, leaving the South with reduced access to new technologies and higher costs for technological goods, even those that are substantially derivative from the knowledge and resources of the South.

An OpenBio presence in research into indigenous crops and knowledge has the potential to reduce biopiracy. This is beneficial to developing countries who fear that foreign firms will end up with "pirated" IP rights that constrain indigenous users. Such an OpenBio effort may also foster local capabilities for innovation. But developing countries are sure to be interested in the revenue stream that might be harvested from local biological diversity and traditional knowledge, and open development is unlikely to directly support this. Whether OpenBio will generate large complementary advantages, as discussed earlier, remains an

open question.

## Conclusion

The biotechnology industries are dynamic and innovative. There is a substantial public interest in keeping them that way. While it seems likely that IP policies will prove important, we cannot predict whether stronger IPRs will promote biotech innovation or hinder it. Indeed, the role of IPRs in promoting innovation is likely to differ by industry and by manufacturing stage. Research activities that generate large sunk costs in the production of final consumer products appear most likely to be well served by strong IPRs, especially if the products allow easy reverse engineering. Research activity that resembles basic research or is focused on research tools appears least likely to be well served by strong IPRs, which may constrain innovation by creating "thickets" of IPRs or by raising the costs of research tools (even to academic researchers).

Despite a growing understanding of the problems posed by overlapping and fragmented IP claims to innovation in industries characterized by sequential and cumulative innovation, the public policy momentum of the last quarter century has favored an increasingly expansive understanding of what constitutes appropriate subject matter for IP protection. Today there is little evidence of a public policy commitment to constrain an expansive biotech industry demand for IP protection. Even when industry participants would find a legislative constraint beneficial, we expect that they will often find it difficult to constrain themselves: group agreements not to assert IPRs are undermined by incentives to defect.

In an interesting development, we observe that industry occasionally overcomes this

"prisoner's dilemma". The SNP Consortium is an outstanding example: important industry participants in gene research chose an open development model and formed a consortium to set SNPs "off limits" to patenting efforts. While such commercially focused efforts are not yet typical of the OpenBio movement, we find them extremely promising. Still, it is important to note that the successes we observe do not imply that legislative constraints are not needed: basic economic considerations suggest that such consortia will be in "undersupply".

The global expansion of IPRs also raises distributional concerns. To many observers, developing countries appear disadvantaged: they are acceding to a regime of global IPR harmonization that will extract substantial payments for developed world IPRs, but they do not possess IP riches of their own. Some observers argue that this disadvantage extends even to the assertion of IPRs in their own biological riches and traditional knowledge: developed countries have been accused of a kind of "biopiracy" as their firms race to establish IPRs in the genetic riches of the developing world.

Some proponents hope that the OpenBio movement will lessen the burden on developing countries. We agree that it is likely to increase developing country access to the data and the research tools that will be needed for indigenous biotech research efforts. Here we are speaking of lawful access: OpenBio developments are freely available to developing countries, which reduces the pressure on these countries to transgress recently harmonized IPR standards. However we are less hopeful that, on its own, OpenBio will lend much stimulus to the development of the biopharmaceutical innovations so desperately needed by the developing world. Instead, in this arena, we expect OpenBio to work best when complementary to targeted government research support. A detailed exploration of this complementarity is an important area for future research.

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