GEORGETOWN UNIVERSITY AND GLOBAL HEALTH LICENSING

LEADING THE WAY IN IMPROVING ACCESS TO ESSENTIAL MEDICINES IN DEVELOPING COUNTRIES

A Revised Proposal

Sponsored by:

The Georgetown Essential Medicines Consortium

Universities Allied for Essential Medicines*

January 2008

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I. EXECUTIVE SUMMARY

The problem

Every day, 6,000 people die of AIDS in Africa while only 49 die in all of North America.[1] Vaccine-preventable diseases, virtually extinct in developed countries, kill hundreds of thousands of people annually in Africa and South Asia.[2] These are just a few examples of how injustice and ill health go hand-in-hand when it comes to the burden of disease in poor countries. According to the World Health Organization, one-third of the world's population lacks access to medicines necessary for life.[3]

University research plays a key role in developing the world's most important medicines and vaccines, and universities can help in the struggle to bring treatment to those suffering in the developing world. Georgetown research has contributed to numerous health-related innovations, including the development of the new HPV vaccine. At the same time, Georgetown has an avowed commitment to advancing the public good, to social justice, and, in the words of our current President, "to creating men and women for others" who will tackle the global health crises of our day. It is in keeping with the mission of Georgetown as a Jesuit institution to help stem the tide of suffering and death among the world's most vulnerable by conducting socially responsible research and management of intellectual property.

Our unique solution

We propose that Georgetown become the first university to comprehensively institute a technology transfer program that facilitates access to essential medicines in low- and middle-income countries. We believe that Georgetown's commitment to the aforementioned principles supports a change in the university's licensing policy, to ensure that Georgetown innovations are made available in resource-limited settings. We propose a broad-based solution with three key features:

1. **Global Health Licensing Program.** A standing committee of interested Georgetown community members would assess every license for developing country potential and apply appropriate licensing language, from a toolbox of options created specifically for Georgetown. The Global Health Licensing Program reflects a more thoughtful, innovation-specific approach to humanitarian licensing – rather than a one-size fits all approach. As such it is a compromise recognizing that not all Georgetown licenses would need to contain access-oriented licensing language.

2. **Neglected diseases alumni research fund**. Georgetown 's research priorities reflect the urgent need for new drugs and vaccines for neglected diseases. This goal could be met with an Alumni Neglected Disease Research Fund to build our institutional expertise and engage our talented alumni.

3. **University pressure to facilitate affordable access to the HPV vaccine**. Lastly, Georgetown must use its position as an ethical and research leader to agitate for better global pricing and access to the current and future HPV vaccines, which have benefited from the contributions of our researchers.

Why Georgetown should seize this opportunity

These policy changes have the potential for significant impact on patient populations in LMI countries. If implemented carefully and thoughtfully, the changes suggested here need not interfere with Georgetown's ability to work with private entities, either as funding sources or developers. This proposal comes at a time when Georgetown is increasing its presence on the world stage through involvement in global health concerns. This proposal offers Georgetown an opportunity to advance its role as the leading international university committed to the global public good.

II. INTRODUCTION TO THE PROBLEM

Approximately 10 million people die needlessly each year because they do not have access to existing essential medicines and vaccines.[4] This access gap stems from several factors, including unreliable healthcare delivery systems, lack of political will for public financing of healthcare, and high prices for medicines.[5] These factors are mutually reinforcing, particularly in poor countries. While third-party medical insurance often insulates patients in wealthy countries from the high cost of medicines, patients in poor countries are often not as fortunate. On average, these patients pay more than 70% of medicine costs themselves.[6]

High prices result in large part from the temporary monopolies granted to pharmaceutical companies through patent and regulatory systems.[7] In fact, the introduction of generic competition may be the most important factor in lowering prices in a given country.[8] Importantly, there is little reason to expect that increased generic competition in poor countries would significantly impact the revenues of pharmaceutical companies and thereby impede future innovation. The branded pharmaceutical industry in the United States derives only 5%-7% of its profits from all low- and middle-income (LMI) countries.[9] [See Appendix II for detailed economic analysis]

Some authors have argued that pharmaceutical companies are unlikely to patent in poor countries and thus intellectual property protection has little to do with the access gap.[10] Yet there is widespread evidence that pharmaceutical companies do seek patents in poor countries.[11] For instance, many of the most important antiretrovirals for HIV treatment are widely patented in Africa.[12] Moreover, the presence of patents in one developing country may affect access to generics in countries where no patents exist, as developing countries differ substantially in terms of their capacity to produce medicines.

International trade policy has further exacerbated the access gap. India passed legislation in March 2007 to comply with the World Trade Organization's Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement, jeopardizing the world's most critical supply of generic medicines. The United States continues to exert additional pressure on developing countries by imposing so-called "TRIPS-plus" standards on these countries in bilateral trade agreements.[13] These standards extend monopoly rights and make it more difficult for governments to promote generic competition or import generic drugs from other countries.

An access gap also exists with respect to medical and preventive technologies, such that people in developing countries are at higher risk of certain diseases, such as cervical cancer, that can be prevented by regular screenings.[14] Women in developing countries are the ones primarily affected by cervical cancer, and in many such countries, cervical cancer is the number one cause of cancer deaths in women.[15] As such, the HPV vaccine developed using Georgetown research is needed greatly in developing country contexts, and Georgetown could prevent a significant number of deaths among the world's most vulnerable by taking action and leveraging its position as a key research contributor to make the vaccine more readily available in poor countries.

In addition to the inequitable distribution of existing pharmaceutical and preventive technologies, disparities in funding for research and development further limit treatment availability for developing-world indications. Countless people suffer from neglected tropical diseases, but drug companies lack the financial incentive to develop medicines for them because the afflicted populations are unlikely to be able to afford such drugs. Indeed, it is estimated that only 10% of the world's health research funds are devoted to the diseases that are the predominant health burden for 90% of the world's population.[16] As a result of this research gap, safe and effective treatment options are extremely limited.[17]

III. The Role of Universities: The Case For A New Approach to Licensing

Research universities have a unique opportunity to address both the access and research gaps via their research policies and licensing agreements. Multiple studies have confirmed that university research is vital to the development of new medicines.[18] Universities thus increasingly own significant intellectual property rights that are licensed to pharmaceutical and biotech companies and developed into important life-saving health innovations. A recent review indicated that the ownership position of universities as a whole in pharmaceutical technologies is both substantial and increasing.[19] Both the number of patents and, concomitantly, the number of license agreements executed by universities have approximately doubled between 1993 and 2003.[20] Universities can use this leverage in licensing negotiations to ensure that their ingenuity and infrastructure are utilized to maximize global welfare.

Georgetown's research, as noted above, has already contributed to life-saving medical technologies and will only continue to do so in the future. In addition to the innovations and ongoing research related to HPV, Georgetown researchers have recently conducted significant research that could pave the way for a test that could predict efficacy of chemotherapeutic agents in breast cancer patients.[21] Currently, Georgetown has cancer diagnostics, cancer therapeutics, and infectious disease innovations available for licensing, just to name a few.[22] However, we strongly believe that Georgetown's responsibility for those innovations does *not* end at licensing them out for further development under traditional licensing policies.

