CENTER FOR GLOBAL HEALTH R&D POLICY ASSESSMENT

The Global Health Social Enterprise: An Emerging Approach to Global Health Research and Development

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Abbreviations

R&D	research and development
LMIC	low- and middle-income countries
NCD	noncommunicable diseases
WHO	World Health Organization
CVD	cardiovascular disease
UN	United Nations
NTD	neglected tropical diseases
WHA	World Health Assembly
HIC	high income countries
DALY	disability-adjusted life years
HPV	human papillomavirus
CEWG	Consultative Expert Working Group on Research and Development
POC	point-of-care
SMBG	self-monitoring blood glucose
IDA	International Diabetes Association
COPD	chronic obstructive pulmonary diseases
GINA	Global Initiative for Asthma
PEF	peak expiratory flow
SBE	self-breast examination
CBE	clinical breast examination
BHGI	Breast Health Global Intiative
ER	estrogen receptor

EXECUTIVE SUMMARY

The social enterprise movement has gained momentum in the past few years and engendered a new way of thinking about businesses. As part of this movement, "social entrepreneurs" launch private enterprises with the dual objectives of having a positive social impact and earning a financial return.

Although this approach has won much attention from funders and impact investors as a means of expanding the reach of health and other needed services to the poor, the idea of using a social enterprise model to advance high-risk and costly R&D for health technologies for the diseases of low-income countries remains largely untested.

Does this approach have advantages compared to traditional for-profit firms and nonprofit product development partnerships (PDPs) in developing global health technologies? Are investors ready to support social enterprises in global health product development? Can policymakers and funders strengthen the supporting environment for social enterprises conducting global health R&D?

Drawing from a review of existing literature and 12 interviews with senior executives at for-profit and nonprofit global health product development organizations and policy experts in the United States, this report explores these questions relating to the potential of the social enterprise model in global health R&D in the United States.

The report begins by reviewing the main organizational models available for conducting global health R&D and discusses whether social enterprises can overcome the challenges faced by traditional for-profit and nonprofit product developers targeting low- and middle-income country markets. The report concludes with key findings and recommendations for supporting social enterprises in global health R&D.

Organizational Models for Global Health R&D

Currently, there are three main models for organizing global health R&D: the nonprofit product development partnership, the typical for-profit firm, and, the focus of this report, the hybrid global health social enterprise (GHSE). For the purposes of this report, GHSEs refer to for-profit social ventures involved in global health, specifically defined as entrepreneurial organizations that are

1. legally incorporated as for-profit entities, with one or more owners who have a legal right to control the firm and who are entitled to its residual earnings and net assets,[1] and
2. explicitly dedicated to the social purpose of developing new medicines, treatments, or technologies for diseases of low- and middle-income countries while making a profit.

[1]For-profit forms include proprietorships, partnerships, corporations, limited liability companies, cooperatives, and hybrid social enterprises.

These three models form a spectrum, with nonprofits at one end concentrating fully on their social missions and for-profit firms at the other end focusing on generating competitive financial returns. GHSEs fall in between these extremes, driven by both their potential for social impact and generation of profits. A number of distinguishing characteristics differentiate the organizational models.

PDPs. As nonprofit tax-exempt entities, PDPs are free to seek support from foundations and government grant programs. Although they may be able to secure loans, for the most part traditional private financing such as equity investment is out of reach for PDPs. Since they are not designed to earn revenues, PDPs must continually engage in fund-raising efforts but have the freedom to pursue the most socially valuable projects without regard to financial returns. PDPs are legally obligated to pursue their social missions.

Traditional firms. Traditional for-profit biotechnology and pharmaceutical firms are designed to create, manufacture, and sell products that generate profits. They can benefit from federal tax incentives, such as measures included in the Orphan Drug Legislation and the R&D tax credit, and can raise private financing to support their work. Although some firms may leverage their products for social initiatives or participate in corporate social responsibility activities, they are under no obligation to do so.

GHSEs. GHSEs fall in between the two previous models and pursue both financial and social returns. Unlike a PDP, a GHSE must ensure that it has sustainable revenues and that its social mission does not compromise the financial viability of the company. Some GHSEs have adopted explicit legal structures for social enterprise such as the "benefit corporation" and are under legal obligation to focus on their social mission. Others incorporate social impact into their business model while simply relying on traditional legal structures for operation. A GHSE with the latter structure has no long-term legal obligation to pursue its social mission, and the stimulus for doing so usually stems from senior leaders within the company and shareholders. Like traditional firms, GHSEs can tap into private financing and use federal tax incentives. In addition, GHSEs may receive investments from impact investors who are specifically seeking out "double bottom line" firms, and sometimes from foundations.

The most important implications of the differences between these three models for global health R&D are discussed in the next section.

Key Findings

We identified at least 10 U.S. biotechnology companies using the social enterprise model to develop global health technologies. Admittedly, this is a small number, and it suggests that GHSEs are still in their infancy in the United States. None of them has a large volume of sales, and none has yet licensed product, although Napo Pharmaceuticals' New Drug Application for an antidiarrheal treatment is under review. Nevertheless, the GHSEs follow a common business model, which is now firmly established, and the advantages of and drawbacks to the GHSE approach as perceived by their CEOs seem to be increasingly clear.

In interviews, executives of GHSEs cited a number of reasons for adopting a for-profit model, including the ability to access diverse private capital sources in the early and late stages of R&D, the flexibility to set their own agendas and quickly respond to new market opportunities, and the opportunity to leverage "dual markets" by repurposing global health technologies for high-income markets. These potential advantages are described below.

A number of potential weaknesses in the GHSE model also emerged from our interviews and analysis, including restrictions on the kinds of products the companies can pursue, challenges in maintaining their social missions, and lack of suitable metrics for attracting investors. These are also summarized below.

Potential Advantages

GHSEs can leverage private financing not readily available to nonprofits.

Estimates suggest that developing a new health technology can cost hundreds of millions of dollars, demanding robust financing options.[2] The ability to raise financing is especially important for late-stage product development, which requires costly clinical trials. GHSEs can pursue a mix of private financing such as loans, equity, and venture capital. In addition, they can tap into the growing impact investor movement, which may be inaccessible to purely profit-driven firms. Impact investors make investments in firms that can achieve a financial return while having positive social impact.

To carry out their work, nonprofit PDPs rely mostly on grants from foundations and governments, which were originally unavailable to for-profit entities. However, recent moves by foundations to make "program-related investments" are starting to open this funding pool to for-profit firms and GHSEs. GHSEs' ability to access a diverse mix of financing sources for global health R&D may be an important advantage, though this remains to be demonstrated in practice.

GHSEs can flexibly set their own agendas.

GHSEs can be nimble and respond to new opportunities more quickly than nonprofits. PDPs may be limited by the sets of priorities dictated in their grant agreements, whereas a GHSE can react to a new market opportunity allowing an existing technology in its portfolio or a competency within its team to be applied. This also allows GHSEs to tap into opportunities outside global health, enabling them to earn additional revenues to support their main R&D portfolios. For example, Napo Pharmaceuticals is repurposing its antidiarrheal product for the pet care market.

GHSEs can pursue dual markets for their products.

GHSEs are best suited to pursue products that have dual markets—that is, when a product has value in both a developed- and developing-country market or when a particular technology can be leveraged for a neglected disease in addition to another more profitable indication. Diagnostic platform technologies, for instance, may be used for a variety of disease indications. Similarly, Sequella's tuberculosis (TB) drug candidate has the potential to both treat drug-resistant TB in developing countries and address gastric ulcers in high-income markets.

Possible Drawbacks

GHSEs are more restricted in the types of products that they can pursue.

Since GHSEs depend on their own revenue to maintain operations, they cannot pursue products with little or no paying market. This excludes treatments for some of the most neglected diseases, such as intestinal worm infections, affecting the poorest households in low-income countries and other diseases that do not benefit from donor financing.

GHSEs have been successful in maintaining their social missions in short-term operations but may face greater difficulty in maintaining these missions over the long term.

GHSEs are able to incorporate their social missions into day-to-day decision making, but this balance might be difficult to maintain in the long term, especially in the event of a leadership transition or buyout by another company. Current corporate law requires directors to pursue the best deal for their shareholders during a buyout. If the social mission is not explicitly protected, it might be compromised in order

[2]Tufts Center for the Study of Drug Development (CSDD), "Drug Developers Are Aggressively Changing the Way They Do R&D," press release on the Tufts CSDD Outlook 2011 report, 5 January 2011. Matthew Herper, "The Truly Staggering Cost of Inventing New Drugs," *Forbes*, 10 February 2012.

to secure the most profitable outcome for shareholders. New legal structures in the United States, such as the benefit corporation and the flexible purpose corporation, can help for-profits with regard to these concerns, but experience with these legal structures for R&D-driven organizations is limited. Nonprofit counterparts, by contrast, are legally bound to a social goal.

GHSEs lack standard metrics and tools for balancing financial returns and social impact. There is no standard way to measure and describe the trade-offs between financial and social returns for a GHSE, and interviewees cited communicating these trade-offs to investors as a significant challenge. For instance, there is no method for determining whether a 10 percent profit and 20 percent reduction in the disease burden is better than a 20 percent profit and 10 percent reduction in the disease burden. Since there are no widely accepted metrics for this purpose that balance measures such as quality-adjusted life years or reductions in disease burdens with profits, GHSEs may struggle to balance their missions to improve health through product development with financial goals and to find investors who share similar objectives.

The inability to measure these trade-offs limits the ability of impact investors to invest across firms and sectors. Without language to compare health R&D opportunities to other potential investments and a way to gauge future health outcomes, an impact investor may be unable to assess how socially driven a particular company is or how potentially significant the future social impact of that company's product portfolio will be. Current initiatives are under way to develop impact metrics and common language more broadly for impact investors,[3] but interviewees noted that these metrics do not directly address biotechnology and pharmaceutical innovation.

Conclusion

GHSEs represent a nascent and rapidly evolving model of for-profit product development that may help meet important needs in global health and bring greater levels of private financing into product development for neglected diseases. Since investment in global health R&D is inadequate despite being urgently needed from a public health impact perspective, mechanisms such as GHSEs that can bring fresh resources to priority disease areas and complement the existing landscape of nonprofits and traditional companies conducting global health R&D should be carefully considered for support.

GHSEs cannot solve the global R&D imbalance on their own, nor are they suited to product classes with little or no financial returns, such as treatments for visceral leishmaniasis and African trypanosomiasis. They can, however, potentially help pursue R&D opportunities where commercial and global health priorities intersect, for example, in antibiotics, platform technologies, and other dual-market product areas.

[3]Global Impact Investing Network, "Impact Reporting and Investment Standards," www.thegiin.org/cgi-bin/iowa/reporting/index.html.

CHAPTER 1
INTRODUCTION

1

Technological breakthroughs fueled by billions of investment dollars have transformed health care for affluent patients in wealthy countries, yet investment in health technologies for resource-poor countries has not kept pace.

Because most patients in low- and middle-income (LMI) countries lack the purchasing power to afford high-quality care, pharmaceutical and biotechnology companies have not traditionally viewed such countries as lucrative markets. In the past, this trend has given rise to the term *neglected tropical diseases* (NTDs), referencing diseases that attract negligible investment but nonetheless have significant impact on populations of LMI countries. The tendency of companies to shy away from product development in areas of NTD research is in part due to the costs and risks of such research and development (R&D) being too high relative to the market potential. This disparity has reinforced the stereotype of the "for-profit company"—that shareholders, officers, and directors of biotechnology companies are concerned with and responsible for the financial return on investment only, and not the social impact of their investment.

This view is slowly changing. The past decade has seen a significant rise in what can be termed a *third sector* that is distinct from the purely for-profit and nonprofit sectors—the *social enterprise* and *social entrepreneurship* model to target social issues such as climate change, poverty, education, and international development.[4] *Social enterprise*, in the context of this report, refers to for-profit organizations that take particular efforts to balance a social mission with a financial bottom line, and *social entrepreneurs* refers to the people founding or leading those organizations. Such social entrepreneurs are aggressively seeking ways to marry the business model of for-profit companies with the mission-driven approach of nonprofit organizations.[5] At the same time, commercial opportunities are improving in emerging markets, either through major increases to the economic productivity of many developing countries or through governments and foundations increasingly subsidizing payments for these treatments for NTDs. Likewise, in the past decade, health care experts have started to recognize that the same technologies that have revolutionized health care for affluent populations can be repurposed to yield powerful new vaccines, drugs, and diagnostics for NTDs with a lower required investment and commitment. All of these recent trends create more favorable conditions for the development of new health products for the diseases predominantly affecting low-income families in LMI countries.

However, the environment for these for-profit global health social enterprises (GHSEs) can be further improved. First, better tools are needed to help connect GHSEs to funding organizations aligned with their priorities. For example, certifications that identify the companies that are making a focused effort on diseases in LMI countries could help investors and stakeholders better identify those companies that

[4]Christian Seelos and Johanna Mair, "Social Entrepreneurship: Creating New Business Models to Serve the Poor," *Business Horizons* 48, no. 3 (2005): 241–246.

[5]Ibid.

have fully embraced both a social purpose and a financial bottom line. Further, industrywide metrics that help simultaneously communicate the health impact of early and preclinical research in the context of financial return on investment would be valuable in maintaining the humanitarian priorities of the social enterprises. Finally, ensuring that a social mission remains a long-term priority of GHSEs through legal mechanisms would help preserve the original humanitarian intent of the founding social entrepreneurs, even in the event of company sale or merger. Two new, hybrid legal corporate structures in the United States—the *benefit corporation* and the *flexible purpose corporation*—might be suitable to address this last issue and help secure a focus on the health of LMI countries as part of the long-term corporate mission.[6]

This paper examines the potential impact of the social enterprise model in furthering health product innovation for LMI countries. In particular, this paper draws from experiences and challenges faced by for-profit GHSEs in terms of funding and dedication to a global health mission, in comparison with nonprofit and traditional business models. We address two key questions:

- What role can the social enterprise model play in health product innovation targeting LMI countries? How do social enterprises balance the social mission of health innovation for LMI countries with the need for profits?
- What limitations do social enterprises face in health product innovation within LMI countries, and how can those limitations be mitigated?

