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Foreword - Global Access to Health: Legal, Business, and Policy Obstacles

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INTRODUCTION

Thomas Jefferson — scientist, philosopher, and United States president — firmly believed in the power of innovation. A bit of a tinkerer himself, he devoured new applications while serving as America's first patent examiner and often engaged in enthusiastic correspondence with hopeful inventors. He was a pioneer in the development of American patent law and shaped its attention to the utility, novelty, and non-obviousness of inventions. But Jefferson also believed that inventions were only meaningful if they were used to benefit the quality of life in society as a whole.[1] In a letter to Robert Morris written in 1794, he told the inventor of waterproof cloth that his valuable discovery "will be truly great if the process be so cheap as it will admit to be used for the laboring part of mankind. The rich have so many resources already for taking care of themselves, that an advantage the more, if confined to them, would not excite our interest; but if it can be introduced commonly for laborers, then it becomes valuable indeed."[2]

Jefferson's philosophy offers a glimpse of the solution to our global struggle to address the diseases of the poor. Despite improved health and reduced mortality globally in the last half-century,[3] too many people are still

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[1] Jeffrey H. Matsura, *Thomas Jefferson and the Evolution of a Populist Vision of Intellectual Property Rights and Democratic Values*, www.archipelago.org/vol10-34/matsuura.htm.

[2] Thomas Jefferson, The Papers of Thomas Jefferson 1 January 1794 to 29 February 1796 (Princeton University Press 2000).

[3] World Health Organization, *The World Health Report 1998*, Chapter 8, www.who.int/entity/whr/1998/en/whr98_ch8.pdf.

not being treated for these diseases.[4] Millions of people in developing countries – most of them children – die every year from diseases that are preventable and treatable. A measles vaccine costs 15 cents, yet nearly 675 infants die of measles every day.[5] Some 26 million children per year under the age of five are not immunized with simple, inexpensive vaccines most of us take for granted.[6] The number of women at risk of death during childbirth in low-income countries compared with wealthy ones is 500 to one.[7] Tuberculosis, HIV/AIDS, diarrheal diseases and childhood pneumonia, complications of pregnancy and neonatal deaths — each partially preventable with vaccines or treatable or manageable with therapeutics available in rich nations — cause 29% of all deaths in low- and middle-income countries. Every year, HIV/AIDS, malaria, and TB together kill six million people, mostly in sub-Saharan Africa and Asia.[8] This is the equivalent of everyone in Los Angeles and Houston[9] dying from these diseases each and every year.

These tragedies persist, despite the many billions of dollars[10] spent annually to develop new products to enhance and extend human life. New health solutions – drugs, vaccines, diagnostics, monitoring tools, and related platforms – are clearly needed. However, due in part to an historical lack of market incentives for the pharmaceutical industry, only 21 of the 1,556 new drugs put on the market in the three decades prior to 2004 specifically targeted neglected diseases, meaning those that disproportionately affect developing countries.[11] Even when these interventions are appropriate, they quickly run into the many legal, policy and infrastructure challenges that make delivery in resource-poor countries enormously difficult.

UNRIVALLED OPPORTUNITY

Nevertheless, there is reason for optimism. We live in a time of unprecedented opportunity when it comes to tackling neglected diseases. This reflects a broader movement in global health that has engaged academia (including the creation of numerous global health institutes or divisions), government (including the creation of the President's Emergency Plan for

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[4] Dean T. Jamison, et al., *Accomplishments, Challenges, and Priorities*, PRIORITIES IN HEALTH, 1, 1-22 (Oxford University Press 2006).

[5] World Health Organization, *Fact Sheet no. 286 (*revised January 2007), www.who.int/mediacentre/factsheets/fs286/en/index.html.

[6] World Health Organization, *Global Immunization Data* (January 2008), www.who.int/immunization/newsroom/Global_Immunization_Data.pdf.

[7] Dean T. Jamison, et al., *The Way Forward: A Blueprint for Action*, PRIORITIES IN HEALTH 179-82 (Oxford University Press 2006).

[8] The Global Fund, www.theglobalfund.org.

[9] U.S. Census Bureau, 2006 estimates, www.census.gov.

[10] Planning Report 07-1, *Economic Analysis of the Technology Infrastructure Needs of the U.S. Biopharmaceutical Industry*, RTI International, Nov. 2007 (prepared for National Institute of Standards & Technology) (biopharma firms spend some $21 billion a year on research and development).

[11] *Global Framework on Essential Health R&D*, 367 THE LANCET 1560 (2006). Although there are many ways of defining "Developing Countries," the World Bank's categorization of "low-income economies" or "lower middle-income economies" are often referenced. Depending on the context and the parties offering a definition, such term might also include certain markets or countries within the categorization of "upper middle-income economies."