The institutional principles of the university are well-aligned with the goal of increasing access to medicines globally. According to Georgetown's Office of Technology Licensing, "Georgetown is committed to the policy that ideas or creative works produced at Georgetown should be used for the greatest possible public benefit, and believes that every reasonable incentive should be provided for the prompt introduction of such ideas into public use, all in a manner consistent with the public interest."[23]

Additionally, Georgetown is committed to developing "men and women for others," who, as recently noted by President DeGioia, will tackle the great global health crises of our day.[24] President DeGioia said at a recent White House meeting that, "At Georgetown, we seek to identify new and innovative ways by which the unique and considerable resources of an American research university, grounded in faith and guided by the ideal of compassion in action, can be brought to bear in combating global health threats." Socially responsible licensing policies are just such a way.

Georgetown and other universities are at a turning point, at which we are making the transition from national to truly global universities, and addressing the inequalities in global health today is a key part of this transition. In the words of our university president, "I think all of us know we're going to look back on this period and be asking ourselves where we were when 6,000 people a day are dying in Africa [of AIDS]."[25]

IV. Specific Proposals

International guidelines on intellectual property play a clear and significant role in increased prices for pharmaceuticals worldwide. However, given the current international political climate, systemic reform of intellectual property protection seems unlikely to occur in the near future. Therefore, we propose a modest intervention that works within existing trade-law and drug-development paradigms to circumvent both national and international obstacles to generic medicine production. Our proposal utilizes a three prong-approach to maximize Georgetown's role in increasing access to essential medicines: (1) Institute a

Global Health Licensing Program (2) Establish an Alumni Giving Campaign & Neglected Disease Research Fund (3) Leverage Georgetown's role in HPV vaccine research to facilitate affordable access to these vaccines.

1. Addressing the Access Gap – Instituting an Innovative Global Health Licensing Program

The Global Health Licensing approach

The ultimate goal of this proposal is to achieve marginal cost pricing for health-related end products, including medicines, biologics, diagnostic tests, and medical devices, in low- and middle-income (LMI) countries. To achieve this, we propose a thoughtful, innovation-specific approach to humanitarian licensing – rather than a one-size fits all approach. We propose that Georgetown's technology transfer agreements facilitate access to essential medicines in LMI countries by utilizing licensing language that is crafted to appropriately meet the need but tailored to the innovation to be licensed. The end result of such language could be allowing generic manufacturers the right to produce the innovation in LMI markets, regardless of patents, or could be a customized solution suitable to the drug, device, or biologic, that enhances access to that innovation.

It is important to note that the global health licensing approach we are suggesting is a *compromise approach* – it recognizes that not all Georgetown licenses would need to contain access-oriented licensing language. It also recognizes that a one-size fits all approach is not tenable, as access-oriented licensing language which may work for drugs may not work for biologics or diagnostic tests.[26] Or similarly, the need in LMI countries for one type of health-related innovation may be greater than the need for others. Thus, our approach attempts to strike an appropriate balance, one that addresses the challenges to previously proposed humanitarian licensing schemes while effectively ensuring that essential health-related innovations are made available and affordable in LMI countries.

The Global Health Licensing Approach v. Other Approaches

While a 'fair pricing' approach—obliging the manufacturer of a medicine to make it available at a low markup on marginal cost of production—might seem like a plausible (or even preferable) alternative to using university licensing to facilitate access, it would require a credible threat of enforcement for breach of contract. A licensing approach, on the other hand, does not require universities to take an active role in monitoring or enforcement. A licensing approach may also provide LMI patients with less expensive medicines than the fair pricing approach would. The balance of the evidence indicates that competition has been a more reliable method of lowering prices than voluntary "at cost" pricing.[27] Finally, a licensing approach has the advantage of fostering a more sustainable and locally appropriate supply of low-cost medicines in developing countries.

Though the access gap has attracted attention from a number of interested parties and various proposals have been debated, no systematic solution has been agreed upon. Some proposals utilize an Equal Access License (a mechanism that uses cross-licensing and grant back of rights to facilitate generic competition), compulsory licensing (the right of WTO member countries to issue their own licenses for production of specific medicines, governed by TRIPS), or voluntary differential pricing (relying on pharmaceutical companies to provide different prices for different markets). However, after exhaustive research and meetings with a variety of stakeholders, it is apparent that none of these options provides a singular solution to the access gap. Rather, each one has shortcomings that render them ineffective on their own. As such, to respond to the concerns of the university community and to address the issues raised by relevant stakeholders, we propose a unique and novel program for enhancing access to essential medicines via university licensing.

The Global Health Licensing Program at Georgetown[1]

The first prong of our strategy for maximizing Georgetown's role in increasing access to essential medicines involves implementing an innovative Global Health Licensing Program at Georgetown. The first of its kind, the program would recognize that each health-related innovation is produced, manufactured, and distributed differently, and that each has a different potential to positively impact health in LMI countries. As such, the Georgetown program would uniquely analyze each and every Georgetown health-related innovation available for licensing, and utilize the most appropriate access-oriented licensing language for those capable of having a positive health impact in LMI countries.

The Georgetown program would consist of two novel components: First, a standing committee to review each health innovation available for licensing, and, second, a toolbox of access-oriented licensing language from which the committee can select the most appropriate language when it deems the innovation could have a significant positive impact on health in LMI countries.

A. The Global Health Licensing Committee

The Global Health Licensing Committee would be a standing committee, hosted by the Georgetown Office of Technology Licensing, which would consist of technology transfer experts, researchers, patent attorneys, global health faculty members & clinicians, clergy, and students. The Committee would be charged with reviewing on a semi-annual basis all health-related innovations ready for licensing. When reviewing each innovation, the Committee must determine whether the expected resultant health product could have a significant positive impact on health in LMI countries. If so, the Committee must ensure that the license for the technology includes access-oriented language that goes beyond traditional, largely ineffective and unenforced, due diligence clauses.

B. The Global Health Licensing Toolbox

When the Committee determines that an innovation requires access-oriented licensing language, it must then select the most appropriate and effective language from a host of options to be created especially for the Georgetown Global Health Licensing Program. This Global Health Licensing Toolbox would consist of existing access licensing options as well as newly devised access licensing language, to be developed exclusively for the Toolbox by the Georgetown Essential Medicines Consortium. These newly devised options would seek to identify licensing language that is effective and appropriate for different types of health-related innovations. For example, the Consortium will seek to develop language that facilitates access to biologics, which require a wholly different manufacturing process than traditional drugs, presenting challenges for generic production. Or the Consortium will seek to develop language for diagnostic tests and other non-drug health innovations. Ultimately, the goal is for the Toolbox to provide an array of licensing options, such that the most effective, tailored, access-enhancing license is utilized.

Thus, the Global Health Licensing Program we propose presents an opportunity for Georgetown to take the lead in enhancing access to essential medicines. While other universities have engaged in socially responsible licensing efforts, none have implemented a comprehensive program designed to maximize impact and efficacy, as the Global Health Licensing Program would do. As such, Georgetown could augment its efforts to be the first truly "global" university, by being the first to institute an across-the-board effort to enhance access to medicines in LMI countries.

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[1] The Global Health Licensing Program was created and developed by the Georgetown Essential Medicines Consortium.