Section II reviews the traditional for-profit and nonprofit business models of global health organizations, as well as the emergence of the social enterprise approach. Sections III and IV focus on stakeholder and industry interviews to analyze how GHSEs have strategically developed to overcome those challenges faced by for-profit and nonprofit companies, and explore the new challenge of balancing the demands of a for-profit organization with the global health–focused social mission. Section V concludes with recommendations for a new entrepreneur entering global health as well as suggestions for policymakers when attempting to lower the barriers to global health innovation.

A. Methodology

This report was developed through extensive literature review, research regarding for-profit and nonprofit product development partnership (PDP) organizations focusing on global health, and a comprehensive review of exemplary U.S. state law concerning corporations, shareholders' rights, and the fiduciary responsibilities of directors and officers. Further, focused interviews were conducted with senior officers working at nonprofit PDPs, executives within biotechnology companies focusing on NTD research, and experts in social enterprise. Interviewee responses are generally referenced as anonymous to protect potentially sensitive information that may be adverse to the interests of the interviewee's organization. A full list of interviewees can be found in the appendix.

B. Key Findings

The social enterprise model in global health is largely untested; only in the past decade have we seen companies and business models emerge that deliberately integrate a social benefit mission with the need for financial returns. The recent emergence of GHSEs is in part due to an evolving global health backdrop, consisting of increasing competition for foundation funding, demands for new business models in biotech R&D, a growing sector of impact and double-bottom-line investors, and a new generation of social entrepreneurs seeking to "do well while doing

[6]Other countries have also begun to introduce such hybrid legal corporate structures. For example, social enterprise legal structures in the U.K. include the community interest company and the community benefit society.

good." As funding and commercial markets continue to change, a third approach to the development of health technologies for LMI countries—aside from the PDP and primarily for-profit corporations—will become increasingly critical.

The nonprofit PDP and for-profit GHSE models are in some ways similar. For example, both organizational models can license and sell technologies to create an additional source of revenue, can readily partner with larger pharmaceutical companies to further product development, and have the operational freedom to pursue diseases that affect LMI countries if consistent with their organizational mission. However, key distinctions exist that highlight some advantages and drawbacks of using the for-profit social enterprise model in future global health R&D.

1. GHSEs can draw from forms of capital not readily available to nonprofit organizations

GHSE organizations have the option of accessing types of early- and late-stage capital not traditionally available to nonprofit PDP organizations. Early-stage venture financing, equity ownership, and government small business grants, for example, are at present available only to for-profit companies. Notably, GHSEs can access the growing *impact investor* movement, which recent estimates suggest ranges from $400 billion to $1 trillion. Likewise, GHSEs have access to additional methods of late-stage capital expansion, such as loans and debt financing, to support clinical testing, while PDPs are primarily dependent on foundations, government support, and partnerships with larger pharmaceutical companies.

Access to capital is an important consideration when weighing the potential impact of GHSEs in health product innovation. Looking forward, several interviewees noted that the competitive space for PDPs has become significantly crowded, as foundations have established funding priorities and favor supporting organizations with proven track records. Consequentially, newly founded global health organizations will likely have greater success in securing early-stage capital as a for-profit company than as a non-profit PDP.

2. GHSEs are limited to portfolios that allow for profitability through a dual market

GHSEs face greater constraint in their project selection than do PDPs and limit their R&D to areas that have market potential in both developed and LMI countries. In general, these strategies fall into the "technological" and "geographical" dual markets, focusing respectively on the repurposing of a platform technology to a developed-world product, or the resale of a product to a developed-world market. However, these strategies limit the projects that the GHSEs pursue; truly neglected diseases are often not included in their portfolios, except in situations where upstream platform technologies focusing on rare or neglected diseases could also be applied to drug discovery for a developed world market.

By contrast, PDPs enjoy somewhat greater freedom in portfolio selection and do not have as great a need to consider product sales when determining their R&D portfolios. The potential health impact of a product portfolio will almost always take precedence over financial returns. However, PDPs are still limited by the funding priorities of their benefactors, who in turn often demonstrate a preference for indications where the dual-market potential is small or nonexistent. As such, developing new products for diseases such as cancer, heart disease, or diabetes, which have a significant health impact in both developing and developed countries, would be an unlikely focus of nonprofit organizations.

3. GHSEs can incorporate a social mission within short-term operations but face uncertainty in securing long-term adherence to social goals

The social mission is a key asset to global health R&D organizations, for example, in recruiting talent, maintaining morale, attracting funding, and establishing partnerships. Despite the legal requirements that for-profit companies seek to maximize profits

for shareholders, many GHSEs cited no significant difficulty in adhering to a social mission in day-to-day operations and project selection. Communicating to investors the trade-offs between revenue-seeking activities and the social mission is perhaps the biggest challenge, and directors must spend a significant amount of time negotiating with shareholders, selecting operational priorities, and selecting investors that have aligned social interests. To this end, tools to help communicate the trade-off could be valuable, such as metrics incorporating both social return and return on investment, composite lists of impact investor networks, and clear signaling tools to help GHSEs reach out to impact investors and signal potential double-bottom-line investment opportunities.[7]

Although GHSEs are comfortable with a pursuit of a social mission within day-to-day operations, the ability to maintain a global health mission for the long-term life of the company is less certain. During a company sale or merger, for example, GHSEs may be forced to abandon their global health objectives in favor of more lucrative markets. The 2000 takeover of the ice cream company Ben & Jerry's by Unilever serves as a cautionary example, as Ben & Jerry's was forced to prioritize shareholder profits over its nationally recognized social mission.[8] In such situations, newly formed hybrid corporate models—such as the B Corp and the Flex C (defined later in this paper)—could be potential solutions. Directors of identified GHSEs formed their companies prior to the availability of such corporate forms; however, during interviews many expressed an interest in adopting such hybrid models either with their current company or in a future venture.

[7]Although some funds, such as the Acumen Fund and the Global Health Investment Fund, have begun to channel impact investing toward for-profit companies working in global health, the method for selecting investment targets is often opaque to GHSEs.

[8]See "The Scoop on Ben & Jerry's Sellout," *Slate Magazine*, 12 April 2000, www.slate.com/articles/business/moneybox/2000/04/the_scoop_on_ben_jerrys_sellout.html.

CHAPTER 2
ORGANIZATION MODELS: NONPROFIT, FOR-PROFIT, AND SOCIAL ENTERPRISE

2

Over the past two decades, organizations entering the medical innovation space have entered either with a mission-driven motive to create social benefit or with the explicit aim to reap financial return on investment.

In the context of global health, these types of organizations mark ends of a spectrum, represented on one end by the nonprofit PDP and on the other by the for-profit pharmaceutical and biotechnology companies. Recently, a small number of organizations adopting the social enterprise model—such as for-profit companies adopting a social mission or, less commonly, nonprofit PDPs adopting corporate practices—have emerged in global health, accompanied by new legal corporate forms. Each of these various corporate structures comes with its respective benefits and drawbacks.

A. Nonprofit Drug Development Organizations

In the global health space, PDPs arose at the end of the 20th century as nonprofit organizations dedicated to investing in health technologies that specifically address NTDs.[9] Nonprofit organizations generally perform socially necessary work that governments and traditional businesses allow to slip through the cracks. Nonprofits are not owned by any individuals and thus do not aim to make any profits for shareholders. On the contrary, nonprofits must be driven by a social welfare mission per state law and the federal tax rules governing their structure. All of a nonprofit's activity must be related to its social mission, and any income from unrelated activity is subject to taxation.[10]

PDPs adopted the "portfolio" model used by pharmaceutical companies, which involved investing in R&D for a variety of promising treatments for a single disease or single disease indication, as opposed to directing all of their investment resources toward developing one approach. Rather than conduct R&D in house, however, PDPs often save costs by outsourcing some aspects of the drug development process to smaller biotech companies or laboratories. Philanthropies such as the Bill and Melinda Gates Foundation (the "Gates Foundation") and the Rockefeller Foundation as well as government grants and "in-kind" contributions from for-profit biotechnology and pharmaceutical companies often provide initial financial support.[11]

This model has been generally successful in directing financial resources toward the development of new medicines and health products for LMI countries. A recent study of 348 organizations involved in NTD product development found that the 26 identified PDPs were involved in the development of more than 40 percent of the most promising products.[12] In addition, PDPs have

[9]Estimates suggest that more than 16 PDPs were founded between 1999 and 2003. FSG, *Combating Diseases Associated with Poverty*, November 2004; Global Forum for Health Research, *Health Partnership Review*, May 2008.

[10]See Internal Revenue Service, "Unrelated Business Income Tax," www.irs.gov/charities/article/0,,id=156395,00.html.

[11]C. Grace, *Product Development Partnerships (PDPs): Lessons from PDPs Established to Develop New Health Technologies for Neglected Diseases*, Department for International Development, United Kingdom, 2010; USAID, Report to Congress: Coordinate Strategy to Accelerate Development of Vaccines for Infectious Diseases, 2009.

[12]E. Ponder, *Developing New Drugs and Vaccines for Neglected Diseases of the Poor: The Product Developer Landscape*, BIO Ventures for Global Health, March 2012.

served as important advocates for increased innovation in global health technologies, focusing on unmet needs and the importance of downstream access within LMI countries to approved products.

B. For-Profit Companies in Global Health

At the other end of the spectrum, for-profit companies are firms that primarily have a market-driven mission to create financial profits. They produce goods and services that the marketplace wants, and they use the profits they generate to pay investors and taxes as well as to expand and grow the corporation. If a for-profit fails to generate profits or secure funding, then it ceases to function independently and will be either taken over by another for-profit company or forced into some form of bankruptcy.

Although for-profit companies are focused primarily on market opportunity, at times market opportunities can converge with social need. In the health care industry, for-profit companies have invested in global health in ways that tie into financial gain. For example, the increasing pressure on for-profit companies to appear socially responsible has motivated several large pharmaceutical and biotech companies to donate medicines to LMI countries, donate licenses and intellectual property to neglected disease researchers, and pay premium prices to outsource research or clinical trials to LMI countries.[13] Also, in recent years, for-profit biotechnology companies started viewing NTD markets as financially lucrative in and of themselves and structuring their business models to serve those markets for financial gain.

A recent report by BIO Ventures for Global Health highlighted the participation of for-profit biotechnology companies, citing their involvement in 41 percent of all R&D projects for new medicines for NTDs, matching PDP involvement in neglected disease research.[14,15]

C. Nontraditional Business Models: The Social Enterprise

Combining the social welfare focus of a nonprofit and the financial goals of a for-profit company, a new model of business—the social enterprise—has arisen in the past decade to address social issues such as climate change, poverty, education, and international development.[16] Many commercial enterprises would consider themselves to have social objectives, but commitment to those objectives is motivated by the perception that it will ultimately make the enterprise more financially valuable. Social enterprises differ in that they do not aim to offer any benefit to their investors except where they believe that doing so will ultimately further their capacity to realize their social welfare goals.

1. Defining and recognizing the social enterprise

Myriad definitions have emerged that are directly applicable to specific organizations operating in the space between traditional nonprofit companies and for-profit companies. Specifically, some in the literature define social enterprise as a more efficient outgrowth of nonprofit institutions,[17] whereas others see the concept as a for-profit business attempting to

[13]See, for example, Simeon Bennett, "AIDS Drugs Flow to the Third World," *Bloomberg Businessweek*, 5 August 2010, www.businessweek.com/magazine/content/10_33/b4191021714150.htm?campaign_id=rss_null.

[14]BIO Ventures for Global Health (BVGH) and the Biotech Industry Organization (BIO), *Biotechnology: Bringing Innovation to Neglected Disease Research and Development*, June 2012, www.bvgh.org/LinkClick.aspx?fileticket=XeOgiPLC9Rc%3d&tabid=235.

[15]Ponder, *Developing New Drugs and Vaccines*.

[16]Seelos and Mair, "Social Entrepreneurship."

[17]Raymond Dart, "The Legitimacy of Social Enterprise," *NonProfit Management and Leadership* 4 (Summer 2004): 411–424.

Table 1. Overview Comparison of Nonprofit, Social Enterprise, and For-Profit Corporate Models

	NONPROFIT	SOCIAL ENTERPRISE	FOR-PROFIT
MOTIVES	Appeal to goodwill	Mixed motives	Appeal to self-interest
DRIVERS	Mission driven	Balance of mission and market	Market driven
GOALS	Social value creation	Social and economic value creation	Economic value creation
SUPPORT	Primarily philanthropic	Investors/profit	Investors/profit
DESTINATION OF INCOME/PROFITS	Directed toward mission activities of nonprofit organization (required by law or organizational policy)	Reinvested in mission activities or operational expenses and/or retained for business growth and development, or redistributed to shareholders and owners	Reinvested in operational expenses and/or business growth, or distributed to shareholders and owners

address social needs in the marketplace.[18] As early as 1996 the Roberts Foundation Homeless Economic Development Fund defined social enterprise as "a revenue generating venture founded to create economic opportunities for very low income individuals, while simultaneously operating with reference to the financial bottom-line."[19]

Social enterprise, in the context of this report, refers to a for-profit organization that makes particular efforts to balance a social mission with a financial bottom line. The term *double bottom line* refers to a social enterprise's goal of achieving both social benefits as well as financial returns. Perhaps the most notable example is the Grameen Bank that more than 20 years ago reached profitability by extending credit to poor populations in Bangladesh, and for which its founder Muhammed Yunus was awarded a Nobel Prize for Peace in 2006. A more recent example of a successful double-bottom-line company is Tesla Motors. Founded in 2003, Tesla has maintained a long-term strategic goal to create affordable mass market electric vehicles to have a material impact on oil consumption,[20] and by 2010 it had acquired more than $710 million in assets.

For the purposes of this report, *global health social enterprises*, or GHSEs, refer to for-profit social ventures involved in global health, specifically defined as entrepreneurial organizations that are

1. legally incorporated as for-profit entities, with one or more owners who have a legal right to control the firm and who are entitled to its residual earnings and net assets;[21] and

[18]Rebecca Harding, "Social Enterprise: The New Economic Engine?" *Business Strategy Review*, Winter 2004, 40–43.