AIDS Relief and the President's Malaria Initiative), as well as the developing countries themselves. The net result of this surge in resources and political will can be witnessed in the successes of the Global Fund to Fight AIDS, Tuberculosis and Malaria, and the GAVI Alliance. Mechanisms are being created to incentivize product development and ensure that the right ones will be purchased and used, and lives will be saved.

The science is moving ahead as well. A growing number of universities, for-profit companies and not-for-profit research and development (R&D) initiatives house life-sciences projects that are focused on developing global health solutions. They include a broad array of health technologies, products, approaches and strategies for the prevention, diagnosis or treatment of neglected diseases. For example, in comparison to a decade ago, when the pipelines for malaria and TB drugs were virtually non-existent, today there are more than 20 malaria drug candidates and six TB drug candidates under development.[12]

At the same time, there are still far too many legal and policy hurdles that stand in the way of delivering the emerging global health solutions. It is not enough to design these interventions to be effective in the communities where they are needed. They must also be tested in these communities, and approved or accepted by the appropriate regulatory or international bodies. Companies must feel secure that their products will not be misused, counterfeited or otherwise misappropriated. The products must then be priced reasonably, produced in sufficient quantities, and distributed efficiently so they will be accepted and used by the governments and people who need them.

ARTICLES WITHIN THIS SYMPOSIUM

The articles in this symposium issue of the American Journal of Law & Medicine concentrate on an important subset of these legal and policy hurdles to achieving global access. One author describes the need to efficiently forecast product demand within such countries, while the remaining authors explore a range of topics pertaining to intellectual property (IP) rights, including analysis of complex issues relating to the management and licensing of IP, proposals for the use or modification of patent systems, and discussion of international IP organizations, collaborations and agreements.

Ruth Levine focuses on the importance of improving demand forecasting for the purchase of global health solutions in order to reduce the risks for suppliers. This will lower costs and decrease supply shortages, she argues, and will help persuade the private equity and biopharmaceutical sectors that R&D for such products is a viable investment. Levine describes how establishing dependable demand forecasts will allow donors, health ministers, and other purchasers to more efficiently spend their limited funds and plan their supply chain logistics. According to Levine, weak forecasting exasperates already misaligned incentives that impede access to essential medicines. Better demand forecasting will streamline global health markets

[12] Medicines for Malaria Venture, www.mmv.org; TB Alliance, www.tballiance.org.

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and enhance the cooperative relationships among stakeholders, including funders, suppliers, intermediaries and local health systems. Levine recommends a set of actions that she believes will facilitate a more appropriate allocation of risk and alignment of incentives.

Most of the authors chose to examine the many IP dilemmas affecting global access to health solutions. Brook Baker takes a critical look at the manner in which the United States appears to use the U.S. patent system to defend the interests of the pharmaceutical industry, even when establishing policies aimed at addressing global health concerns. Baker points to the fact that, following the conclusion of multilateral negotiations to establish a uniform baseline of international IP rights under the TRIPs Agreement, Washington nevertheless pursued bilateral trade negotiations to increase IP protections. Baker also points to the U.S. government's allowance of a five-year period of data exclusivity for newly registered medicines, and the practice of linking the rights of drug registration to patent status, both of which hinder the ability of generic competitors to quickly enter the market with less expensive products. He describes how data exclusivity is distinct from IP regimes and could not be overcome by compulsory licenses, meaning that a fractured regulatory system is also contributing to the global health challenge. Baker believes, however, that momentum is building internationally and within the U.S. Congress to weaken a trenchant defense of drug company prerogatives that has had a deeply negative impact on access to affordable generic medicines.

Aaron Kesselheim also evaluates U.S. drug policies, particularly with regard to IP laws and generic drugs, and argues that such policies could be modified to significantly improve access to global health solutions in low- and middle-income countries. Pharmaceutical markets are increasingly interdependent, with policy decisions in wealthier nations more directly affecting access to essential medicines in developing countries. The author describes how the growth of pharmaceutical developers and manufacturers within developing countries (such as India, Brazil and South Africa) has relaxed the dichotomy between developed and developing countries because of their unprecedented penetration into wealthy pharmaceutical markets. Kesselheim illustrates how stronger U.S. policy support for the purchase of generic drugs would help build greater pharmaceutical manufacturing capacity within developing countries. This would both create local employment opportunities and improve the quality and quantity of essential drugs available in those countries. These policy changes, according to the author, should be coupled with a critical review of IP policies so as to ensure that IP protections are not misused to prevent the necessary rights from entering the public domain within a reasonable time.