2. Establishing an Alumni Neglected Disease Research Fund

In its effort to be the first "global" university, Georgetown should also seek to become a leader in neglected disease research, and, in so doing, to attract nontraditional partners and funding for neglected disease research from non-profit grant sources, public-private partnerships (PPPs), and pharmaceutical firms. In particular, we propose instituting an alumni giving campaign and establishing an Alumni Neglected Disease Research Fund to jumpstart Georgetown research in this area. Recognizing that the 10-90 gap represents a lack of profit motive for pharmaceutical companies to engage in neglected disease research, we believe strongly that to address the diseases afflicting those in LMI countries, universities like Georgetown must take the lead and seek other sources of funding for such research.

Many interactions designed to facilitate neglected research have been designed in recent years, including: patent donation, dual-market licensing, and straightforward exclusive/non-exclusive licensing. Public-private partnerships, such as the Medicines for Malaria Venture, and new funding streams like that from the Bill & Melinda Gates Foundation are addressing the development gap, pushing an unprecedented number of compounds through clinical trials.

However, these projects depend on universities and other scientific institutions to fill the discovery gap. Therefore, it is essential that we seek out new ways to encourage work in these areas. The burgeoning field of public-private partnerships for global health research has attracted over $1.2 billion in funding from sources such as the Gates Foundation, the vast majority of which is contracted out to research scientists.[28]

Georgetown should ensure that its scientists are not excluded from benefiting from these nontraditional sources of neglected disease funding. However, we recognize that Georgetown researchers are best poised to secure grants from these funding sources when the university has an existing program dedicated to neglected disease research. As such, we propose that Georgetown institute an alumni giving campaign designed to establish an Alumni Neglected Disease Research Fund. The Fund would be used to hire neglected disease researchers and support a neglected disease research program. Once such a fund is established and Georgetown has shown itself to be a university dedicated to this research, our ability to garner support from other funding streams will be enhanced. The existence of such a Fund will also enhance our ability to secure faculty seeking to engage in neglected disease research.

Additionally, Georgetown should seek to strengthen their neglected disease research program by placing a premium on potential for contribution to neglected disease research during the process of hiring new faculty. Furthermore, Georgetown should recognize the difficulty of translating basic science research into end products in considerations of faculty promotion; hence, the University should develop alternative methods for evaluating neglected disease researchers that extend beyond publications authored and grants received.

Georgetown should also seek to increase interest in neglected disease research at the early stages of researchers' development – particularly by incorporating information on the 10-90 gap and the access gap in the medical school curriculum. A framework for doing so already exists in the social justice curriculum available to medical students at Georgetown.

Finally, the University should encourage neglected disease researchers' participation in preclinical development projects for neglected diseases, particularly open-source initiatives seeking to pool research resources for the purpose of speeding commercialization [e.g. Tropical Disease Initiative and Biological Innovation for Open Society.]

3. Taking Action to Facilitate Affordable Access to HPV Vaccines

In a milestone achievement in the fight against cancer, Gardasil, the Merck vaccine that is the first-ever to prevent cervical cancer, has now been approved for use in 50 countries.[29] GlaxoSmithKline is seeking FDA approval of its similar HPV vaccine, Cervarix, and has been approved for use in Europe.[30]

Both of these vaccines were developed using parallel research conducted at Georgetown and several other research institutions. Dr. Richard Schlegel, chair of the Department of Pathology at the Lombardi Comprehensive Cancer Center, and a team of Georgetown researchers, including Drs. A. Bennett Jenson and Shin-je Ghim have been instrumental in researching the L1 protein, which forms the basis of the vaccine.[31] The university is, and should be, immensely proud of their accomplishments. The researchers first "express[ed] the capsid protein of an HPV in the laboratory", then "over-expressed [it] in either yeast or insect cells," until it formed "virus-like particles, or VLPs, which look very similar to the 'real' virus."[32] It is this research that forms the basis of both HPV vaccines – both contain a mixture of VLPs that induce the body to generate protective antibodies to the virus, which is found in 99% of cervical cancer cases.[33]

Georgetown licensed its research to biotech company Medimmune to produce large amounts of the necessary protein for use in clinical trials, who then sublicensed it to GlaxoSmithKline to conduct the clinical trials which allowed the vaccine to be mass produced and approved.[34] Georgetown's decision to share its intellectual property and innovations with industry played a key role in developing this life-saving technology.

The vaccines are very expensive, however, reflecting the high costs of vaccine development. It costs approximately $360 for a course of three shots in the United States, and though the companies have pledged to reduce prices for poor countries, significant reductions would be necessary to make the vaccine truly accessible, as low-income countries can only spend about $8 per person on all health service provision annually, and middle-income countries about $49 per person.[35]

Merck has said it will offer the vaccine at "dramatically lower prices" in developing countries, and GSK has said it will use "tiered pricing," discounting it based on GDP, but neither company has agreed to forego profits from sales in poor countries. [36] Merck has partnered with the Clinton Global Initiative to donate enough doses to vaccinate one million women over the next several years. This is a wonderful gesture, but there are over two million women who need the vaccine and the donated doses will not convey many epidemiological benefits. Experts predict that "price is likely to be the main obstacle to HPV vaccination in the developing world."[37]

In particular, costs of the HPV vaccine are likely to be much higher in developing countries than other vaccines.[38] Prices for most vaccines bought by poor countries through the World Health Organization/UNICEF Expanded Program on Immunization are pennies a dose, and newer vaccines such as the Hib and Hepatitis B vaccines are underutilized at a price of $3.65 per dose, largely because of cost.[39] Even if the vaccine were priced at $25 a dose in poor countries, it would require a significant increase in national health spending to vaccinate the majority of eligible girls.[40] As such, experts predict significant external funding or specialized funding schemes will be necessary to finance the vaccine in poor countries.

As noted above, cervical cancer primarily affects women in developing countries. Women in developing countries account for 85% of new cervical cancer cases and deaths each year, and 200,000 women die of the disease in poor countries annually, compared with 3,000 in the United States.[41] In many developing countries, cervical cancer is the number one cause of cancer deaths in women.[42] This is largely because women in developing countries lack access to pap smears and preventive screenings available in

developed countries – only about 5% of women in developing countries have been screened for cervical cancer in the past five years, compared with as much as 50% in developed countries.[43] Additionally, developing countries have the largest percentage of girls in the target age group for the vaccine, with respect to their total population.[44]

The HPV vaccines developed with contributions from the Georgetown research team are needed even more so in developing country contexts, where pap screening is not readily available. Attempting to solve this problem by ameliorating the root causes – poor health care infrastructure, lack of skilled health workers, etc. – could take decades. In contrast, administering a vaccine that is nearly 100% effective and protects against the HPV types that cause 75% of all cervical cancers, would not take nearly as long to implement. Though current versions of the vaccine may require refrigeration,[45] which can present a hurdle to administration in developing countries, Georgetown researchers currently are developing versions which would not require refrigeration, and which could easily be reproduced by generic manufacturers.[46] Howard Zucker, WHO Assistant Director-General for Health Technology and Pharmaceuticals, says that HPV vaccines "could save hundreds of thousands of lives if delivered effectively" in the developing world.[47]

Georgetown has a long history of research in this area, and the next-generation vaccines being investigated by scientists led by Dr. Schlegel could have both preventive and therapeutic benefits for women worldwide.[48] In particular, the second-generation vaccine currently being developed would consist of a powder that could be easily reconstituted with water, presenting a cheaper and more easily distributed vaccine that holds serious promise for developing country settings. The third generation vaccine, which is being developed with a Gates Grand Challenge Grant, will hopefully be a single dose powder with therepeutic benefits.