[19]Jed Emerson and Fay Twersky, *New Social Entrepreneurs: The Success, Challenge, and Lessons of Nonprofit Enterprise Creation* (Roberts Foundation Homeless Economic Development Fund, 1996).

[20]Katie Fehrenbacher, "Elon Musk Envisions Tesla Electric Car as Low as $20K," Gigaom.com, 17 September 2008, retrieved 3 October 2010.

[21]For-profit forms include proprietorships, partnerships, corporations, limited liability companies, cooperatives, and hybrid social enterprises.

2. explicitly dedicated to the social purpose of developing new medicines, treatments, or technologies for diseases of LMI countries while making a profit.

Social enterprises differ from traditional nonprofit institutions in that they must earn profits to continue operating. Likewise, social enterprises differ from traditional for-profit models in that their profits are used, at least in part, to support social causes rather than to increase the wealth of investors, managers, and owners. This trade-off between social mission and financial return, and the degrees by which a social enterprise is more socially driven than a for-profit, or more profit driven than a nonprofit, can vary. Table 1 shows a comparison of the three organizational approaches.

To help further define the focus of this paper, the social enterprise should be distinguished from three other corporate models working in the social space:

Socially responsible businesses. A socially responsible business achieves commercial success in ways that respect ethical values, people, communities, and the environment.[22] Such businesses may even provide resources to and actively engage with public or nonprofit organizations to serve a specific social cause. However, unlike social enterprises, their primary goal is the creation of economic value. UPS, for example, has revenues exceeding $50 billion a year, while deploying more than 1,500 alternative energy vehicles powered by electricity, natural gas, and hydrogen.

Purely profit-motivated firms operating in the social sector. The boundary-blurring of recent years has seen some firms enter the social sector simply in search of profits. These organizations typically do not place inherent value on the social impact they create. For example, Lockheed Martin's focus on improving employment within local communities in order to increase profitability through diversification does not qualify the firm as a social enterprise.

Corporations practicing corporate social responsibility. Corporations practicing corporate social responsibility (CSR) are for-profit businesses whose motives are financially driven, but who engage in philanthropy. "Strategic philanthropy" helps companies achieve profit maximization and market share objectives while contributing to the public good. A private company or corporation engages in socially beneficial activities such as grant making, community involvement, volunteering company personnel, and sponsorship as a means to improve public image, employee satisfaction, sales, and customer loyalty. CSR is not classified as social enterprise, although philanthropic activities may support social enterprises, make a positive social impact, or contribute significantly to a public good.

In the last decade, there has been a growing pool of social entrepreneurs looking to engage in social missions, including global health, through market-based solutions using social enterprises.[23] Some estimates suggest that globally this "third sector" employs around 40 million people, with 200 million volunteers. Ten years ago only Michael Young's School for Social Entrepreneurs provided courses; now more than 30 universities around the world run fully fledged programs.[24] Although there are no reliable data on social enterprise company revenues, an aggregation of businesses belonging to membership associations generally identified with the sustainable business movement reveals a marketplace of more than 65,000 businesses with more than $40 billion in revenues.[25] A 2010 survey of 400 social enterprises in

[22]See Business for Social Responsibility, http://www.bsr.org.

[23]D. Bornstein, *How to Change the World: Social Entrepreneurs and the Power of New Ideas*, updated edition (New York: Oxford University Press, 2007).

[24]Charles Leadbeater, "Mainstreaming of the Mavericks," *The Guardian*, 24 March 2007, www.guardian.co.uk/society/2007/mar/25/voluntary-sector.business.

[25]A partial listing of these associations includes Green America, Social Venture Network, Investors' Circle, Business Alliance for Local Living Economies, Transfair USA, Social Investment Forum, National Cooperative Business Association, and National Center for Employee Ownership.

Snapshots: GHSEs in Phase 3 Clinical Development (continued)

Name: ***Sequella Inc.***
Founded: ***1997***
Employees: ***10–25 (approx.)***
Revenue: ***$1 million/year (approx.)***
Location: ***Rockville, Maryland, United States***

Background: Sequella Inc. is a privately held clinical-stage biopharmaceutical company that develops and commercializes products for diagnosis and treatment of infectious diseases. Sequella was originally incorporated in 1997 to develop new therapeutics for tuberculosis (TB), and several of its founding members continued to create Sequella Global TB Foundation, now known as the Aeras Global TB Vaccine Foundation. In 1999, Sequella received its first National Institutes of Health Small Business Innovation Research grant, and over the next nine years received more than $16 million in additional nondilutive grant support. In 2007, Sequella commercialized a revenue-generating out-license of the company's first product, a veterinary TB diagnostic.

NTD Product: Sequella's lead drug candidate, SQ109, completed three Phase 1 studies in the United States and one Phase 2 efficacy study in TB patients in Africa, and is currently undergoing Phase 3 studies in Russia and the Baltic States. SQ109 has promising activity against both drug-susceptible and MDR TB bacteria, including XDR-TB strains, and may also enhance the activity of the antitubercular drugs isoniazid and rifampin. If approved, SQ109 could replace one or more of the current first-line antitubercular drugs, simplify therapy, and shorten the current TB treatment regimen. SQ109 also has a dual market potential for the treatment of *Helicobacter pylori* infections, the key pathogen responsible for gastric ulcers and related indications, and as a potent antifungal agent. Sequella estimates that SQ109's worldwide TB market potential is approximately $564 million, with the majority of expected sales forecast from developed economies; more than $650 million for *H. pylori*–related duodenal ulcer and carcinoma markets; and $350–400 million for a new antifungal agent.

Key Partnerships: In April, 2011, Sequella and Maxwell Biotech Venture Fund announced their agreement to complete the clinical development (Phase 3) and commercialize SQ109 for treatment of TB in the Russian Federation and neighboring Commonwealth of Independent States countries, including Armenia, Azerbaijan, Belorussia, Kazakhstan, Kyrgyzstan, Moldova, Tajikistan, Turkmenistan, and Ukraine. The structure of the exclusive license in this territory for TB includes an equity investment, clinical trial supply purchase, milestones, and royalty payments that, contingent upon successful development and commercialization, could be worth up to $50 million to Sequella over the duration of the license.

Name: ***PaxVax***
Founded: ***2007***
Employees: ***30 (approx.)***
Revenue: ***$3.2 million/year (approx.)***
Location: ***San Diego, California, United States***

Background: PaxVax is a privately held company established in 2007 to develop and commercialize innovative and socially responsible vaccines against infectious diseases. PaxVax has a clinical-stage product portfolio, including a cholera vaccine entering Phase 3 and a pandemic H5N1 influenza vaccine entering Phase 2. The company also has vaccines in development for HIV and anthrax under R&D contracts with the National Institutes of Health (NIH). The company's proprietary adenoviral-based technology platform enables the rapid development of oral vaccines that can target any viral or bacterial protein antigen. The company's vaccine candidates are designed to be easier to manufacture, store, distribute, administer, and deliver across the globe than conventional injectable vaccines while enhancing the desired immune response to the vaccine antigens.

Product Pipeline: PaxVax has many products in development. Among them is PXVX-0200, a single-dose, oral, live, attenuated vaccine against cholera, which was previously approved and marketed in six countries under the brand name Orochol. Unlike currently available cholera vaccines requiring two doses over the course of weeks before effectiveness, PXVX-0200 provides rapid onset of protection in as little as seven days after a single administration, making it ideal for rapid response to low-resource settings and following natural disasters. Further, PXVX-0200 has a potential dual market as a travel vaccine for people preparing to travel to areas where cholera is endemic or where it has recently caused an epidemic.

Key Partnerships: PaxVax has partnered with SynCo Bio Partners BV, a biopharmaceutical GMP contract manufacturing organization with specific expertise in live microbial biotherapeutics located in Amsterdam, Netherlands, to manufacture the initial material for the cholera vaccine for clinical trials. PaxVax has raised more than $50 million from investors including Ignition Partners and the Wellcome Trust, and is supported by grants from the NIH through the National Institute of Allergy and Infectious Diseases and its Division of Acquired Immunodeficiency Syndrome, as well as the Bill and Melinda Gates Foundation.

Snapshots: GHSEs in Phase 3 Clinical Development (continued)

Name: ***Napo Pharmaceuticals***
Founded: ***2001***
Employees: ***20–30 (approx.)***
Revenue: ***$1.4 million/year (approx.)***
Location: ***San Francisco, California, United States***

Background: Napo Pharmaceuticals Inc. is a privately held company that develops and commercializes proprietary pharmaceuticals for the global marketplace in collaboration with local partners. Napo's strategy focuses on both higher-volume business in the emerging economies of the world and high-value novel medicines in the Western market. In accordance with its social mission, Napo is the parent company of CAP Global LLC, a wholly owned subsidiary and certified B Corp (benefit corporation). CAP Global's mission is to accelerate the development of Napo's lead drug crofelemer for pediatric populations in the treatment of multiple diarrheal diseases (such as cholera), and to provide crofelemer cost-effectively to relief organizations in LMI countries. Napo aims to maximize shareholder return through the creation of partnerships that provide incentives for the harmonization of these global pursuits.

NTD Product: Napo's lead drug candidate is crofelemer, a compound derived from the Croton lechleri tree in the Amazon River Basin and formulated to combat debilitating diarrhea. Napo offers its products for the HIV, acute cholera, and pediatric markets. Peak sales for the drug's HIV/AIDs indication are expected to be in the range of $150 million to $200 million. In November 2010 Napo completed its first successful Phase 3 study of crofelemer in HIV/AIDS patients, and demonstrated that the drug exceeded endpoints for efficacy and demonstrated the same safety/tolerance profile as the placebo. Further, label extensions to treat other gastrointestinal problems, such as irritable bowel syndrome, as well as for canine diseases, could help Napo access a $14 billion market. A new drug application submitted to the FDA in 2011 is currently being reviewed.

Key Partnerships: Napo entered into two partnership agreements in 2005 and 2008 to accelerate the development and commercialization of crofelemer for treatment of HIV/AIDS patients, exchanging marketing rights in North America, Europe, and Japan for a $5 million licensing fee and future milestone payments. Recently, however, Napo has sought to regain development control of crofelemer to accelerate plans for drug launch and postapproval marketing.

the United States found that greater than 30 percent reported annual revenues of more than $1 million.[26]

Within the global health space, some for-profit companies that adopt the social purpose of addressing disease in LMI countries are beginning to emerge. Out of all the for-profit companies investing in NTDs,[27] a review of public documents, literature, reports, product pipelines, and available mission statements identified 10 such companies that meet the GHSE definition. Companies such as Sequella Pharmaceuticals, Napo Pharmaceuticals, Anacor Pharmaceuticals, PaxVax, Inviragen, and 60° Pharma have developed business models allowing for product development targeting NTDs while realizing a financial return on shareholder investment. (See the appendix for a brief description of each company.) This list is by no means comprehensive. However, these companies have products targeting LMI countries at various stages of development, ranging from early stage / preclinical through Phase 3 clinical trials.

2. New legal tools are emerging to help GHSE organizations

Since 2010, two new legal corporate forms—the benefit corporation (B Corp) and the flexible purpose corporation (Flex C)—have emerged in 16 U.S. states to help social enterprises balance their goals of advancing

[26]Community Wealth Ventures, Social Enterprise Alliance, and Center for the Advancement of Social Entrepreneurship, *Social Enterprise: A Portrait of the Field*, 2010, www.communitywealth.com/pdf-doc/Field%20Study%20FINAL.pdf.

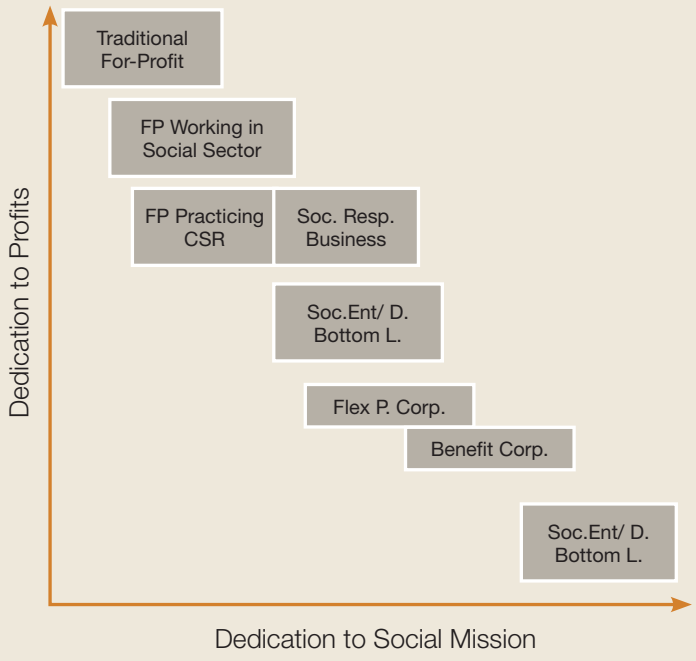
[27]BVGH and BIO, *Biotechnology*.

social welfare while creating profits and value for their shareholders.[28] These corporate structures are hybrids between for-profit and nonprofit corporate forms that legally permit corporations to pursue profits as well as social benefit goals. Further, both B Corps and Flex Cs create transparency and accountability in the implementation of social benefit goals by requiring the company to publish an annual report that provides an assessment of the successes, failures, and hurdles to be overcome in achieving those goals. A third, nonlegal tool for assisting social enterprises is the "B Corp certification," run by the third-party nonprofit B Lab. Corporations that have B Corp certification carry a brand certification verifying that the corporation meets certain standards of social and environmental performance, accountability, and transparency. Organizing a business as a B Corp or Flex C is different from carrying a B Corp certification, but those entities are well suited to such certification.

Generally speaking, a Flex C offers more flexibility with regard to determining the purpose(s) of the company and provides directors with a high level of discretion in how they balance and prioritize both traditional economic and special purpose goals. By contrast, the B Corp requires—rather than merely permits—directors to consider particular social goals in executing day-to-day and long-term operations. Likewise, while both B Corps and Flex Cs must provide an annual report to shareholders detailing their progress toward a social end, only B Corps are subject to audit by a third-party standard.