Peter Drahos moves away from a U.S.-focused critique. Instead he evaluates the role of patent offices more generally in maintaining the structure of pharmaceutical markets, and describes the impact of patent rules on the structure and evolution of such markets. Drahos outlines how the Trilaterals (the European Patent Office, Japanese Patent Office, and U.S. Patent and Trademark Office), through their technical assistance programs, have influenced the design and operation of patent offices within developing countries, to the point of integrating them into a global system of patent

administration. Such a system, Drahos explains, facilitates efficiency and maximizes the outputs of patents at minimum cost, which he argues results in poor-quality patents that then complicate access to medicines for people living in developing countries. Drahos suggests that each developing country lessen its reliance on the Trilateral technical assistance and instead design its own system of patent administration, including standards of patentability, based on its own needs and with the assistance of local scientific expertise. In so doing, the offices would be re-integrated into a national regulatory strategy, resulting in much better levels of access to medicines.

Peter Yu explores how collaborations among the BRICS countries (Brazil, Russia, India, China and South Africa), as well as among less-developed countries, can promote access to essential medicines in the developing world. Yu begins his article by introducing the BRICS countries and their respective approaches to international intellectual property protection. He describes how these five countries could wield sufficient power to halt a push by the United States and Europe to ratchet up global intellectual property standards, but also evaluates whether these five countries could, in light of their different historical backgrounds, build a sustained coalition to accomplish such a task. Yu advances the premise that cooperation and solidarity among these countries, as well as lesser developed nations, are critical to their ability to advance their interests in the WTO and the international intellectual property regime, and offers proposals for promoting access to essential medicines in the less developed world.

Gail Evans considers the strategic use of patent licensing agreements and other mechanisms to manage intellectual property. Responding to a call by the Kenyan and Brazilian governments for public health tools that could build research capacity of developing countries, Evans recommends the strategic use of patent licensing arrangements to transfer knowledge between public research organizations within developed and developing countries. Evans poses that compulsory licensing and parallel importing, while necessary to address national emergencies of epidemic disease, are not the means to build a sustainable public health program that will ensure access to necessary medicines. She examines the various approaches and opportunities in structuring voluntary license agreements within the framework of international patent and competition laws. Creative, tailored agreements would support a sustained cycle of research for drug development, and appropriate competition laws would reinforce licensing strategies designed to promote the production of medicines. This approach, Evans argues, would help developing countries strike a balance between the pharmaceutical industry's need to seek patent protection and the need of public research organizations to broadly disseminate new scientific knowledge. Evans also considers collaborative mechanisms, including patent pools, as alternative means of managing IP to support multi-institutional research networks.

The articles by Graham Dutfield, Jack Lerner and Kevin Outterson consider aspects of international IP agreements, organizations, and multi-lateral negotiations, respectively. Dutfield's article discusses the scale of global health problems and whether IP rights have exacerbated them. He assesses whether patent systems have successfully balanced the interests of inventors, users of inventions and society as a whole, particularly now that

compulsory license provisions are included in national laws and international agreements. He explores more specifically whether patents contribute to an existing lack of access to life-saving medicines by the poor in developing countries, and evaluates data exclusivity protections by local governments and certain free-trade agreements, which many claim will further stifle such access. Dutfield then considers WTO members' compulsory license rights, as permitted under the TRIPs agreement, and whether Paragraph 6 of the Doha Declaration, coupled with the 2005 Amendment, has furthered its intended aim of facilitating access to patented medicines by way of compulsory licenses for those countries that lack manufacturing capacity, and whether such mechanisms are workable in practice.

Lerner points out that the international intellectual property system has a strong effect on global health in developing countries, and in his article explores the various initiatives involving intellectual property that are being developed and negotiated within major intergovernmental organizations. These initiatives include the World Intellectual Property Organization's (WIPO) Development Agenda and the World Health Organization's (WHO) draft Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property under consideration by the WHO Intergovernmental Working Group on Public Health, Innovation and Intellectual Property (commonly referred to as the IGWG). Lerner describes these initiatives, and takes a close look at how they can expect to interact, overlap and/or conflict, as well as how they might facilitate collaboration among these intergovernmental organizations.