Unfortunately, Georgetown's relationship to the current vaccine has been attenuated by paralell research at several institutions, cross-licensing between Merck and GSK, and lengthy interferrence proceedings to determine the legal holder of the dominant patent, which went to Dr. Ian Frazer at the University of Queensland on appeal this August. However, Georgetown has over twenty years of experience on HPV research, and recently received the patent for the second generation vaccine. We believe that Georgetown, given its Jesuit mission and its significant intellectual property rights related to second-generation HPV vaccines, is still in a position to lead the public charge for access to HPV vaccines.

As such, we call on Georgetown to begin a dialogue with its industry partners to discuss pricing and distribution of the HPV vaccine in LMI countries and to explore options for increasing access to the vaccine in these contexts, to ensure that Georgetown's current and future HPV innovations are utilized to the best public benefit.

V. Other Institutions Supporting Socially Responsible Licensing

Georgetown would not be alone in considering creative solutions to the problem of limited access to medicines in the developing world. Several ideas have been promulgated in academic and policy circles over the past few years. Most recently, in March 2007, eleven top research institutions and the American Association of Medical Colleges published a white paper on the topic, stating that "universities should strive to construct licensing arrangements in ways that ensure that these underprivileged populations have low- or no-cost access to adequate quantities of [university developed] medical innovations."[49] Many of the sponsoring universities, such as Harvard, Yale, Stanford, and Cornell are peers of Georgetown in the elite upper echelon of American universities. [See Appendix III for full text of the AAMC white paper].

The AAMC paper follows publication of the Universities Allied for Essential Medicines *Philadelphia Consensus Statement*, which calls on universities to promote equal access to research as well as research on neglected diseases and has been endorsed by over a hundred top scientists and public health luminaries, as well as thousands of students and others at 135 campuses around the world.[50]

And Sen. Patrick Leahy, chair of the Senate Judiciary Meeting and a Georgetown alumni, introduced a bill in the fall of 2006 that would require all federally-funded research institutions to ensure that the drugs they develop are supplied to poor countries at the lowest possible cost.[51] "I have introduced this legislation because the leaders of universities have not yet been able to come together around a different approach," Leahy said. [52] Leahy's bill, though unsuccessful, would have conditioned federal research funds on a university's adoption of socially responsible licensing policies. Sen. Leahy remains committed to seeking university-based solutions to the access gap, and his staff has expressed interest in highlighting on a national stage any university efforts to combat the access problem via innovative licensing programs.

Additionally, a 2005 report published by the American Association for the Advancement of Science explored ways to license university discoveries to drug companies in a way that ensures that the drugs can be accessed for humanitarian uses.[53] The report argued that humanitarian licensing practices would involve "a provision in a license whereby inventors and technology suppliers protect in advance the possibility of sharing their proprietary technology with third parties for the benefit of people in need." Likewise, the Association of University Technology Managers (AUTM) has convened a group known as Technology Managers for Global Health to look at how university research can be optimally advanced to improve global health outcomes.[54] Proposals for universities to institute policies which would promote neglected-disease research have also been put forth, most recently in the AAMC white paper.[55]

1. Specific action at peer universities

In addition, universities across the country have taken specific actions to increase access to their university innovations in the developing world.

Yale University
In 2001, the humanitarian organization Médecins Sans Frontières (MSF) requested a license from Yale University to buy generic stavudine – an HIV medication – from an Indian company which had offered to sell it in South Africa for approximately three percent of the price of the branded version.[56] Though Bristol-Myers Squibb (BMS) had an exclusive license to sell the drug, Yale was the key patent-holder.[57] Within weeks of receiving the request from MSF, Yale and
BMS announced that they would permit the sale of generics in South Africa and that the price of brand-name stavudine would be slashed thirty-fold for the government and for non-governmental organizations.[58]

Additionally, in 2003, Yale and the University of Washington issued a license to Institute for One World Health, to develop a Chagas' disease treatment specifically for use in developing countries. The universities retained the ability to issue a different license for developed-world applications, likely as a for-profit venture.[59] This represents another method of socially responsible licensing that preserves developed-world markets for pharmaceutical companies and maintains profits for such companies and universities, while facilitating low-cost access to medicines in poor countries.

University of Washington
More recently, the Intellectual Property Management Advisory Committee at the University of Washington adopted a resolution on Jan. 4, 2007, that will help increase access to University of Washington health technologies and innovations in the developing world.[60] The policy "values distributing UW intellectual properties worldwide and the societal good that can come from such

innovations over the revenue they might generate if licensed only through exclusive agreements, if a choice must be made between the two."[61] The policy recognizes that the primary goal of university innovations should be worldwide use and societal benefit and recommends that an *ad hoc* faculty committee examine cases in which specific conflicts between societal benefit and commercial interests arise.[62]

University of California-Berkeley
Berkeley has had pieces of a socially responsible licensing program for approximately three years, which especially recognize that socially responsible licensing can be a strategy for stimulating research support, in addition to maximizing societal benefit of Berkeley technologies.[63] The Office of Intellectual Property and Industry Research Alliances notes that the program "can stimulate business & societal change through the creation of new markets for additional nonprofit pharmaceutical companies."[64] Additionally, the Office recognizes that utilizing licensing such as an Equal Access License can attract collaborations, new streams of research funding, donations and other forms of support.[65] Significantly, Berkeley has negotiated numerous contacts and licenses under the socially responsible licensing program, including many prospective commitments to grant royalty-free licenses for humanitarian use. Examples include:

1. TB Vaccine – The university negotiated an agreement with a for-profit biotech company such that if a TB vaccine is developed using Berkeley research, it will be distributed royalty free in developing countries.
2. Malaria – Berkeley also issued a royalty-free license to provide artemisinin, a high-demand treatment for drug-resistant malaria, to a biotech company that will provide the drug at cost to developing countries and a non-profit pharmaceutical company that will do the work necessary for regulatory approval. The project was funded by a $42.6 million grant from the Gates Foundation, indicating that socially responsible licensing can be funded through new revenue streams and do not require a loss of profits for universities and drug companies.[66]
3. Dengue Fever – The university has issued a royalty-free license to a non-profit organization to distribute a diagnostic for Dengue fever to the developing world.

In March 2006, Chancellor Birgeneau of the University of California-Berkeley, agreed to change the online mission statement of its technology licensing program to note that for technology and intellectual property relevant to global health, "our primary goal is to improve global human welfare." The university has also begun marketing its 'Socially Responsible Licensing Initiative' as a way to attract nontraditional funding, and it has already signed a handful of deals with foundations and nonprofits under that licensing rubric.[67]

University of Nebraska
The University of Nebraska negotiated a deal in 2003 with Medicines for Malaria Venture, whereby the university issued a royalty-free license for Ranbaxy Laboratories to develop and produce an anti-malarial compound derived from wormwood.

2. An opportunity for Georgetown

Despite this significant progress, to date no university has established a comprehensive access scheme for licensing health related innovations with significant promise for the developing world. Progressive technology transfer for neglected diseases has also been slow to move beyond isolated deals. We believe our proposal presents a novel, practicable, and informed approach. Since our initial proposal we have met with many significant stakeholders and reflected on the best practices and realistic concerns in implementing such a comprehensive plan. We feel even more strongly than before, and present evidence

via this paper, that Georgetown is ideally situated and perfectly poised to play a leading role in addressing the access and research gaps currently plaguing the developing world.