These corporate forms have not yet been widely adopted. Professional groups estimate there are about 70 B Corps in the United States, but only two Flex Cs are known thus far.[29] However, some large international brands have taken advantage of these legal tools—Patagonia, the outdoor clothing company, registered as

Figure 1. Comparison of Various Corporate Models



[28]Benefit corporation laws exist in California, Hawaii, Maryland, Illinois, Massachusetts, Louisiana, New Jersey, New York, South Carolina, Vermont, and Virginia, and legislation is moving forward in Pennsylvania, Colorado, and Washington, D.C. Currently, California and Washington are the only U.S. states with Flex C corporate structures (Washington State Corporate form is referred to as a "social purpose corporation."). See the state-by-state legislative status at http://www.benefitcorp.net/state-by-state-legislative-status, accessed 12 October 2012.

[29]Trista Morrison, "Mission-Based Biz Model Might Benefit Biotechs," BioWorld, 2012, www.bioworld.com/content/mission-based-biz-model-might-benefit-biotechs-0.

a B Corp the day the law went into effect in California. No B Corp or Flex C corporations focused in global health have been identified through either research or industry interviews, likely reflecting the relative infancy of these laws. In contrast, more than 650 certified B Corps exist according to B Lab, at least two of which are focused on global health technologies. Notably, Cap Global, a certified B Corp and subsidiary of Napo Pharmaceuticals, has been recognized as "Best for the World" in a list of all businesses creating the most overall positive community impact appearing in the *2012 B Corp Annual Report* released on March 7, 2012.[30]

These corporate forms, along with the traditional for-profit and nonprofit organizational structure, are perhaps best categorized along two continuums: commitment to a social benefit and commitment to the profit motive. (See Figure 1.)

[30]"Best for the World" businesses earned a score in the top 10 percent of all certified B corporations against metrics created by B Lab. Napo Pharmaceuticals, press release, https://docs.google.com/viewer?url=http%3A%2F%2Fwww.napopharma.com%2FCap_Global_Recognized.pdf.

CHAPTER 3
ANALYZING OPTIONS FOR GLOBAL HEALTH PRODUCT DEVELOPMENT

3

Organizations focusing on the development of new health products for global health have a number of options regarding corporate form—as referenced earlier, these are the nonprofit PDP, the for-profit social enterprise (GHSEs), and the new, hybrid corporate structures, such as the B Corp and the Flex C corporate entities.

Although GHSEs are still relatively few in number, six key areas were identified through literature reviews and interviews that constitute differences between the nonprofit PDP and the for-profit social enterprise. They are as follows:

1. The ability to raise pre-revenue capital
2. The ability for late-stage capital expansion
3. The ability to leverage federal tax incentives
4. The need to develop sustainable revenue models
5. The ability to balance financial returns with social benefits
6. The ability to anchor the social mission into the long-term organizational mission

Comparisons across these categories show one advantage of the GHSE approach in being able to leverage equity stakes in the company to access new lines of revenue. Further, GHSEs are able to adhere to a social mission within daily operations—much like the PDPs—but do face some pressure from investors in demonstrating the future potential of profits. Consequentially, GHSEs are confined to the development of products that have dual-market potential, either through the sale of the drug in developed countries or the repurposing of drug discovery platforms for the development of products for wealthy markets. Finally, the ability of GHSEs to adhere in the long term to a social mission is uncertain—it is here that the hybrid B Corp and Flex C business models could play a future role.

Understanding how these differences affect operational capacity could help determine the potential contribution made by GHSEs, and potentially assist policymakers in identifying areas for improvement.

A. GHSEs Leverage Multiple Sources of Pre-Revenue Capital

Stakeholder and industry interviews made clear that cost and the ability to tap into financial resources at various stages of product development were the primary considerations in selecting corporate structure. Estimates show that developing a new biological vaccine or drug takes 10 to 15 years, and cost estimates can range from $1 billion to $4 billion per approved drug.[31] Developing a more traditional small-molecule drug usually involves a slightly shorter development time frame, but cost estimates are still high. For

[31]Tufts Center for the Study of Drug Development (CSDD), "Drug Developers Are Aggressively Changing the Way They Do R&D," press release on the Tufts CSDD *Outlook 2011* report, 5 January 2011. Matthew Herper, "The Truly Staggering Cost of Inventing New Drugs," *Forbes*, 10 February 2012.

neglected diseases, these estimates are lower but still significant—after reduction for tax credits and the possibility of accelerated review by the U.S. Food and Drug Administration (FDA),[32] some economists have estimated the cost of clinical testing for a neglected disease to be between $300 and $600 million.[33]

The expense of research, regulatory approval from the FDA, and the difficulty in bringing a product to market makes positive net income in biotechnology a rare occurrence. Within the United States, only about 32 of the 294 public biotechnology companies in drug development are profitable.[34] Exit strategies, or ways to liquefy investments in drug development, are generally available only after a product has been brought through the early phases of development. At that point, companies generally aim for the product to be acquired, optioned, or licensed by a larger company or look to partner with a larger pharmaceutical company to help bring the product to market. Alternatively, the company itself may be acquired by a larger organization. However, it is critical that companies manage to finance the early stages of R&D through the stage of negative revenue, either self-sufficiently or by accessing alternative financing mechanisms.

Various sources of financing exist at the early stage including foundations, governments, loans, and private investment. Each of these comes with its own strings attached, and each is accessible only to certain types of organizations.

1. GHSEs face difficulty in efficiently accessing foundation grants

Federal tax regulations require foundations to spend at least 5 percent of their assets per year.[35] These grants and donations, however, must be directed to organizations within the scope of the foundation's priority subject areas. In general, recipients must be nonprofit organizations; however, federal tax regulations do allow foundations to make certain investments, program-related investments (PRIs)—rather than grants—in for-profit companies that can count toward their 5 percent spending mandate. The IRS has strict rules in determining whether an investment qualifies as a PRI,[36] including for example, whether the investment significantly furthers the foundation's exempt activities, and whether a for-profit investor would make a similar investment.

Demonstrating this level of compliance is burdensome for smaller investors, but large foundations are beginning to take advantage of this flexibility. In 2009, the Gates Foundation created a $400 million program-related pool (increased to $1 billion in 2010), a quarter of which is used to make equity investments or to finance debt instruments in profit-making ventures.[37] The Gates Foundation made its first PRI in 2011 by investing $10 million in Liquidia Technologies,[38] and in 2012 it completed a $30 million equity investment in Genocea Biosciences and a $13 million equity investment in Visterra—all companies focusing on vaccine research.[39] However, navigating the technical, financial, and legal issues can still be a significant challenge—the Liquidia investment took over a year between initial interest and final purchase.[40]

[32]For a background of the Priority Review Voucher Program, see www.bvgh.org/What-We-Do/Incentives/Priority-Review-Vouchers.aspx.

[33]David B. Ridley, Henry G. Grabowski, and Jeffrey L. Moe, "Developing Drugs for Developing Countries," *Health Affairs* 25, no.2 (2006): 313–324.

[34]David Thomas, "Only a Few Public Biotechs Are Profitable, But There Are More of Them Today," 24 May 2012, www.biotech-now.org/business-and-investments/inside-bio-ia/2012/05/only-a-few-public-biotechs-are-profitable-but-there-are-more-of-them.

[35]Internal Revenue Service, "Private Foundations," www.irs.gov/charities/charitable/article/0,,id=96114,00.html.

[36]Internal Revenue Service, "Program-Related Investments," www.irs.gov/charities/foundations/article/0,,id=137793,00.html.

[37]Stephanie Strom, "To Advance Their Cause, Foundations Buy Stocks," *New York Times*, 24 November 2011.

[38]Luke Timmerman, "Gates Foundation Makes First Equity Investment in a Biotech Startup, Liquidia Technologies," *Xconomy*, 8 March 2011, www.xconomy.com/seattle/2011/03/08/gates-foundation-makes-first-equity-investment-in-a-biotech-startup-liquidia-technologies/.

[39]Luke Timmerman, "Genocea Snags $30M from Gates Foundation, VCs for New Vaccines," *Xconomy*, 10 October 2012, www.xconomy.com/boston/2012/10/10/genocea-snags-30m-from-gates-foundation-vcs-for-new-vaccines/.

[40]Timmerman, "Gates Foundation."

PDPs are most reliant on grant fundraising to maintain operations, and as such they are forced to spend significant resources seeking contributions from foundations, governments, for-profit biotech and pharmaceutical companies, and the public, all of which grow increasingly scarce in challenging economic conditions.[41] Interviewees from GHSEs and PDPs highlighted the challenge faced by nonprofit drug development companies due to heavy reliance on a small number of philanthropic organizations, the largest of which include groups such as the Wellcome Trust and the Gates Foundation, and on flow-through organizations such as the Global Alliance for TB Drug Development.

Newly formed PDPs may face even greater challenges. As multiple interviewees stated, large philanthropic organizations have by and large already determined their funding priorities, and often elect to fund PDPs with recognized track records, posing significant financial challenges for newly founded PDPs.

Many interviewees noted that although PRIs allow foundation investment in for-profit companies, receiving funds directly from a foundation is significantly harder as a for-profit, even a GHSE. Legal and tax constraints on foundations and philanthropies can present significant hurdles to direct charitable donations to a for-profit biotech or pharmaceutical company—however, nonprofit organizations face no such hurdles and can partner with for-profit companies much more readily. As such, foundations have been able to channel funds to for-profit companies and GHSEs through third-party PDPs.

While several interviewees from both PDPs and for-profit organizations cited examples where this indirect investment has worked smoothly, instances have arisen where miscommunications, delays, and disagreements have prevented funds from being distributed to for-profit companies. For example, one interviewee PDP recounted an instance where funding was delayed due to disagreements regarding downstream marketing rights, oversight provisions, and agreements to provide regular progress reports. Likewise, one for-profit social enterprise focusing on neglected disease research cited disagreements concerning royalty rates and ownership of downstream intellectual property. Another for-profit company further cited an instance where a funding agreement with one PDP took 15 months between the partnership agreement and actual receipt of funds. Such hurdles can discourage for-profit companies from relying solely on foundation grants, and they will instead turn toward more traditional forms of pre-revenue financial support.

2. GHSEs can efficiently access private investment and venture capital

Private investment funds, which include angel investors and venture capital (VC) firms, provide financial support to pre-revenue companies in exchange for partial equity ownership. Only for-profit companies, including GHSEs, can take advantage of this type of funding because they can sell an equity stake in their companies, whereas PDPs cannot because they are nonprofit organizations. As with all private funding, biotechnology investors primarily look for significant returns on their investment, and typically attempt to ensure such a return through asserting control over the corporate direction. Many private investors hold seats on their portfolio companies' boards of directors and can influence the companies' strategic decisions.

As for-profit companies, GHSEs depend greatly on VC funding in their early stages.[42] Biotech investment is often characterized as too risky or requiring profit horizons that are too long term for the appetite of most VC investors.[43] However, GHSEs may

[41]William H. Clark and Larry Vranka, "The Need and Rationale for the Benefit Corporation: Why It Is the Legal Form That Best Addresses the Needs of Social Entrepreneurs, Investors, and, Ultimately, the Public," Appendix B, 16 November 2011, https://docs.google.com/viewer?url=http://www.benefitcorp.net/storage/The_Need_and_Rational_for_Benefit_Corporations__11-16_version.pdf&pli=1.

[42]BioCentury global venture capital investment data, 2012.

[43]Bruce Booth, "The Biotech Venture Capital Math Problem," Forbes, 15 March 2012, www.forbes.com/sites/brucebooth/2012/03/15/the-biotech-venture-capital-math-problem/.

attract a niche investor group interested in orphan diseases, an area becoming more attractive as federal policy developments have promised orphan drugs faster regulatory approval and thus easier access to untapped markets for desperately needed products.[44c] In fact, orphan diseases are one of the few areas where VC firms are expected to increase investment over the next three years, compared with cardiovascular disease, diabetes, neurology, and other high-prevalence indications where investment decreases are expected.[45] The orphan drug program benefits those affected by rare and neglected diseases, and drugs for the treatment of the neglected diseases of the developing world generally also qualify as orphan drugs because most neglected diseases affect fewer than 200,000 persons in the United States.[46]

Significantly, all of the interviewed GHSEs opted for the for-profit model in order to better access early-stage private investment. While pre-revenue financing for for-profits is still a challenge, companies cited a much greater flexibility to find investors to support early-stage and preclinical R&D. For one, there are a relatively high number of equity investors when compared with the number of philanthropic donors, including family-run foundations Second, interviewees noted that negotiations with equity investors typically focus on issues such as ownership stake, voting rights, and price per share. As one company noted, "raising pre-revenue funds is easy—I just have to lower the cost of equity." The consequence of this is that many newly formed organizations that elect to focus on product development for diseases in LMI countries, and that are selecting between a nonprofit and a for-profit model, may find it easier to select a for-profit approach in order to secure the necessary start-up and pre-revenue capital.

3. GHSEs can access capital through the growing impact investor movement

Many GHSEs interviewed noted that their social mission allowed them to draw from a growing genre of investors: *impact investors*. In what is often referred to as double-bottom-line (referring to the focuses on profits and social impact) or triple-bottom-line (focusing on profits, social impact, and environmental impact) investing,[47] these investors seek to create a social impact through targeted direct equity and debt investments in businesses such as community banks, microfinance institutions, clean tech or green businesses, or social venture funds investing globally across developed and emerging markets.[48] The impact investing movement is still in development, but by some accounts it could become an institutionalized sector of the VC industry, representing individual investors seeking values-aligned investment opportunities.

By presenting themselves as socially focused companies, many GHSEs were able to leverage these impact investor groups. Sequella Inc., for example, stated that 80 to 90 percent of its investments were from double-bottom-line investment sources that required the company to focus in part on a social mission, raising more than $5 million in 2011 for Phase 2 clinical trials of a TB drug candidate.[49] PaxVax, self-described as a double-bottom-line company, draws investment almost exclusively from impact investors that are pursuing both financial and social returns, and

[44]C. Shaffer, "Pfizer Explores Rare Disease Path," *Nature Biotechnology* 28 (2010): 881–882.

[45]National Venture Capital Association (NVCA), *Vital Signs* (NVCA and MedIC, October 2011).