Outterson explains the work of WHO's IGWG in its structuring of a global strategy and Plan of Action to address diseases that "disproportionately affect the developing world." He evaluates the plight of the developing countries from the perspective of two kinds of markets: their markets for medicine, often bolstered by government subsidies, and their markets for innovation, meaning the ability of the local institutions and companies to conduct research and development, often through governmental funding and tax credits. A primary aim of the article is to assess the meaning of "disproportionately" in the context of the IGWG negotiations. Outterson explains that this is a term often used as a synonym for Type II diseases, which occur in high-income countries but are predominately incident in developing countries, and Type III diseases, which are overwhelmingly or exclusively incident in developing countries. The use of such a term, according to the author, is unwarranted and has the detrimental effect of supporting the position that the TRIPs flexibilities, such as the compulsory licensing mechanisms, are limited to a specific set of diseases. This position is taken most typically by the pharmaceutical industry and developed country governments. The author concludes that the use of the word "disproportionate" should not support an agenda that limits the utilization of TRIPs flexibilities. Instead, it should be an important reminder of a weakness in the developing country markets, both in terms of access to medicines and the ability to develop new health innovations.

Gerald Keusch brings the unique perspective of a physician scientist who has the personal experience of good intentions gone awry. He developed new technology at his university, only to see it licensed to a company and

successfully translated into a product that is not being made accessible to the poor within developing countries. Keusch has come to recognize that to ensure that the fruits of their labor are made available for a broader humanitarian purpose, scientists must take a more active role in how technologies are managed once they leave their laboratories. Keusch is critical of the adage that the career path of physician-scientists is defined as "publish or perish," and argues that all scientists should embrace an understanding of all aspects of knowledge — including its generation, dissemination, translation, application, implementation and evaluation. Keusch describes the dangers of rejecting this new scientific paradigm, reflects on his own experience, and strongly supports the growing partnership between researchers and university technology-transfer officers as a necessary bridge between scientific discovery and an accessible product.

BREADTH OF LEGAL, POLICY AND OTHER ISSUES

Most of the articles described above discuss the impact of IP regimes on global health, with many authors exploring novel methods to appropriately secure, manage and allocate IP rights in a way that best achieves global access to improve the lives of the poor within developing countries. This symposium also brings together a broad spectrum of scholars and key stakeholders from the legal, medical, and economic fields to address what is today one of the most pressing issues confronting the world. Although the legal issues extend beyond technology access and IP alone, addressing a problem of this magnitude cannot be done in one single symposium. This publication addresses one important aspect of a multifaceted problem, raises awareness about various aspects of this critical challenge, and promotes the importance of global health consciousness across professions.

The scope of the work needed to address the disparities within global health illustrates the complexity of the legal and policy hurdles associated with achieving global access on the ground. The legal issues include the appropriate structuring of complex international collaborations, preparing research and supply agreements, and managing antitrust concerns. Other potential roadblocks involve international trade and taxes, including the risk of parallel trade. We must seek better ways of capturing counterfeit and mislabeled drugs, ensuring the safety of participants in international clinical trials, working with international activists and civil societies, and complying with regulatory frameworks.

These challenges are why we at the Bill & Melinda Gates Foundation also look beyond intellectual property issues to address access to global health. Intellectual property is neither an evil weapon to abuse the downtrodden, nor the cornerstone of all economic development. It is simply a tool (albeit a commonly used and powerful tool) that may at times be used, and at others avoided, to help achieve our broader global access objectives: dissemination of knowledge and access to health interventions.

The Collaboration for AIDS Vaccine Discovery (CAVD) is a promising example of a novel approach to the sharing of data and research materials. The CAVD is an international network of thirteen vaccine discovery consortia and five central service facilities, involving more than 100 universities, non-

profit research institutions, governments, multilaterals and private companies. The Gates Foundation helped launch the collaboration because the current approach of small teams of investigators conducting independent vaccine discovery projects was failing to develop a successful HIV vaccine. Established in 2006 with almost $300 million of philanthropic and government funding, the CAVD was conceived in the spirit of working in an open, collaborative fashion, sharing data and reagents, with the appropriate balance between competition and cooperation. Thus, participating organizations have signed on to a set of Data & Materials Sharing Principles, which outline the type, scope and timing for sharing information and research materials within the CAVD and the broader scientific community.

The CAVD, given that the participants are tackling the very upstream search for an HIV vaccine, focuses primarily on accelerating discovery and development. However, the ultimate access to a vaccine, diagnostic tool or drug depends on many factors, including enabling technologies, established regulatory environments, sufficient supply of the product, and reasonable balanced pricing that encourages both sustainable production and widespread uptake. Access is also a function of economic and public relations incentives for the developer and supplier, dependable regulatory and distribution systems, and the availability of adequate local health systems.