Georgetown has the opportunity to institute intellectual property policies which would ensure that its innovations reach those vulnerable people who need them most. If carefully developed, such policies need not interfere with Georgetown's ability to work with private entities, either as funding sources or as downstream developers. We propose that Georgetown take advantage of this opportunity to become the first truly global university, with technology transfer agreements that facilitate access to essential medicines in LMI countries by utilizing licensing language that is crafted to enhance access. We also propose that Georgetown join the growing list of universities whose research policies reflect a priority for neglected diseases. This goal could be met with an Alumni Neglected Disease Research Fund to build our institutional expertise and engage our talented alumni. Lastly, we propose that Georgetown use its position as a moral and research leader to agitate for better global pricing and access to the current and future HPV vaccines. Clear and sensible policies on intellectual property and the promotion of neglected disease research would elevate Georgetown's reputation as a trailblazer in addressing one of the most challenging humanitarian crises of our time.

VI. IMPACT ASSESSMENT

1. Impact on Low- and Middle-Income Countries

The impact of these proposals on patients in low- and middle- income countries is largely dependent on the University's ability to develop novel drugs, diagnostics, or devices useful in treating human disease. As noted above, the ownership position of universities as a whole in pharmaceutical technologies is both substantial and increasing.[68] The number of patents and license agreements executed by universities have approximately doubled between 1993 and 2003.[69] As of 2005, 28,349 licenses currently existed between universities and companies, and 1.25 new products based on academic inventions have been introduced each day over the past eight years.[70] A major share of this university intellectual property is in the biomedical field.[71] For example, universities own patent rights in key pharmaceuticals used in recent years, including the cancer drugs cysplatin and carboplatin,[72] pemetrexed (Alimta),[73] cetuximab (Erbitux);[74] the anemia treatment epoetin alfa (Epogen);[75] the AIDS drugs stavudine (Zerit),[76] lamivudine (Epivir),[77] abacavir (Ziagen),[78] emtricitabine (Emtriva),[79] and T20 (Fuzeon);[80] and the bestselling glaucoma medicine latanoprost (Xalatan).[81]

Georgetown has already played a significant role in globally relevant discovery – the HPV vaccine is just one example, but as one of the foremost research institutions in the nation, Georgetown's research will undoubtedly contribute to future health innovations. The world-renowned faculty at the School of Medicine, School of Nursing & Health Studies, Lombardi Comprehensive Cancer Center, and Biomedical Graduate Research Organization and the $138 million they attracted in sponsored research in 2006 provide the necessary substrates for discovery. Furthermore, Georgetown has added researchers such as prostate cancer pioneer Nancy Dawson to its faculty, who will continue developing novel approaches to cancer treatment, and Dr. Howard Federoff as its new executive director for health sciences, who will help make Georgetown a leader in biomedical science research. [82]

The University's recent research initiatives have already begun to reap dividends, and Georgetown between 2003-2005 submitted 19 new patent applications[83]. In addition to the HPV vaccine, a simple survey of the Office of Technology Licensing reveals technologies currently available for licensing that can impact treatment of diseases with a significant global health burden.[84] In addition to biomarkers that could be used to diagnose cervical cancer – which, as noted above, primarily affects women in the

developing world – Georgetown has developed innovations that could assist in the detection and treatment of prostate and breast cancer, as well as numerous other cancers.[85]

Though LMI countries experience a disproportionate burden of disease from communicable and infectious diseases, rates of chronic diseases such as heart disease, cancer, and obesity are rapidly increasing – leaving these countries facing a double-edged sword.[86] As such, these Georgetown technologies could lead to innovations of significant utility in the developing world and there is great potential for Georgetown licensing to help curb morbidity and mortality caused by non-communicable diseases in developing countries.

Additionally, recent initiatives that promote generic competition within LMI countries – a potential outcome of the Georgetown Global Health Licensing Program – have proven extremely effective in lowering the price of essential medicines.[87] For example, when the Brazilian government began generic production of antiretrovirals in 2000, prices quickly fell by 82%.[88] Additionally, in 2001, Médecins Sans Frontières (MSF) requested a license from Yale University to buy generic stavudine – an HIV medication – from an Indian company which had offered to sell it in South Africa for approximately three percent of the price of the branded version.[89] Though Bristol-Myers Squibb (BMS) had an exclusive license to sell the drug, Yale was the key patent-holder.[90] Yale and BMS announced that they would permit the sale of generics in South Africa and that the price of brand-name stavudine would be slashed thirty-fold for the government and for non-governmental organizations.[91]

The impact of this intervention was unequivocal: rapid expansion of HIV-treatment programs in sub-Saharan Africa would not have been possible without generic stavudine, a WHO-recommended first-line therapy. Prices fell almost immediately from $1600 to $55 per patient year for the branded version, down even further (to $35 per patient year) with generic competition.[92] While a success story in many ways, the change in policy agreed to by BMS occurred retrospectively and only with great public pressure. *Had access-minded licensing*
provisions been in place ex ante, these difficulties would have been avoided and an untold number of lives could have been saved.

The precise impact of a university licensing intervention in improving access remains difficult to appraise. Essentially, this is a problem of measuring missed opportunities. While one might argue that it is difficult to point to cases where university licensing was the limiting factor in expanding access, this misses the crux of why licensing is important. University licensing presents an *opportunity* for increasing access. This opportunity arises because universities lie far upstream in the drug development process and because universities respond to a different set of incentives than companies.

Delineating LMI Countries
Determining which countries fall within the LMI category for purposes of access-oriented licensing and measuring its impact will ultimately be a somewhat arbitrary decision. We believe the most sensible category would include all low- and middle-income countries as defined by the World Bank.[93] We include middle-income countries because many of these countries (e.g., Brazil, Mexico, and South Africa) have highly unequal income distributions and large poor populations that must obtain their own care in the private sector.[94] For example, 613 million people in China live on less than $2 per day.[95] If licenses only enabled generic companies to enter low-income markets, they would leave out many individuals whom universities aim to benefit. Additionally, there is a wealth of evidence demonstrating that the poor of societies with severe income inequalities are actually the worst off, regardless of their income or poverty level.[96] As such, leaving out the poor of middle-income countries with highly unequal income distributions could leave those most needy out in the cold.

It is also important to note that in situations where access-oriented licensing language allowed for generic competition the revenue potential of middle-income countries would help ensure that there are sufficient financial incentives for generic companies to sustain production of a given medicine. Plus, excluding middle-income countries would prevent equitable access provisions from operating where they might work best—for the often chronic, developed-world indications in the developing world. Middle-income countries are in particular need of such medications.[97] Those middle-income countries that do grow sufficiently to be recognized as high-income countries would no longer be able to take advantage of access-oriented licensing language, however.

2. Impact on Georgetown University

As a leading international institution and a university committed to social justice and Jesuit principles, Georgetown has always served as a model in education and public service. Georgetown has also recently sought to redefine its role as a leader in the fight against global health crises, with the creation of the O'Neill Institute on Global and National Health Law, the Center for Law & the Public's Health, and with its designation as a World Health Organization and Pan-American Health Organization Collaborating Center on Public Health Law and Human Rights. President DeGioia has also committed himself and his presidency to making Georgetown the university leading the charge in the fight against global AIDS.[98] As such, we believe that adopting the above proposals is consistent with Georgetown's desire to remain a leader amongst universities with international spheres of influence. Furthermore, the University is likely to derive a substantial public relations boost for its efforts to address the global lack of access to medicines.