[46]Testimony of Jesse L. Goodman, chief scientist and deputy commissioner for science and public health, FDA, before the Senate Subcommittee on Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Committee on Appropriations, 23 June 2010.

[47]The phrase *triple bottom line* was first coined in 1994 by John Elkington, the founder of a British consultancy called SustainAbility. See "Triple Bottom Line: It Consists of Three Ps: Profit, Planet, and People," *The Economist*, 17 November 2009, www.economist.com/node/14301663. Elkington argued that businesses should consider three bottom lines of people, planet, and profit rather than the traditional formula of pure profit as the bottom line of a business. Today, this term, like *mission driven, sustainable*, and other similar terms, is commonly used by social entrepreneurs and investors to refer to businesses that consider other interests in addition to profits and shareholder value maximization.

[48]US SIF: The Forum for Sustainable and Responsible Investment, *2010 Report on Socially Responsible Investing*, 2010, http://ussif.org/. See also "Sustainable and Responsible Investing Facts," http://ussif.org/resources/sriguide/srifacts.cfm, accessed 9 September 2011.

[49]"Sequella Awarded $4.6 Million in New NIH Grants to Expand Anti-Infectives Pipeline," *Business Wire*, www.businesswire.com/news/home/20110404006080/en.

since founding in 2007 it has secured more than $50 million from investors such as Ignition Partners and the Wellcome Trust, in addition to nondilutive grants.[50] Companies that have taken advantage of the new impact investor pool emphasized that such investors see the "bigger picture" in pursuing both a global health benefit as well as profits.

Importantly, the impact investor movement appears to be growing. A November 2010 report by J.P. Morgan estimates the size of this market opportunity at between $400 billion and $1 trillion.[51] This included only investment opportunities in emerging markets across five sectors: housing, rural water delivery, maternal health, primary education, and financial services. J.P. Morgan estimates the 10-year profit potential from these opportunities alone ranged between $183 billion and $667 billion.[52] Approaching it from the demand side of the equation, and focusing only on U.S. individual investors, a June 2010 report from Hope Consulting, Money for Good, estimates a demand for impact investments among U.S. high-net-worth individuals at $120 billion.[53]

Regardless, some interviewees from GHSEs responded with some skepticism and frustration when discussing impact investors. Two companies interviewed had actively sought investment through impact investor groups such as Ashoka (www.Ashoka.org), Mission Markets (www.missionmarkets.com), the Global Health Investment Fund,[54] the Global Impact Investing Network (www.thegiin.org), and the Acumen Fund (www.acumenfund.org/ten/), but with varying success. Such groups are focused on growing the impact investor movement and developing tools to help investors find and fund social enterprises, such as the development of guidelines and metrics. However, these funds focus on areas of global development and social benefit, with only a small effort dedicated to medical innovation.

Although the concept of seeking a return on investment through impact investing may be appealing on the surface, this investor group is still in its infancy[55] and practical implementation can be difficult.[56] One interviewee specializing in impact investing highlighted a "philosophical barrier" that many impact investors face—specifically, they are still working to balance the goal of social impact with the goal of securing financial return of their investment.[57] The inability to reconcile these two conflicting objectives is in many ways discouraging the impact investor movement and driving investors to seek either financial returns or social benefits. Further, investors that focus on the social impact as their priority typically treat their investments as charitable contributions, directing them toward nonprofit companies where the perceived social benefit is the highest and the legal barriers to donation are much lower than contributions directed toward for-profit enterprises.

To further complicate the issue, many independent impact investors lack the bandwidth and technical understanding to assess the social impact of GHSEs, particularly in terms of trade-offs with financial returns. Financial returns are easy to measure, being a function

[50]"FDA Accepts PaxVax's IND for Single-Dose Oral Cholera Vaccine," *Business Wire*, 19 March 2012, www.businesswire.com/news/home/20120319005396/en/FDA-Accepts-PaxVax%E2%80%99s-IND-Single-Dose-Oral-Cholera. See also http://paxvax.com/vision-strategy/.

[51]J.P. Morgan Global Research, *Impact Investments: An Emerging Asset Class*, 29 November 2010, www.jpmorgan.com/pages/jpmorgan/investbk/research/impactinvestments. See also a summary of the J.P. Morgan report: Nicholas Timmons, "Impact Investment 'a Burgeoning Asset Class,' " *Financial Times*, 28 November 2010, www.ft.com/intl/cms/s/0/e875dda6-fae6-11df-b576-00144feab49a.html?ftcamp=rss#axzz1XUogcz2a.

[52]Ibid.

[53]Hope Consulting, Strategies for Social Change, *Money for Good*, 2010, www.hopeconsulting.us/money-for-good.

[54]David Bank, "Global Health Investment Fund Lifts Capo on Returns," 27 September 2012, http://impactiq.org/global-health-investment-fund-lifts-cap-on-returns/.

[55]J. Gregory Dees and Beth Battle Anderson, "For-Profit Social Ventures," ch. 2, in Social Entrepreneurship, edited by Marilyn L. Kourilsky and William B. Walstad, 12 (Senate Hall Academic Publishing, 2003); Jed Emerson, *The Nature of Returns: A Social Capital Markets Inquiry into Elements of Investment and the Blended Value Proposition*, Harvard Business School, Social Enterprise Series, no. 17, 2000, www.hbs.edu/socialenterprise/download/.

[56]Erin Bailey of JPMorgan Chase.

[57]Ibid.

of profit levels, perceived risk, and growth prospects. In contrast, investors looking to "do well by doing good" are still struggling to identify for-profit companies that have a legitimate social mission and measure the social benefit derived from their investment. The lack of transparency and credibility in how funds define, track, and report on the social and environmental performance of their capital leads to a limited ability to understand the impact of investments.[58] Financial performance data alone are insufficient. Some organizations, such as the Global Impact Investing Network, are working to standardize the impact investing community through a common framework for performance reporting.[59] However, although such efforts are in progress, they are still fragmented, and they focus less on upstream R&D and more on downstream sustainability and community impact.

In summary, while the GHSEs are perhaps poised to take advantage of the growing impact investor community, that community is still developing and maturing. Tools to help measure and communicate impact in both financial and social benefit terms would help develop this investing sector, and help support GHSEs in the future.

4. Government grants provide an important source of capital for GHSEs

Interviewees from for-profit companies, GHSEs, and PDPs cited government funding as an important source of capital, particularly in the early stages of their respective companies. Government funds are disbursed through a variety of programs and are available in the form of grants, contracts, and advanced purchase agreements.

Interviewees from GHSEs cited the importance of government grants specifically for businesses, such as the Small Business Innovation Research (SBIR) Program grants and the Small Business Technology Transfer (STTR) Program grants offered to small start-up companies by government organizations such as the Department of Defense/DARPA and the NIH. These grant programs are exclusive to small businesses and typically supply amounts of up to $150,000 for Phase 1 funding and $1 million over two years for Phase 2 funding.[60] In fiscal year 2011 (October 1, 2010–September 30, 2011), the NIH made SBIR grant and contract awards totaling more than $609 million and STTR grant awards totaling more than $73 million.[61]

Likewise, all GHSEs interviewed had pursued or intend to pursue government spending dedicated to the development of new technologies for public health emergencies. In 2004, Congress allocated $5.6 billion for this purpose through the Project Bioshield Act,[62] and in 2007 it created the Biomedical Advanced Research and Development Authority (BARDA) through the Pandemic All Hazards Preparedness Act[63] to help oversee government procurements. These government programs oversee funding for the development and advanced procurement of drugs, vaccines, and diagnostics that are deemed necessary in a public health emergency, with a focus in three key areas: biodefense, pandemic influenza, and emerging infectious diseases. Interviewees noted the partial overlap with these focus areas and neglected diseases—dengue, cholera, and drug-resistant strains of TB, for example, are all listed as BARDA priorities.[64] It should be noted, however, that this nondilutive funding is not exclusive

[58]Global Impact Investing Network, "Impact Reporting and Investment Standards," www.thegiin.org/cgi-bin/iowa/reporting/index.html.

[59]See "Impact Reporting and Investment Standards," http://iris.thegiin.org, and Global Impact Investing Ratings System, www.giirs.org.s

[60]Currently, 11 federal agencies participate in the SBIR Program: the departments of Health and Human Services (DHHS), Agriculture, Commerce, Defense (DOD), Education, Energy (DOE), Homeland Security, and Transportation; the Environmental Protection Agency; the National Aeronautics and Space Administration (NASA); and the National Science Foundation (NSF). Currently, five federal agencies participate in the STTR Program: DOD, DOE, DHHS (NIH), NASA, and NSF.

[61]See National Institutes of Health, "Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Programs," http://grants.nih.gov/grants/funding/sbirsttr_programs.htm.

[62]P.L. 108-276.

[63]P.L. 109-417.

[64]*BARDA Strategic Plan, 2011–2016*, https://docs.google.com/viewer?url=http%3A%2F%2Fwww.phe.gov%2Fabout%2Fbarda%2FDocuments%2Fbarda-strategic-plan.pdf.

to for-profit companies. In 2010, two PDPs—PATH and the Infectious Disease Research Institute (IDRI)—both received funding from BARDA, $5.2 million and $1.8 million, for their work in vaccines and vaccine technologies.[65]

5. GHSEs can leverage equity to rapidly secure late-stage capital

Late-stage capital expansion—the ability to rapidly leverage equity to scale up operations—is another advantage of GHSEs cited by interviewees. Assuming a company's early-stage initial investment yields positive and promising results, other large influxes of capital are required for biotech companies to do further testing and particularly to pay for clinical trials. The cost of clinical trials can be as much as $800 million.[66] Thus, the ability to raise subsequent larger rounds of capital is critical to a company's success. The general sources of capital are the same as those available at the early stage; however, the actual funding entities that can supply the larger amounts of capital needed at the later stage are much fewer and farther between.

If companies can show that their results are particularly promising, then they can often draw funds from VC firms that have already invested in the earlier stages, and possibly additional funds from other VC firms who didn't want to take the early-stage risk. This has happened in a few instances—Napo Pharmaceuticals, for example, was able to raise funding for Phase 3 testing of its antidiarrheal drug product in exchange for marketing and royalty rights.[67] Debt financing is also a possibility and is often used to supplement the equity funding at these stages.[68] Lenders providing loans at this stage, however, often include financial and reporting covenants in their terms to help secure their investment.

Some GHSE interviewees cited late-stage capital expansion as a reason for electing a for-profit model over a PDP approach. Inviragen, for example, cited the need to raise late-stage capital for Phase 3 clinical trial funding as a central consideration in forming as a for-profit company. By forming as a GHSE, Inviragen is able to access typical for-profit sources of capital and secured funding from VC and private investment. This money is not insignificant—for example, a 2009 series A financing allowed Inviragen to raise $15 million to further support its dengue vaccine efforts.[69] While not sufficient in and of itself, such financing can help a company transition to mid- and late-stage clinical testing.

In general, nonprofits face greater challenges in securing late-stage funding, and as a result must spend significant time and resources raising funds from foundations, governments, and the public.[70] Several interviewees from PDPs stressed how only a few funding sources—in particular the Gates Foundation and, to a lesser extent, government grants—are available to finance late-stage clinical trials for the development of new medicines for neglected diseases (although several other sources of funding are available for early-stage R&D, such as smaller family foundations and licensing arrangements). This small pool of investors often reduces the flexibility and operational freedom of PDPs, since funding is restricted to specific activities. In contrast,

[65]PATH, "PATH Awarded $5.2 Million BARDA Contract to Stabilize Pandemic Influenza Vaccines," www.path.org/news/an100915-barda.php; IDRI, "IDRI Awarded Contract from BARDA to Develop Next Generation Adjuvants for Pandemic Influenza," www.idri.org/press-12-3-10.html.

[66]Avik S. Roy, *Stifling New Cures: The True Cost of Lengthy Clinical Drug Trials*, April 2005, www.manhattan-institute.org/html/fda_05.htm.

[67]Camille Ricketts, "Napo Pharm Raises Seed Money for Its Anti-diarrheal Drug," *Venture Beat*, 5 February 2009, http://venturebeat.com/2009/02/05/napo-pharm-raises-seed-money-for-its-anti-diarrheal-drug/.

[68]Avance, *Non-dilutive Financing Alternatives for Biotech Companies*, March 2008, https://docs.google.com/viewer?url=http%3A%2F%2Fwww.avance.ch%2Fnewsletter%2Fdocs%2Favance_on_funding_alternatives.pdf; Robert Weisman, "Biotechs Are Spending Less on Drug Discovery," *Boston Globe*, June 2011.

[69]AltAssets, "Inviragen Merges with SingVax, Raises $15m to Combat Dengue Fever," 9 October 2009, www.altassets.net/private-equity-news/inviragen-merges-with-singvax-raises-15m-to-combat-dengue-fever.html.

[70]William H. Clark and Larry Vranka, "The Need and Rationale for the Benefit Corporation: Why It Is the Legal Form that Best Addresses the Needs of Social Entrepreneurs, Investors, and, Ultimately, the Public," 16 November 2011, https://docs.google.com/viewer?url=http://www.benefitcorp.net/storage/The_Need_and_Rational_for_Benefit_Corporations__11-16_version.pdf&pli=1.

GHSEs found that they could retain a higher level of flexibility to pursue partnership opportunities since shareholders and investors generally place fewer constraints on organizations than do philanthropic funders, such as large foundations.

Finally, GHSEs have an added fundraising advantage through debt financing. Debt financing is in theory available for nonprofits but is much more limited and expensive than in the for-profit context. PDPs would be required to pursue only products that have financial returns, and would need to reassure lenders of their interest in seeking financial returns. Lenders view these entities as more risky investments—considering that no individuals have invested their own money in the company's equity, it thus has more limited "skin in the game."[71]

B. GHSEs Must Use Dual-Market Strategies to Generate Revenues

By definition, directors of GHSEs are required to seek, in part, some financial return for the benefit of their shareholders. Those GHSEs interviewed generally pursued two business strategies to generate a social benefit while providing a return on investment:

1. Geographic dual-market business model

One strategy adopted by GHSEs is to focus on diseases that have potential markets in LMI countries as well as markets in developed countries and emerging markets in the BRIICS countries.[72] Such research areas typically include novel therapeutics and diagnostics for TB, HIV/AIDS, malaria, Chagas disease, and dengue. Inviragen, for example, developed a social mission and business mission having significant overlap—developing vaccines for diseases such as dengue is in itself a viable profit model and could produce a suitable return on investment for its investors. Likewise, Sequella Pharmaceuticals, for example, cited its decision to license its TB drug candidate in Russia as a pure market-based decision required for profitability, and one that a PDP may not have needed to pursue.