To achieve global access, a multi-stakeholder approach that acknowledges and capitalizes on synergies is essential. The stakeholders — public and private, for-profit and philanthropic, national and multinational — must cooperate to identify opportunities and useful technologies, build partnerships, negotiate responsibilities for appropriate research projects, and work to foster an environment that facilitates access. In a typical scenario, academia provides the initial innovation and research; the private sector contributes tools, development, processes, manufacturing capacity, and distribution capabilities; non-profits bring in the humanitarian mission along with funding, and tend to manage and facilitate the collaboration. Finally, the public sector provides direction, policy, implementation mechanisms, and funding.

A relatively new, but now readily accepted and appreciated, mechanism used in managing R&D for global health is the product development partnership (also referred to as the public-private partnership). These alliances bring together key players from both the public and private sectors, from donors and government to private industry and academia, to manage a portfolio of development projects. One example is the Aeras Global TB Vaccine Foundation. Aeras was founded in 1997 to help develop new concepts and tools to control the global tuberculosis epidemic, focusing on the development of new vaccines against TB and ensuring their availability to all who need them.[13] Its goal is to develop, test, characterize, license, manufacture and distribute at least one new TB vaccine within the next decade. Aeras, a non-profit organization, will develop candidate vaccines in its own laboratories as well as actively pursue and help fund joint development activities with leading biotechnology and pharmaceutical companies such as Crucell and GlaxoSmithKline. Aeras and its partner

[13] The Aeras Global TB Vaccine Foundation, www.aeras.org.

companies strike a balance between philanthropic goals and commercial interests by working to develop a TB vaccine that is both accessible by the poor and is commercially sustainable.

Another promising approach to access is the creation of innovative new financing mechanisms that encourage R&D and the introduction of new tools for global health. The GAVI Alliance was established to help create a viable market for vaccines that were not being introduced in a timely way into developing country immunization systems. GAVI provides funding to procure vaccines in response to country requests. As a complement to their funding, GAVI supported the establishment of organizations — referred to as Accelerated Development and Introduction Plans (ADIPs) — that were tasked to work with companies and countries to create better information about which products were needed where. ADIPs were piloted with rotavirus and pneumococal vaccines. The International Finance Facility for Immunisation Company (IFFIm) has also significantly increased the pool of resources available to purchase existing and future childhood vaccines for the world's 70 poorest countries. As an additional mechanism to "pull" forward new vaccines targeted specifically at developing countries, a number of donors have supported the idea of Advance Market Commitments (AMCs) to guarantee future markets for vaccines against specific diseases. Unlike the GAVI model, which does not provide companies with a guarantee that money will be available if certain vaccines are developed, the AMC designates funds for the purchase of specific vaccines in an attempt to motivate companies to plan for (and ultimately supply to) developing countries.[14]

All of these approaches recognize the importance of involving the private sector in global health, and are designed to work with and complement the biopharmaceutical industry's ability to discover, develop and deliver vaccines, drugs and diagnostics. This is in large part because developing a new global health product is not very different from developing any other health product. It requires a motive, basic research, a market, attention to legal and ethical requirements, clinical trials, manufacturing and distribution capacity, and an environment conducive to introduction. The fact that a profit component is included will offer an incentive to companies. All sectors must be creative in "finding approaches that meet the needs of the poor in ways that generate profits for business" in order to find sustainable solutions – a concept referred to by Bill Gates in a speech at the 2008 World Economic Forum in Davos, Switzerland, as "creative capitalism."

All this business savvy, brought to bear by both the non-profit organizations as well as private industry, must take aim at coupling commercial interests with a humanitarian focus. Creativity and cooperation among stakeholders within the many sectors of global health are the only ways to ensure that the appropriate products will be inexpensive to produce, easy to distribute, and simple to use within a wide range of political, social, legal, health and business systems around the world.

The authors of the papers presented in this symposium issue have embraced one of the greatest challenges of our time: how to overcome the

[14] *See* The GAVI Alliance, www.gavialliance.org, for GAVI, IFFm, and ADIPs; *see* The Center for Global Development, *Making Markets for Vaccines*, www.cgdev.org/section/initiatives/_active/vaccinedevelopment, for AMCs.

legal and policy obstacles standing in the way of access to health care for all people, no matter where they live. We share their belief that this goal is achievable. We also share Jefferson's belief that a fundamental purpose of innovation is to benefit humankind. In his time, nearly 200 years ago, the United States relied on Europe for new ideas. "In an infant country like ours we must depend for improvement on science of other countries, longer established, possessing better means, and more advanced than we are," he wrote in 1821. "To prohibit us from the benefit of a foreign light, is to consign us to darkness."[15] When it comes to matters of global health, it is time for all of us to ensure access to health solutions so that the people most in need will not be consigned to darkness.

[15] Thomas Jefferson: A Chronology of His Thoughts (Jerry Holmes, ed. 2002).

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