The Global Health Licensing Program Meets the Need for Collective Action
As with any new and innovative approach to technology transfer, Georgetown may hesitate to be the first to change its licensing practices due to concerns that industry might shy away from a solo actor. It is therefore critical that major research institutions work together to bring these new approaches forward, as exemplified by the recent White Paper published by the American Association of Medical Colleges and several top research institutions. [See Section V and Appendix III for more information].[99] The ultimate goal is for all universities to collectively adopt access-minded licensing practices, thereby maximizing impact and bargaining power with industry partners. The Georgetown Global Health Licensing Program represents an opportunity to promote collective action – this unique and innovative program could be shared with lawmakers and other universities as a model for positive university action. Georgetown implementing such a comprehensive program will inspire other universities to follow suit.

In addition to leading the way through its own policies, specific venues at which Georgetown could promote the Global Health Licensing Program include the biannual meetings of senior research officers at major research institutions, meetings of the American Association of Universities, and the Association of University Technology Managers (AUTM). This movement is already occurring to some extent, as evidenced by the AAMC White Paper, and Georgetown would not be alone in pushing things forward.

Many universities have negotiated individual access-minded licensing agreements, and others have begun to alter their broader approach to research and development.[100] However, no university has engaged in a comprehensive, innovative approach like the Global Health Licensing Program outlined in this proposal. As such, it is to Georgetown's advantage, both from a global health and a public relations perspective, to implement this program, be a model to other universities, and play a catalytic role in identifying practicable ways for universities to enhance access to essential medicines.

University- Industry Relations
When entering into early negotiations, it will be important to keep in mind that our industry partners are not averse to tackling global health problems. Indeed, many pharmaceutical companies are outspokenly

committed to improving global human welfare.[101] However, the lawyers dedicated solely to contract negotiation are not necessarily the most appropriate representatives of pharmaceutical companies' priorities. Top scientists and CEOs may be more likely to value advancement of global health, especially considering the interest in repairing the industry's public image. Georgetown has good relationships with industry leaders and is well-suited to start this dialogue. Through engaging appropriate actors, Georgetown's ability to adopt innovative licensing policies increases significantly.

Economic Impact
While we strongly emphasize the great potential for a positive impact around the world from the Global Health Licensing Program, we recognize that the university is also concerned about its obligation to continue creating and disseminating new knowledge through its ties to industry. The revenues gained from technology transfer are used to re-invest in research and are critical to ensure that new advances are quickly developed into technology that will improve quality of life.

An initial Georgetown-specific economic analysis indicates that implementing the Global Health Licensing Program will not pose a serious threat to university profits. The analysis evaluated the impact of including open-licensing language in ALL health related innovations (a much broader proposition than what is suggested by the Global Health Licensing Program in this proposal), and found that even instituting this approach across the board, Georgetown would lose only one-half of one percent of its total operating expenditures. [See Appendix II for the complete analysis].

This analysis also did not include any potential revenues from royalties that would be due to Georgetown under the open-licensing language used, and also assumed pharmaceutical companies would require Georgetown to compensate them for any shortfall in the value of the license – an assumption which may not prove true in licensing negotiations. Thus, the analysis indicates that using a more conservative approach, such as that suggested by the Global Health Licensing Approach, and applying access-oriented licensing language to only those health innovations with significant applicability in LMI countries, would have little if any impact on Georgetown's bottom line.

3. Impact on Pharmaceutical Companies

As stated above, sales in low- and middle-income countries represent a small proportion of pharmaceutical industry revenue – 5-7% on average.[102] Sub-Saharan Africa represents only 1.3%. A former CEO of Eli Lilly put this in perspective, stating that complete loss of this market would cost "about three days fluctuation in exchange rates."[103] Additionally, access-oriented licensing and preferential pricing agreements that would be utilized in the Global Health Licensing Program could benefit pharmaceutical companies by providing a convenient way for them to take advantage of the fact that the markets for their products—individual countries—are perfectly segmented. [See Appendix II for more information]. When markets are perfectly segmented, companies can charge different prices in different markets, a practice known as price discrimination. Price discrimination allows companies to increase profits because they are able to select an optimal price in each individual market, rather than being restricted to a single world-wide price.

Access-oriented licensing could be a useful way for pharmaceutical companies to take advantage of segmented markets, because companies may be hesitant to charge lower prices in LMI countries for fear of a negative reaction in developed countries. For example, pharmaceutical companies may be concerned that selling drugs at lower prices in developing countries could lead to pressure to sell at the same low prices in developed countries. With access-oriented licensing, however, often foreign generic partners would produce drugs for foreign sales, providing an intuitive answer for why prices may differ across countries. [See Appendix II for more information].

Diversion

One potential concern with access-oriented licensing, however, is the potential for diversion of drugs from poor countries for illicit resale in rich countries. Historically, however, diversion from poor countries has rarely been observed. Generic drugs have been produced in India for decades without apparently infiltrating or undermining Western markets.[104]

Meanwhile, the only significant media reports of diversion have been shown to be overblown. For example, GlaxoSmithKline alleged in 2002 that 36,000 packages of HIV medicines worth approximately $18 million were found to have been diverted from a charitable initiative in West Africa to the EU.[105] It turned out that 99% of the packages handled by the parallel trader were not part of Glaxo's charitable access initiative but rather ordinary commercial sales at prices approximating EU prices. Also, Glaxo did not label the packages as ineligible for sale or re-importation in the EU.[106]

Insofar as diversion is a concern, it can be addressed in the same manner that the World Trade Organization has addressed it—by requiring use of different packaging, pill color, and pill shape in different countries to facilitate the identification of illegal imports.[107] The access-licensing approach actually reduces the risk that medicines would be diverted to markets in high-income countries compared to a drug-donation or voluntary differential pricing approach. Differentially-priced products sold by the original, branded company (as in Canada) may be susceptible to parallel trade, particularly if they are similar in appearance. Regulatory barriers exist to prevent these medicines from entering high-income markets easily, though they are sometimes not enforced.[108] Generic versions of the same medicines have to overcome a second legal barrier (due to patent protection) governed by customs procedures. Moreover, consumer demand for these generics is likely to be low compared to reimported branded products.

Access Gaps in High-Income Countries

Another potential concern pharmaceutical companies may have is the perception that these novel licensing practices only address the access gap abroad while ignoring the significant access gap that exists in the U.S. Indeed, an access gap clearly does exist within the U.S. and the Global Health Licensing Program would not provide a domestic solution. Access-oriented licensing and similar mechanisms, however, often rely on the ability to divide markets into two groups—those with branded-drug exclusivity and those with generic competition. Application of these strategies within the U.S. would necessitate a neat division of poor and rich markets, which is clearly infeasible. For this reason, we suggest that governments are more aptly situated to enact domestic solutions to this problem than universities.

Though licensing provisions are unlikely to provide a solution to the access gap in the U.S., the use of access-oriented licensing should not present a public relations liability for the pharmaceutical industry. The American public's interest in and concern for global health matters have grown substantially in recent years. Additionally, often it would be generic manufacturers, not brand-name companies, selling at low prices. While lower prices for identical branded drugs invite public criticism, generic products do not.

VII. CONCLUSION

Global access to medicines represents a life or death scenario for millions of people worldwide. The problem is, in one sense, attributable to societal ingenuity. As a result of biomedical innovations that allow treatment and prevention of disease, we are continuously challenged to distribute the product equitably. For other patients, those suffering from neglected diseases, the economic principles underlying our society seem to have failed them entirely.