Napo Pharmaceuticals noted that its criteria for disease target selection is focused on those products that have dual geographic markets. For example, their principal product, crofelemer, is being developed specifically to serve those in LMI countries suffering from cholera and diarrhea associated with HIV/AIDS, but it also has significant markets in the United States to treat populations suffering from other diarrheal diseases such as irritable bowel syndrome, a diseases that afflicts 20 percent of the U.S. population and has a possible market of more than $4 billion annually. A new drug application for crofelemer is currently being reviewed by the FDA. Napo is also pursuing treatments for type II diabetes—an indication selected specifically for its potential market in developed countries, as well as its significant prevalence in LMI countries.

However, developing a viable business model around a geographical dual market would inevitably preclude GHSEs from addressing some NTDs. Interviewees emphasized that point, specifying that developing medicines for certain target neglected diseases, such as visceral leishmaniasis and African trypanosomiasis, is unsustainable as the principal activity in a for-profit organization without some revenue-generating activity to subsidize this investment. Exceptions to this rule are rare, and would apply only to situations where the drug discovery platform could be applied to a developed world market (see the following section) or where the FDA would require smaller clinical studies due to an absence of alternative treatments and the disease would be eligible for an alternative incentive reward, such as an innovation prize or priority review voucher. For example, one interviewee reasoned that research into a new vaccine for Buruli ulcer would have a relatively low regulatory bar because no modern treatment exists, and that coupled with the receipt of a priority review voucher, pursuit of vaccines for Buruli could constitute a profitable business

[71]Thad D. Calabrese, "The Accumulation of Nonprofit Profits: A Dynamic Analysis," *Nonprofit and Voluntary Sector Quarterly* 41 (2011): 300–324.
[72]The *BRIICS countries* are Brazil, Russia, India, Indonesia, China, and South Africa.

model. Regardless, in the absence of a low regulatory hurdle and additional non-market-based incentives, social enterprises cited a reluctance to pursue a disease that had little or no market in the developed or BRIICS countries.

2. Technological dual-market business model

Social enterprises also pursued the development of drugs or technological platforms that could be repurposed toward opportunities for other disease markets. Several examples were cited during the interviews—for example, Sequella Pharmaceuticals is currently testing the same compound for both TB as well as *H. pylori*, the etiological agent that causes more than 90 percent of duodenal ulcers and 80 percent of gastric ulcers, and has an estimated U.S. market of more than $1 billion annually.[73] Further, interviewed GHSEs tend to focus on repurposing drugs and vaccines toward specialized markets within the United States, such as animal health, biodefense (including pandemic influenza), and travelers' vaccines.

Some GHSEs working toward technological dual markets used a "piggybacking" approach toward funding their neglected disease research portfolio. Under this approach, research activities for NTDs piggybacked on the core operations of the company, utilizing a certain percentage of infrastructure, resources, lab materials, manpower, and expertise.

Anacor Pharmaceuticals, for example, has developed a sophisticated boron chemistry platform to design and test new compounds against diseases with significant U.S. markets, such as oncomycosis and psoriasis. Further, Anacor has developed additional programs using the boron chemistry platform and company infrastructure toward diseases such as visceral leishmaniasis, Chagas disease, malaria, and river blindness. While many of these projects are still in early research, Anacor has started early clinical testing of at least one candidate for human African trypanosomiasis. The marginal costs for these additional programs are supported exclusively through grants and development agreements with groups including the Institute of One World Health, the Medicines for Malaria Venture, and the Drugs for Neglected Disease initiative, and by funding by the Gates Foundation through a grant to University of California, San Francisco.

Interviewees generally noted that for-profit organizations had greater flexibility in selecting target markets. For-profits have considerable freedom as to which markets they choose, and they can base the decision solely upon core competencies, market opportunities, resources available to them, and ultimately, profit potential—the "normal" strategic, visionary, and financial constraints. PDPs, on the other hand, have less freedom in market consideration, as their market is usually an intrinsic part of the organization's mission, is laid out in the charter, or is intertwined with its specific grant funding. A PDP founded to develop vaccines for malaria is limited to that particular social mission and generally cannot switch gears to serve an entirely different population without violating its responsibilities to its grantees, charter, supporters, employees, volunteers, and end clients, as well as, possibly, legal guidelines.

One common misconception of the for-profit sector is that for-profit companies and GHSEs may have higher success rates than PDP organizations, which are reliant on continued donations from third-party organizations. On the contrary, there is no compelling evidence that for-profit companies including GHSEs have a greater chance of survival than nonprofits. Business failure rates are high, and there is no reason to believe that for-profit ventures will be immune to the forces and factors that have led so many businesses to fail.[74] Further, while most GHSEs studied were required to adopt one of the dual-market business strategies described earlier, some PDPs used similar opportunities to minimize their reliance on philanthropic donations and elected to pay tax on unrelated income as necessary.

[73]Sequella Pharmaceuticals, http://sequella.com/pipeline/productsummaries.htm.

[74]Dees and Anderson, "For-Profit Social Ventures."

C. Nonprofit Tax Exemption Is Not Essential to GHSE Operations

Whereas nonprofits cited some advantage to their tax-exempt status, GHSEs found that the lack of tax exemption was not critical to operations. From the PDP perspective, interviewees expressed the view that the nonprofit tax status did make fundraising easier while lowering operational costs. Some PDPs interviewed noted the importance of retaining their 501(c)(3) status, particularly for attracting financial support from individual donors and smaller family foundations.

Regardless, GHSEs did not cite the lack of nonprofit tax exemptions or tax deductions for donors as a significant disadvantage. On the contrary, it was often viewed as a "cost of doing business" and was only a minor consideration in deciding to favor incorporating as a for-profit rather than a nonprofit company. Further, some interviewees noted that significant tax incentives—such as tax credits—exist for smaller biotechnology companies. For example, the 2010 Patient Protection and Affordable Care Act in the United States included a major 50 percent tax credit for qualified small- and medium-sized biotechnology companies with less than 250 employees for tax years 2009 and 2010.[75] Interviewees from GHSEs also cited the tax advantages provided by the Orphan Drug Act of 1983, which, among its many incentives, provided to companies developing a new drug for a rare disease a tax credit of 50 percent of the cost of conducting human clinical testing.[76]

Nonprofits are able to generate income.[77,78] IDRI, a PDP based in Seattle, Washington, is an excellent example of how a PDP can help sustain operations through operating as a business. Established in 1993, IDRI's mission is to "develop novel, advanced products for the diagnosis, prevention and treatment of neglected diseases of poverty."[79] IDRI's emphasis, however, is on "product-focused" research portfolios, which have yielded several products with dual geographical or technological market potential. As a result, IDRI has spun off at least two for-profit companies since 1994 and generated licensing revenues based on their adjuvant portfolio technologies initially developed as part of their neglected disease research. For example, in 2008, IDRI licensed its glycopyranosyl lipid adjuvant to the for-profit vaccine development company Immune Design. In return, IDRI received an upfront payment, milestone payments on success in testing, royalties from future product sales, and equity shares in Immune Design, which raised $18 million and $32 million in series A and B venture funding, respectively. Corixa, another spinoff founded in 1994, likewise generated revenues for IDRI through a series of development contracts with GSK, concluding with its 2005 acquisition for $300 million. Although taxable, these activities have provided close to 40 percent of IDRI's $50 million annual budget.[80]

[75]D. Zerbe, "Health Reform Will Set Off Biotech Tax Credit Rush," *Forbes*, 26 March 2010; A. Philippidis, "Revival of Tax Credit Program Depends on Job Creation and Scientific Results," *Genetic Engineering and Biotechnology News*, 18 July 2011.

[76]Orphan Drug Act, P.L. 97-414, as amended, www.fda.gov/regulatoryinformation/legislation/federalfooddrugandcosmeticactfdcact/significantamendmentstothefdcact/orphandrugact/default.htm.

[77]Brenda Zimmerman and Raymond Dart, "Charities Doing Commercial Ventures: Societal and Organizational Implications," in *A Reader in Social Enterprise*, edited by Kelvin Sealey, Jerr Boschee, Jed Emerson, and Wendy Sealey (Boston: Pearson Custom Publishing, 2000).

[78]Traditional commercial activities were primarily carried out to provide services to constituencies and included things such as gift shops and used clothing stores, such as Oxfam and Goodwill.

[79]Infectious Disease Research Institute, www.idri.org/dev/mission-vision.html.

[80]Curt Malloy, "Licensing of IP for Development and Production of Vaccines in Developing Countries," presentation given at the World Health Organization's Intellectual Property Rights and Vaccines: Promoting R&D and Production in Developing Countries, Tokyo, 16–17 November 2009, www.who.int/vaccine_research/documents/IVR_IPR_Tokyo_Session5_Malloy_presentation.pdf.

CHAPTER 4
BALANCING SOCIAL MISSION WITH FINANCIAL RETURNS

4

In addition to raising enough capital in the early and late stages of development, GHSEs in their mission aim to maintain a focus on neglected diseases, which often do not have the best market returns.

This can pose particular legal challenges, as courts often find that the primary purpose of traditional for-profit corporations is to promote growth of long-term value and maximize shareholder profit.[81] Other purposes, such as social benefit, are not traditionally allowed to conflict with those primary goals, and if they do, shareholders can bring suit against the corporation's directors for breach of fiduciary duties.[82] Although some for-profit corporations are currently able to devote resources to advancing social benefit goals—for example, through practicing CSR—such efforts are often justified to shareholders as ultimately part of a plan to maximize profit.

Perhaps the most high-profile example of the legal challenges social enterprises face is the acquisition of Ben and Jerry's by Unilever, in what ultimately became a forced takeover. Initially, Ben and Jerry's rejected Unilever's purchase offer and moved to accept a lesser offer that promised to honor their corporate mission. In response, Unilever sued, and won, on the grounds that Ben and Jerry's had a fiduciary obligation to ensure the maximum return to its shareholders and accept the higher offer. Ben and Jerry's had always had a very strong sense of corporate responsibility, and certainly did not want to lose control of that by being swallowed up by a large corporate entity like Unilever. In spite of its best efforts, ultimately Ben and Jerry's was acquired by Unilever, and the original leadership lost control of their own company.[83]

Directors of GHSEs likewise maintain a fine line between serving the social purpose that their corporation was founded to serve and bringing in financial returns high enough to satisfy shareholders. Although no GHSE has yet been sued for adhering to a social mission, the threat of suit is present and the fiduciary responsibilities of directors might affect corporate operations.[84]

A. GHSEs Can Maintain Focus on Social Mission in Day-to-Day Operations

The level of scrutiny given to the decisions of a director depends in part on the context and the state in which the decisions are being made. Generally, courts have distinguished between director decisions made in the context of day-to-day operations and those decisions that would affect the operational

[81] *Revlon, Inc. v. MacAndrews & Forbes Holding, Inc.*, 506 A.2d 173, 182 (Del. 1986).

[82] *Dodge v. Ford Motor Company.*

[83] Aiden Livingston, "To B or Not to B? Weighing the Benefits of Benefit Corporations," *Mashable Business*, 2 March 2012, http://mashable.com/2012/03/02/benefit-corporations/.

[84] As a general legal matter, the level of scrutiny the decisions of a director are given depends in part on the context and the state in which the decisions are being made. As a typical example, Delaware courts review director decision making in three broad categories, or scenarios: (1) day-to-day operational decisions; (2) defensive decisions (those taken by directors in an effort to ward off potential bidders, whether friendly or hostile); and (3) change-of-control decisions (those taken during a pending sale or merger). The ability of a director within a for-profit company to pursue a social goal is dependent on which of these situations applies.

structure of an organization, such as a corporate sale or merger.

In the day-to-day context, directors of for-profit corporations can consider nonshareholder interests—such as social benefit—as long as they can show a rational connection between that consideration and shareholder value.[85] This is because courts review director decisions in the day-to-day context under the deferential "business judgment rule."[86] In other words, courts assume that decisions made in the context of day-to-day operations are in the long-term interests of the shareholders, even if in the short term they appear to be promoting nonshareholder interests (such as a corporation's decision to pursue medicines for a less profitable neglected disease).[87] Regardless, over the long term, operational decisions must show some connection to shareholder value.

When asked directly, GHSE interviewees were at ease with maintaining their legal obligations to shareholders while pursuing their respective social missions, due in large part to their investors and their business strategy. Interviewees credited their investors as being very understanding of their respective company's social commitment to global health, and in granting significant flexibility in pursuing opportunities that may not be maximally profitable in the short term. One company described how its neglected disease research portfolio, while using core corporate infrastructure, was supported using nonshareholder funds; as such, the directors' fiduciary duties did not require seeking approval from shareholders for the NTD programs. Further, companies such as Inviragen and Napo Pharmaceuticals specified that their pursuit of social benefit and their obligations to shareholder profits are in direct alignment.

Although GHSEs were comfortable in fulfilling their legal obligation in regular operational decision making, interviewees said that they often grappled with how to best serve their social mission in light of financial pressures. Although several companies were formed for the purpose of developing medicines for neglected diseases, one interviewee observed that pursuing a more lucrative market in the short term could also help generate revenues to support longer-term investment in neglected diseases R&D. For example, Sequella Pharmaceuticals' TB drug candidates face tough FDA regulatory requirements and clinical testing and an extended regulatory approval process, during which time it would earn no revenue from the product. To diversify its portfolio during this extended period, Sequella made the business decision to devote part of its resources and expertise to diseases with larger markets and lower regulatory hurdles, such as *H. pylori* and *C. difficile*. Even though these investments diverge from the social purpose with which Sequella was founded, Sequella interviewees felt that the diversification ultimately supported the company's work in TB because it kept the company's financial assets safe from the risk of total failure.