Yet this is not a time for the global community to concede defeat. Indeed, recent years have brought about numerous reasons for hope. The Bill and Melinda Gates Foundation has invested billions of dollars into

its global health mission in the past six years. The Global Fund to fight AIDS, Tuberculosis, and Malaria involves a multilateral commitment targeting three of the world's biggest sources of disease burden. President George W. Bush has reinforced the United States' leadership role through the creation of the President's Emergency Plan for AIDS Relief. The Drugs for Neglected Diseases Initiative oversees both the research and distribution of novel drugs. While each of these initiatives is associated with its own set of positive and negative attributes, the current climate is ripe for the enactment of new and creative solutions.

As presented in this proposal, we envision Georgetown University playing a significant role in addressing both the access and the research gap. As a leading research institution, Georgetown can play a catalytic role in reaffirming the notion that universities have an obligation to enhance global welfare. Georgetown's research endeavors ensure that sufficient innovation will be produced by the University for the policy changes to be meaningful. Lastly, our proposal comes at a time when Georgetown is actively seeking to enhance its worldwide reputation through global engagement. With careful consideration and thoughtful implementation, Georgetown has an opportunity to live up to its potential as a true global university and ensure that its globally relevant discoveries enhance the welfare of those in greatest need.

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For more evidence, *see* Evelyn M. Hauser and Philip M. Kitagaqa, *Differential Mortality in the United States: A Study of Socio-Economic Epidemiology* (Cambridge, MA: Harvard University Press, 1973); Michael G. Marmot and G.D. Smith, "Health Inequalities Among British Civil Servants: The Whitehall II Study," *Lancet*, 337 (1991): 1387-93; Donald Acheson, ed., *Independent Inquiry Into Inequalities in Health* (London: Stationery Office Books, 1998); Stephen J. Kunitz, with Irena Pesis-Katz, "Mortality of White Americans, African Americans, and Canadians: The Causes and Consequences for Health of Welfare State Institutions and Policies," *Milbank Quarterly*, 83 (2005): 5-39 (finding that life expectancy of African Americans has been substantially lower than that of white Americans for as long as records are available and that life expectancy of all Americans has been lower than that of all Canadians since the beginning of the twentieth century); Johan P. Mackenbach, "Health Inequalities: Europe in Profile," *UK Presidency of the EU* (February 2006), www.dh.gov.uk/assetRoot/04/12/15/84/04121584.pdf (finding "substantial inequalities" in health in all European countries based on education, occupational class, and income); Ken Judge, Stephen Platt, Caroline Costongs, et al., "Health Inequalities: A Challenge for Europe," *UK Presidency of the EU* (2006), www.dh.gov.uk/assetRoot/04/12/15/83/04121583.pdf (reviewing European efforts to reduce health disparities including programs for social justice, social inclusion, and poverty reduction). For a comparison of health disparities outcomes and politics across states and countries, see "Special Issue: Comparative Perspectives on Health Disparities," *Journal of Health Politics, Policy & Law*, 31 (2006): 1-281. Health disparities in the United States are vast even by international standards, which cannot be explained by race, income, or health care access alone. Christopher J.L. Murray, Sandeep C. Kulkarni, Catherine Michaud, et al., "Eight Americas: Investigating Mortality Disparities Across Races, Counties, and Race-Counties in the United States, PLoS Medicine, 3 (2006), http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0030260 (a black man living in a high-crime city can expect to live 21 fewer years than an Asian woman); Eugene Rogot, Paul Sorlie, Norman Johnson, et al., eds., *A Mortality Study of 1.3 Million Persons by Demographic, Social and Economic Factors: 1979-1985 Follow-Up* (Bethesda, MD: National Institutes of Health, 1992); S. Leonard Syme, "Social and Economic Disparities in Health: Thoughts about Intervention," *Milbank Quarterly*, 76 (1998): 493–505. In 2005, the WHO established a Commission on Social Determinants of Health with the mission to link knowledge with action. Michael Marmot, "Social Determinants of Health Inequalities," *Lancet*, 365 (2005): 1099-1104; Barbara Starfield, "State of the Art in Research on Equity in Health," *Journal of Health Politics, Policy & Law*, 31 (2006): 11-32.

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Appendix I: Sponsoring Organizations

This proposal was developed by the Georgetown Essential Medicines Consortium with significant assistance and input from Dave A. Chokski and others at Universities Allied for Essential Medicines. We are grateful for their assistance and support. Other sponsoring organizations include:

The Georgetown AIDS Law Movement
The Georgetown Society for Health Law & Bioethics
American Medical Students Association – Georgetown Chapter
OurMoment
The American Constitution Society at Georgetown
The Asian Pacific American Law Student Association at Georgetown
La Allianza del Derecho
Law Students for Choice
Outlaw
Caribbean Law Students Association
Corporate Law Association

Appendix II: Initial Economic Impact Assessment for Georgetown University

This appendix describes some of the potential implications of requiring open licensing/preferential pricing clauses in ALL of Georgetown's health-related licensing agreements. It is important to note that *this assessment assumes the use of a single open-licensing mechanism in every license created for every Georgetown health-related innovation.* Thus, this assessment goes well beyond the Global Health Licensing Program that is being proposed here. The Global Health Licensing Program reflects a more thoughtful, innovation-specific approach to humanitarian licensing – rather than a one-size fits all approach. As such it is a compromise recognizing that not all Georgetown licenses would need to contain access-oriented licensing language. Thus, this assessment likely overestimates the potential economic impact to Georgetown from our proposal.

This assessment begins by estimating the portion of Georgetown's licensing revenue attributable to sales from lower income countries (LICs) and lower middle-income countries (LMCs). Next, it provides an estimate of the financial implications of open licensing for Georgetown. It concludes with a discussion of ways in which open licensing could potentially increase profits for pharmaceutical companies and increase licensing revenue for Georgetown.

Georgetown's Licensing Revenue from Sales in LICs and LMCs is Small

From 2000 to 2006, we estimate that the portion of Georgetown University's medical licensing revenue attributable to sales in LICs and LMCs was 6 one-hundredths of 1 percent of total operating expenditures. [See Table 1.] This revenue ranged from a high of 3 tenths of 1 percent in 2000 to a low of 1 one thousandth of 1 percent in 2001. Regardless of the year, and certainly when considering the annual average, licensing payments attributable to sales in LICs and LMCs are a minor source of revenue for Georgetown.

The calculations used to derive these estimates are straightforward. Data on licensing revenue were obtained from the Office of Technology Licensing. The portion of this revenue based on sales to LICs and LMCs is based on an industry-wide average reported by the Pharmaceutical Research and Manufacturers of America, a trade association of pharmaceutical companies.

Compensating Pharmaceutical Companies May Increase the Cost of Open Licensing

Table 2 provides an estimate of the total cost to Georgetown of requiring open licensing or preferential pricing agreements in its medical licensing contracts. It is important to note that these estimates are *based on several assumptions that greatly increase the calculated cost*, relative to alternative choices. For example, the calculations in Table 2 assume that pharmaceutical companies would lose all revenue generated in LICs and LMCs as a result of open licensing, which is almost certainly not the case.[1] In short, when making decisions about how to assess the cost of open licensing, we always chose to bias the costs upward, rather than downward.