GHSEs noted that the lack of clear metrics to measure progress toward a social mission presented challenges when communicating with investors about these types of trade-offs. Metrics on social returns are vague—for example, it's hard to compare the value of a 20 percent reduction in malarial cases in Africa with a 10 percent reduction in malarial cases coupled with a greater increase in financial return on investment. While GHSEs found that their particular investors were by and large supportive of the neglected disease programs, they also found that explaining the selection of a social benefit instead of a financial opportunity was difficult. One interviewee said that it was critical to discuss with investors upfront about the investors' expectations regarding developing profits for shareholders and educate them at the outset about the measurements that would be available to measure the social impact.

[85]See *Aronson v. Lewis*, 473 A.2d 805, 812 (Del. 1984) (stating that a director's decisions must be "on an informed basis, in good faith, and in the honest belief that the action taken was in the best interests of the company").

[86]*Gimbel v. Signal Cos.*, 316 A.2d 599, 608 (Del. Ch. 1974).

[87]*Holdings, Inc. v. Newmark,* 16 A.3d 1, 33 (Del. Ch. 2010) *("eBay")*

GHSEs interviewed have taken efforts to attract socially minded investors through various ways, including adopting the "double-bottom-line" label or demonstrating strong commitment toward clinical studies for medicines targeting neglected diseases. For example, Napo Pharmaceuticals, whose antidiarrheal drug crofelemer is currently in Phase 3 clinical testing, created the Crofelemer Access Program (CAP) Global, a wholly owned subsidiary committed to sustainably providing its antidiarrheal drug crofelemer to populations in LMI countries.[88] CAP Global helps "signal" to potential investors through a dedicated social mission, and through obtaining a B Corp certification by B Lab. Funds raised through Napo's CAP Global are earmarked exclusively for the development, testing, and marketing of crofelemer in LMI countries. In short, the creation of CAP Global has allowed Napo to communicate to shareholders and other business partners the importance of considering social and financial interests when evaluating various strategic business opportunities.

Development of tools to better communicate the social commitment of a biotechnology company could help further attract investors. The B Corp and Flex C corporate structures may help in this vein, as these corporate forms have specific reporting and transparency requirements. Both the B Corp's annual benefit report and the Flex C's annual management discussion and analysis report are required to include statements and assessments of the company's pursuit of its respective social cause. The B Corp corporate form goes even further, as most states require a third-party audit of the benefit report to determine the accuracy of the statements and the validity of the company's efforts. However, no standard way to measure this social benefit exists—for this, it is clear that an industry standard is needed that correlates the health impact in LMI countries to the revenues generated.

B. GHSEs May Face Challenges in Long-Term Preservation of a Social Mission

In contrast with day-to-day operations, preserving the social mission as a long-term corporate strategy can be difficult for GHSEs, particularly with regard to corporate mergers, sales, and takeovers. Almost universally, directors are legally required to maximize shareholder value in these situations.[89] In other words, most courts will seek to limit the "purely philanthropic ends" of mission-driven companies and social enterprises.[90] Some possible exceptions exist in states that have enacted "constituency" statutes to provide some legal protection to directors seeking to consider nonshareholder interests when making decisions regarding corporate structure.[91] However, there are limited guidelines, examples, and case studies of how those would work.

The long-term preservation of the social mission was of particular concern to GHSE interviewees. One interviewee within a company developing technological platforms for dual technological markets said the thought that his company could be bought and the neglected disease program abandoned "keeps [him]

[88]See www.bcorporation.net/capglobal.

[89]Delaware courts will give directors the benefit of the business judgment rule only if the directors can first demonstrate that they were responding to a legitimate threat to corporate policy and effectiveness and that their response was "reasonable in relation to the threat posed." *Unocal Corporation v. Mesa Petroleum Company*, 493 A.2d 946 (Del. 1985). See also *eBay,* 16 A.3d at 33–34. (a public-service mission that "seeks not to maximize the economic value of a for-profit Delaware corporation for the benefit of its stockholders" is an invalid corporate purpose and inconsistent with directors' fiduciary duties).

[90]See, for example, *Baron v. Strawbridge & Clothier*, 646 F. Supp. 690, 697 (E.D. Pa. 1986) (stating that while it was proper for directors facing takeover attempts to consider the corporation's employees, customers, and community, their fiduciary duty was still "to act in the best interests of the corporation's shareholders").

[91]Constituency statutes are one of the main statutory differentiators from state to state with respect to fiduciary duties. Developed mainly by state legislatures as a defensive mechanism for local companies that are subject to a hostile takeover, constituency statutes give the target company's board the discretion to favor a deal that is better for the company's employees, the community, and the local economy over a deal with a higher purchase price but more detrimental effects to the community. If no competing deal exists, the constituency statute permits a board to examine the potential transaction's impact on the community and reject it on that basis.

up at night." The interviewees of early- and growth-stage mission-driven biotech companies expressed fear of being pressured to change business practices or pursue strategic alternatives to independent growth by investors whose financial interests often diverge over time from the social mission of the company. One interviewee maintained that their company had to "remain vigilant" in licensing technologies to ensure that the social mission remained intact, particularly with regard to the preservation of marketing provisions to LMI countries. These fears, combined with the prevailing business culture and, in some cases, advice of counsel about the risk of litigation if one fails to maximize shareholder value, can have a chilling effect on corporate behavior as it relates to pursuit of health goals.

GHSEs have managed to devise strategies to help ensure that their respective companies continue to pursue global health missions. In general, interviewees maintained a commitment to a social mission through four strategies. First, companies took great efforts to seek out and secure investors that understood the social mission and the commitment to neglected disease research. Although that approach does limit the pool of potential investors, offsetting some of the potential benefits of the for-profit structure, it nonetheless helps ensure that many of the company's core investors share the dual commitment of social impact and profitability, providing some insulation from pure capital market pressures.

Second, interviewees maintained a commitment to their respective social mission through the selection of and reliance on directors with similar goals. Interviews with Anacor Pharmaceuticals, for example, emphasized the importance of its CEO, David Perry, in maintaining and supporting its neglected disease research efforts. Sequella Pharmaceuticals, similarly, was dependent on the social mission of founder Carol Macey—also a founder of the PDP Aeras TB—in developing its TB therapeutic program. Retaining directors that hold similar visions toward promoting health in LMI countries helps guarantee that such research programs will remain a priority.

Third, and as discussed earlier, a few companies saw no distinction between their social and financial missions. Interviews with Inviragen, for example, demonstrated its view that a focus on vaccine technology platforms would yield the highest returns by pursuing markets in diseases that affect LMI countries, such as dengue and Chikungunya. Likewise, Lisa Conte, Napo's CEO, stated, "There is nothing in our mission or what we've done that is a compromise to shareholders; if the only thing you care about is money, money, money—or the only thing you care about is the unmet need—it doesn't matter. The two are indistinguishable because you achieve both."[92] Regardless, Napo recognizes that this is still a challenge to communicate to investors.

Finally, one organization, 60° Pharmaceuticals, opted to pursue novel medicines for malaria, TB, and Chagas disease by forming as a limited liability company (an LLC) over a typical corporation. LLCs, in contrast to corporations, are contractually created organizations, and they allow for greater flexibility in selecting organizational purpose. In the instance of 60° Pharmaceuticals, it saw that the LLC option would allow for formal inclusion of a social mission allowing for exclusive focus in developing world diseases, while avoiding the reporting and auditing requirements of benefit corporate models. LLCs do have downsides, however—in particular, LLCs cannot go public. As such, scaling up operations and capital expansion during late-stage clinical trials, for example, through an initial public offering, is not possible.

[92]Morrison, "Mission-Based Biz Model."

CHAPTER 5
SUMMARY AND RECOMMENDATIONS

5

GHSEs represent an untested, yet emerging adaptation of the traditional for-profit R&D model that may hold some advantages over traditional for-profit and PDP models in developing new health products for LMI countries.

Although the GHSE model is still being developed, some companies have seen products through to new drug application and late-stage clinical testing.

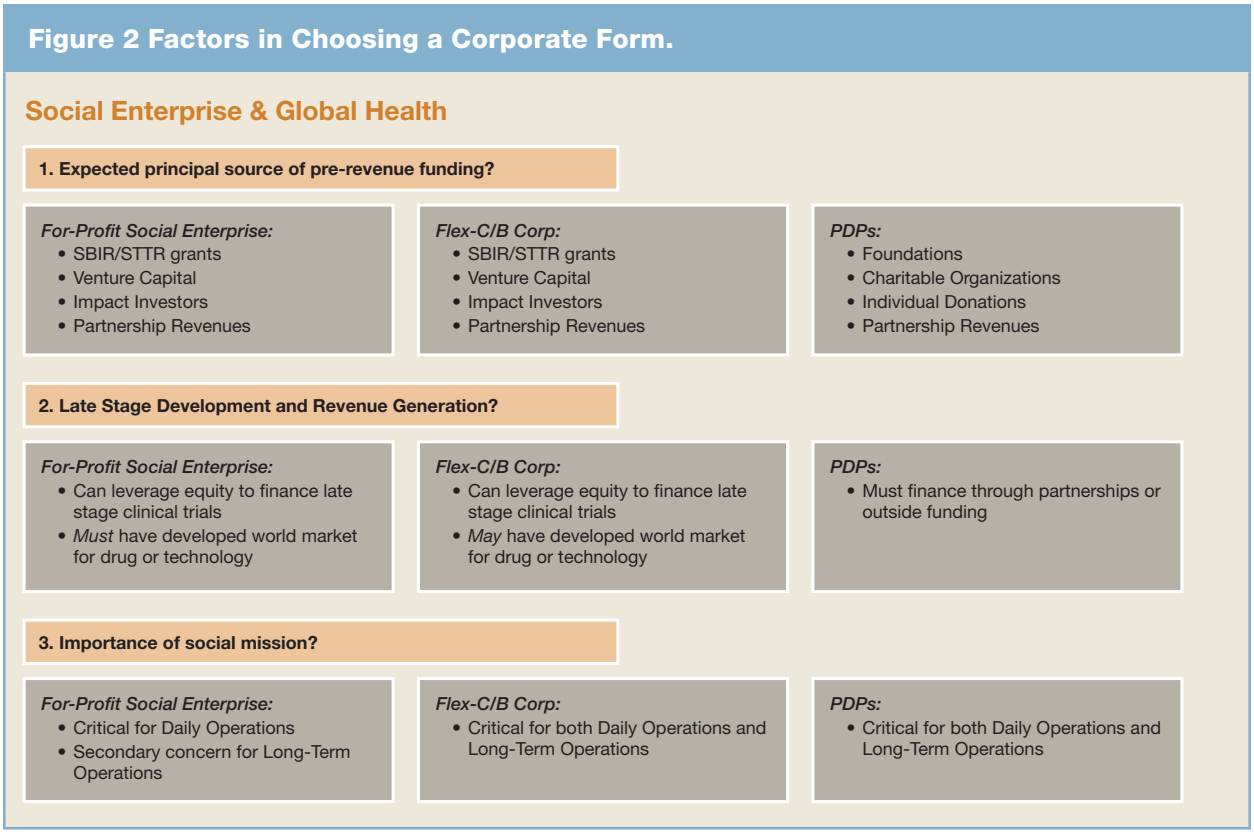
Perhaps the most significant advantage of the GHSE strategy is the availability of a new source of early- and late-stage capital typically not available to PDPs. From interviews with social entrepreneurs and stakeholders, it is apparent that immediate funding sources play a critical role in deciding between corporate forms. (See Figure 2.) Unlike PDPs, GHSEs have the ability to access a source of capital by leveraging equity. Many of the large funders, including the Gates Foundation, have already established funding priorities and have—at least in perception—a historical preference for established PDPs. As funding and commercial markets continue to change in global health, a third approach to the development of health technologies for LMI countries—aside from the PDP and purely for-profit corporate models—will become increasingly critical.

A second potential advantage of the GHSE approach is the apparent flexibility that many of the interviewees have indicated. In particular, GHSEs suggested that the ability to draw from a relatively broad pool of investors and the discretion to select quickly and execute on their priorities provided the freedom to take advantage of scientific and market opportunities in a much more timely manner than PDPs. At the same time, GHSEs were not subject to the priorities and goals of their funding foundations; by not depending on the relatively small number of foundations able to support advanced clinical research, GHSEs are not beholden to a foundation's priorities. Instead, GHSEs can draw from a larger pool of partners and investors, and retain the flexibility to pursue market and social benefit opportunities as they arise.

Regarding the formal adoption of a social mission, GHSEs face only minor legal concerns in embracing a global health objective in their day-to-day operations. Both GHSEs and PDPs cited their social mission as a critical component of their operations, as it helped attract talent, attract funders, and maintain focus on new medicines and technologies for diseases in LMI countries. Nonprofit organizations are, by nature and law, the best suited to fully incorporate a social mission. In contrast, GHSEs are less tailored for this purpose; however, they still enjoy significant discretion, and directors of for-profit social enterprises were by and large comfortable with their legal authority to pursue a globally focused portfolio in their day-to-day operations.

Outside what is legally permissible, companies that aim to balance the profit and social motives eventually face difficult decisions and are forced to make compromises. The practical realities, such as shareholder pressure to maximize profits and the limitations in communicating social impact to investors, make maintaining the initial social cause more challenging. Solutions were varied and included targeting socially minded investors, developing business models where pursuing the social benefit also resulted in a good return on investment, or simply avoiding using corporate core resources and instead obtaining funds for NTD R&D from partnerships and grants. Likewise, GHSEs have to be selective about which specific portfolios to pursue, requiring that they focus on

Figure 2 Factors in Choosing a Corporate Form.



diseases that would present sufficient dual-market opportunities.

Further, the ability to anchor the social mission in light of the need for profits throughout the life of the company, including during sale or merger, was a common concern of interviewees. Hybrid legal structures—such as the B Corp and Flex C corporate models—could help in this respect. These models were designed to assist directors and entrepreneurs to protect a particular social mission throughout the life of the organization. The B Corp model perhaps offers the stronger protection as it requires director pursuit of a stated social goal; however, that model also carries additional auditing and transparency requirements that the Flex C legal structure does not. Regardless, organizations looking to take advantage of an integrated social mission may consider this option looking forward.

The Flex C and B Corp structures can play an additional role in "signaling" a strong social commitment to help attract impact investors. The infancy of the impact investing movement poses a current obstacle to GHSEs, as such investors often lack the sophistication to understand the health challenges in LMI countries, and lack a centralized infrastructure allowing for the identification of and targeted investment in for-profit social enterprises. Strategies to improve the transparency and credibility of GHSEs could be valuable. A common vocabulary and metrics describing the potential health impact of R&D programs could better justify operational decisions and help maintain a social mission as a corporate priority. Some initiatives, such as the Impact Reporting and Investment Standards, are working to provide investors with a common reporting language for impact-related terms and metrics; however, these initiatives are still in development, have yet to be widely adopted, and are not tailored for R&D and early-stage product development. Without improvements in communication tools, investors looking to make socially responsible investments are likely to opt for a more traditional form of contribution—for example, through donations to PDPs or other not-for-profit organizations.

APPENDIX

Table A1. Interviews

INTERVIEWEE	POSITION	ORGANIZATION
Eric Easom	Program leader, neglected diseases	Anacor Pharmaceuticals
Marty Zug	Chief financial officer	Sequella Inc.
Geoff Dow	Chief executive officer (CEO), principal	60° Pharmaceuticals LLC
Dan Stinchcomb	CEO and co-founder	Inviragen Inc.
Lisa Conte	CEO and founder	Napo Pharmaceuticals / CAP Global
Mel Spigeleman	President and CEO	Global Alliance for TB Drug Development
Eugenio L. de Hostos	Director, research and preclinical development	OneWorld Health, an affiliate of PATH
Stewart Parker	CEO	Infectious Disease Research Institute (IDRI)
David Cook	Executive vice president and chief operating officer	International AIDS Vaccine Initiative (IAVI)
Erin Hogan	Vice president, philanthropic services	J.P. Morgan Private Bank
Elizabeth Bailey	Partner (former)	Commons Capital (Currently at Center for Affordable Medical Technology at MGH Center for Global Health)
Todd Johnson	Partner	Jones Day

Table A2. Identified Social Enterprises in Global Health

COMPANY	R&D/MARKET FOCUS	DESCRIPTION
Anacor Pharmaceuticals	Boron-based drug compounds for diseases including: • Onychomycosis • Psoriasis • Atopic dermatitis • Various animal diseases • Sleeping sickness • Visceral leishmaniasis • Chagas disease • Malaria • River blindness • Tuberculosis • Shigellosis	Anacor's objective is to discover, develop, and commercialize proprietary boron-based drug compounds with superior efficacy, safety, and convenience for the treatment of a variety of diseases. Anacor believes boron chemistry has utility in a broad range of diseases outside of their core therapeutic areas. To maximize the value of its boron chemistry platform and to provide nondilutive capital to support development in its core therapeutic areas, Anacor has entered into and will continue to seek partnerships early in development for compounds in noncore areas, such as parasitic, cancer, and ophthalmic indications and for applications in animal health.
Sequella Inc.	New compound therapeutics for: • *H. pylori* (peptic ulcers and related carcinomas) • *C. difficile* • Crohn's disease • Tuberculosis	Sequella is a clinical-stage anti-infectives company focused on commercializing improved treatments for serious infectious diseases. The company leverages its global influence, R&D platforms, and infectious disease expertise to proactively address emerging health threats. Through focused execution, clear commercialization pathways, and strategic partnerships, Sequella intends to commercialize a broad product portfolio designed to treat infectious disease threats with significant market opportunity.
Inviragen Inc.	Vaccines for: • Dengue fever • Hand, foot, and mouth disease • Japanese encephalitis • Chikungunya	Inviragen is focused on developing lifesaving vaccines to protect against emerging infectious diseases worldwide. The global marketplace for vaccines is undergoing fundamental change. While vaccines in the United States and Europe are garnering higher prices, future vaccine industry growth is predicted to be driven outside these traditional markets. The growing middle classes in developing world countries such as India, China, Mexico, and Brazil are creating new market opportunities in the private health care sector. Meanwhile, the continued emergence of devastating infectious diseases has accentuated the need for novel vaccines.
PaxVax Inc.	Vaccines for: • H5N1 bird flu • Cholera • Polio • Malaria • Tuberculosis • Shigella • Human papilloma virus (HPV)	PaxVax's mission is to develop and commercialize innovative and socially responsible vaccines against infectious diseases to improve global health. The company's primary goal is to transform the vaccine industry with revolutionary new platforms to meet the growing global demand for protection against infectious diseases. PaxVax specifically targets diseases that currently lack effective or affordable vaccines. PaxVax is a double-bottom-line company, focusing on both financial and social returns. It is developing vaccines for both people living in the developing world and travelers to the developing world. PaxVax strives to meet global needs responsibly, profitably, and ethically. The company's investors support the pursuit of both financial and social returns: to do well by doing good.

Table A2. Identified Social Enterprises in Global Health (continued)

COMPANY	R&D/MARKET FOCUS	DESCRIPTION
60° Pharmaceuticals LLC	Novel therapeutics for: • Malaria • Tuberculosis • Dengue vaccines	60° Pharmaceuticals LLC is a philanthropic-for-profit drug company. The company has a philanthropic intent in that its focus is on providing a social benefit to its future customers (dengue patients). However, the company is also committed to making a return for investors. These goals are aligned if expectations about financial returns are reasonable and transparent. Investors usually expect at least a threefold multiple from biotechnology companies targeting diseases in developed country markets. The expectations of 60° Pharmaceuticals LLC are more modest. The company will seek to recover commercialization costs and a return that is sustainable given the more modest size of the markets for drugs for neglected diseases. The company also envisions reinvesting a proportion of revenue in excess of commercialization costs in new neglected disease R&D. Potential investors should note that any contributions to 60° Pharmaceuticals LLC are not tax deductible since the company is a for-profit venture. Statements regarding corporate philosophy are provided only for informational purposes.
DesignMedix	Novel therapeutics for: • Drug-resistant malaria • MRSA and other drug-resistant bacterial strains	DesignMedix Inc. develops drugs to address the large medical need caused by the rapid rise in drug resistance in multiple diseases. DesignMedix focuses on globally important infectious diseases where additional drugs are urgently needed. DesignMedix's first objective is to provide a nontoxic cure for drug-resistant malaria that can be used for children and pregnant women. The second project is to develop a safe and potent drug with broad-spectrum activity against blood-stage malaria that can be co-formulated with other antimalarials in a synergistic combination to prevent and treat malaria, thus supporting worldwide eradication of the disease. In a second application of DesignMedix's proprietary approach, the company has produced drug candidates active against a broad spectrum of bacteria, with particular activity against MRSA.
Napo Pharmaceuticals Inc.	Novel drugs for: • Diarrhea-predominant irritable bowel syndrome • HIV/AIDS related diarrhea • Pediatric diarrhea • Insulin-resistant type II diabetes • CFTR inhibitors • Polycystic kidney disease	Napo Pharmaceuticals Inc. is a privately held pharmaceutical company based in San Francisco, California. Napo's lead drug candidate, crofelemer, is under development for gastrointestinal indications including chronic diarrhea in persons living with HIV/AIDS. CAP Global LLC, a wholly owned subsidiary of Napo Pharmaceuticals, is a certified B Corp. CAP Global's mission is to accelerate the development of crofelemer for pediatric populations in the treatment of multiple diarrheal diseases (such as cholera) and to provide crofelemer cost-effectively to relief organizations.

Table A2. Identified Social Enterprises in Global Health (continued)

COMPANY	R&D/MARKET FOCUS	DESCRIPTION
GenVec Inc.	Therapeutics for: • Hearing and balance disorders Vaccine programs for: • HIV (global strains) • respiratory syncytial virus (RSV) • herpes simplex virus (HSV) • Influenza • Dengue fever • Malaria • Animal health/foot and mouth disease	GenVec Inc. is a publicly traded biopharmaceutical company using differentiated, proprietary technologies to create superior therapeutics and vaccines. A key component of its strategy is to develop and commercialize its product candidates through collaborations. GenVec is working with leading companies and organizations such as Novartis, Merial, and the U.S. government to support a portfolio of product programs that address the prevention and treatment of a number of significant human and animal health concerns.
Altravax	Vaccine programs for: • Dengue • Hepatitis B virus (HBV) • HIV-1 • Influenza (seasonal and pandemic)	Altravax is a privately held company focused on the discovery and development of new vaccines to fight infectious diseases. Altravax's mission is to improve human health, individually and globally, by preventing and treating diseases with vaccines. Altravax motivates and empowers its employees to focus on innovative ways to accelerate the development of vaccines that are safe and efficacious. Altravax's proprietary technologies offer unique opportunities to create novel vaccines or improve currently available alternatives to fill unmet medical needs. The company has a robust pipeline of candidates at various stages of development. Altravax also seeks to partner with other companies and organizations to develop vaccines that meet defined health care and market criteria.
Genocea BioSciences	Developing T cell antigen discovery for the development of vaccines targeting: • Herpes simplex virus (HSV)–2 • Pneumococcus • Chlamydia • Malaria	Genocea Biosciences is a venture-backed company focusing on developing the next generation of T cell vaccines. Infectious diseases remain an urgent and persistent global health threat, in both the developed and the developing world. Vaccines are recognized as the most cost-effective and successful approach to managing such diseases, yet traditional methods for discovering and developing vaccines are too slow and insufficiently comprehensive to meaningfully address the complexity of many pathogens. Genocea is working to create vaccines that stimulate the T cell arm of the immune system, which is increasingly recognized as critical to generating protective and long-term immunity against a wide array of diseases.

Table A3. Comparison of Corporate Structures

	For-Profit	GHSE	Flex. Purpose Corp	Benefit Corporation	Nonprofit / PDP
Antecedent Conditions	Focus is on market opportunity.	Focus is on market opportunities that promote a social benefit. Social mission informally adopted in business by-laws.	Focus is on market opportunities that promote a special benefit. Special purpose legally adopted and specified in business charter.	Focus is on market opportunities that promote a social benefit. Specific public benefit legally adopted by company and specified in business charter.	Focus is on social benefit. Social benefit is legally adopted by company; a nonprofit organization is required to specify the manner in which its work benefits the local or global community.
Daily operations	Broad discretion given—profits and social mission *may* be considered.	Broad discretion given—profits and social mission *may* be considered.	Broad discretion given—profits and social mission *may* be considered.	Profits and social mission *must* be considered.	Social mission *must* be considered.
Acquisition and Mergers	Profits are sole consideration; however, constituency states allow some consideration of nonfinancial factors.	Profits are sole consideration; however, constituency states allow some consideration of nonfinancial factors.	Profits must be considered; special purpose *may* be considered.	Profits, special purpose, and general purpose *must* be considered.	Mission must be considered.
Principal Pre-Revenue Financing	Equity / venture investment Government/ nondilutive Funding (SBIR/ STTR grants) Bank loans	Equity/venture investment Government/ nondilutive Funding (SBIR/ STTR grants) Bank loans Socially responsive/ impact investors	Equity / venture investment Government/ nondilutive Funding (SBIR/ STTR grants) Bank loans Socially responsive/ impact investors	Equity/venture investment Government/ nondilutive Funding (SBIR/ STTR grants) Bank loans Socially responsive/ impact investors	Charitable donations Foundation grants Government grants

Table A3. Comparison of Corporate Structures (continued)

	For-Profit	GHSE	Flex. Purpose Corp	Benefit Corporation	Nonprofit / PDP
Revenue Generation	Business model must focus on revenue generation. Profits may be distributed to shareholders or reinvested in company.	Business model balances revenue generation and social mission. Profits may be distributed to shareholders or reinvested in company.	Business model balances revenue generation and social mission. Profits may be distributed to shareholders, reinvested in company, or dedicated to advancing social mission.	Business model balances revenue generation and social mission. Profits may be distributed to shareholders, reinvested in company, or dedicated to advancing social mission.	Profit generation not possible. All revenues must be reinvested in mission.
Tax Exemption	For-profit businesses must pay income taxes on their net income and are required to file returns every year. For-profits are generally protected from making their financial information public. Donations made to a for-profit organization are not tax deductible for the donor.	For-profit businesses must pay income taxes on their net income and are required to file returns every year. For-profits are generally protected from making their financial information public. Donations made to a for-profit organization are not tax deductible for the donor.	For-profit businesses must pay income taxes on their net income and are required to file returns every year. For-profits are generally protected from making their financial information public. Donations made to a for-profit organization are not tax deductible for the donor.	For-profit businesses must pay income taxes on their net income and are required to file returns every year. For-profits are generally protected from making their financial information public. Donations made to a for-profit organization are not tax deductible for the donor.	Designation as a 501(c)(3) may provide a not-for-profit organization with an exemption from paying sales and use tax and an exemption from paying property taxes on real estate owned by the not-for-profit organization. Donations made to a not-for-profit organization with a 501(c)(3) designation are tax deductible for the donor.

Table A3. Comparison of Corporate Structures (continued)

	For-Profit	GHSE	Flex. Purpose Corp	Benefit Corporation	Nonprofit / PDP
Asset Ownership	Assets belong to its owners and shareholders. If the business goes defunct, its assets are usually distributed to the company's shareholders according to each individual's ownership share.	Assets belong to its owners and shareholders. If the business goes defunct, its assets are usually distributed to the company's shareholders according to each individual's ownership share.	Assets belong to its owners and shareholders. If the business goes defunct, its assets are usually distributed to the company's shareholders according to each individual's ownership share.	Assets belong to its owners and shareholders. If the business goes defunct, its assets are usually distributed to the company's shareholders according to each individual's ownership share.	Assets cannot be legally owned by an individual or group of individuals. Its assets belong to the organization itself. If the nonprofit ceases to exist, its assets must be distributed to another nonprofit entity.
Ability to Attract Talent	Profits, equity, and benefits are principal draws.	Social mission, profits, equity, and benefits are principal draws.	Social mission, profits, equity, and benefits are principal draws.	Social mission, profits, equity, and benefits are principal draws.	Social mission is principal draw.

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