The cost estimate in Table 2 contains two components, both of which are based on the assumption that pharmaceutical companies lose all revenue from sales in LICs and LMCs. The first component is the direct cost associated with lost licensing revenue. These costs are simply the revenue estimates provided in Table 1. The second component is a cost associated with

[1] In fact, as discussed below, open-licensing could actually increase revenues in developing countries, by providing an easy way for pharmaceutical companies to set market-specific prices.

compensating pharmaceutical companies for profits lost on sales in LICs and LMCs. In other words, we derive the profits earned by pharmaceutical companies on sales in LICs and LMCs and then assume that Georgetown would pay the drug companies an amount equal to those lost profits.

Clearly, this second component increases the estimated cost to Georgetown of requiring open licensing/preferential pricing clauses in its licensing contracts. In fact, it most likely overstates the cost, because if Georgetown were to simply stop licensing its medical technologies, it would lose at most the direct licensing revenue included in Component 1. We have included the second indirect component of the cost of open licensing as a way to ensure that we do not understate the cost of these provisions, while also incorporating their impact on pharmaceutical companies.

Open Licensing Could Yield Benefits to Pharmaceutical Companies

Open licensing and preferential pricing agreements could benefit pharmaceutical companies by providing a convenient way for them to take advantage of the fact that the markets for their products—individual countries—are perfectly segmented.[2] When markets are perfectly segmented firms are able to charge different prices in different markets, a practice known as price discrimination. Price discrimination allows firms to increase profits because they are able to select an optimal price in each individual market, rather than being restricted to a single world-wide price.

Open licensing, in particular, could be a useful way for pharmaceutical companies to take advantage of segmented markets. Without open licensing, firms may be hesitant to charge lower prices in developing countries, in part because of the reaction in developed countries. For example, pharmaceutical companies may be concerned that selling drugs at lower prices in developing countries could lead to pressure to sell at the same low prices in developed countries. With open licensing, however, foreign partners would produce drugs for foreign sales, providing an intuitive answer for why prices may differ across countries.

In sum, open licensing and/or preferential pricing clauses in licensing agreements may provide pharmaceutical companies with a way to increase profits through price discrimination. To the extent that this increases pharmaceutical company profits, it could also increase Georgetown's licensing revenue.

[2] Perfect segmentation refers to the fact that drugs could not be purchased in a low-price market, such as a developing country and shipped to high-price market in a developed country. This inability to trans-ship is generally due to legislation prohibiting the importation of drugs. The recent debate over the inability of health-care providers in the United States to import lower-priced drugs from Canada provides an example of this situation.

Table 1: Licensing Revenue Attributable to Sales in Low and Lower-Middle Income Countries

	2000	2001	2002	2003	2004	2005	2006	2007	Annual Average	Reference
Georgetown University Royalties from Medical Licensing[1]	26.1	0.07	0.31	0.18	0.75	0.49	8.48	3	4.92	A
Percentage of Pharmaceutical Revenue Coming from Low-Income and Lower-Middle-Income Countries (LICs and LMCs)[2]	7.00%	7.00%	7.00%	7.00%	7.00%	7.00%	7.00%	7.00%	7.00%	B
Georgetown University Royalties Attributable to Sales in LICs and LMCs	1.83	0.00	0.02	0.01	0.05	0.03	0.59	0.21	0.34	C=A*B
Georgetown University Total Operating Expenditures (TOE)[3]	545.138	540.712	584.132	644.221	680.496	711.847	744.101	N/A	635.807	D
Georgetown University Royalties Attributable to Sales in LICs and LMCs as % TOE	0.3%	0.001%	0.004%	0.002%	0.008%	0.005%	0.08%	N/A	0.062%	E=C/D

[1] Source: Carla Demaria, Georgetown University, Office of Technology Licensing

[2] Pharmaceutical Research and Manufacturers of America, Pharmaceutical Industry Profile 2005--From Laboratory to Patient: Pathways to Biopharmaceutical Innovation, 40 (2005). Percentage of revenues from LMI countries: 5-7%.

[3] Financial Statements of Georgetown University, Prepared by PricewaterhouseCoopers

Cost to Georgetown University of Requiring Open Licensing/Preferential Pricing in Medical Licensing Agreements

Component 1: Direct Cost to Georgetown from Loss of Licensing Revenue										
	2000	2001	2002	2003	2004	2005	2006	2007	Annual Average	Reference
Georgetown University Royalties from Medical Licensing[1]	26.1	0.07	0.31	0.18	0.75	0.49	8.48	3	4.92	A
Percentage of Pharmaceutical Revenue Coming from Low-Income and Lower-Middle-Income Countries (LICs and LMCs)[2]	7.00%	7.00%	7.00%	7.00%	7.00%	7.00%	7.00%	7.00%	7.00%	B
Georgetown University Royalties Attributable to Sales in LICs and LMCs	1.83	0.00	0.02	0.01	0.05	0.03	0.59	0.21	0.34	C=A*B
Georgetown University Total Operating Expenditures (TOE)[3]	545.138	540.712	584.132	644.221	680.496	711.847	744.101	N/A	635.807	D
Georgetown University Royalties Attributable to Sales in LICs and LMCs as % TOE	0.3%	0.001%	0.004%	0.002%	0.008%	0.005%	0.08%	N/A	0.062%	E=C/D
Component 2: Indirect Cost to Georgetown from Compensating Pharmaceutical Companies for Lower Profits										
License Fee as Percentage of Pharmaceutical Company Revenue[4]	2.00%	2.00%	2.00%	2.00%	2.00%	2.00%	2.00%	2.00%	2.00%	F
Revenue of Pharmaceutical Companies for Georgetown-Related Products	1,305.0	3.5	15.5	9.0	37.5	24.5	424.0	150.0	246.1	G=A/F
Portion of Revenue from LICs and LMCs	91.4	0.2	1.1	0.6	2.6	1.7	29.7	10.5	17.2	H=G*B
Profit Margin in LICs and LMCs[5]	16.00%	16.00%	16.00%	16.00%	16.00%	16.00%	16.00%	16.00%	16.00%	I
Profit from Sales in LICs and LMCs	14.62	0.04	0.17	0.10	0.42	0.27	4.75	1.68	2.76	J=H*I
Profit Loss of Pharmaceutical Companies as % of Georgetown University TOE	2.7%	0.007%	0.03%	0.02%	0.06%	0.04%	0.64%	N/A	0.50%	K=J/D
Total Cost: Sum of Components 1 and 2										
Total Lost Revenue	16.44	0.04	0.20	0.11	0.47	0.31	5.34	1.89	3.10	L=C+J
Total Lost Revenue as % of Georgetown University TOE	3.0%	0.008%	0.03%	0.02%	0.07%	0.04%	0.72%	N/A	0.56%	M=L/D

[1] Source: Carla Demaria, Georgetown University, Office of Technology Licensing

[2] Pharm. Research & Mfrs. Of Am., Pharmaceutical Industry Profile 2005--From Laboratory to Patent: Pathways to Biopharmaceutical Innovation, 40 (2005). Percentage of revenues from LMI countries: 5-7%.

[3] Financial Statements of Georgetown University, Prepared by PricewaterhouseCoopers

[4] Thursby, M. and J. Thursby (2002). "University Licensing Under Bayh-Dole."

[5] Calculated from "How the Fortune 1000 Stack Up In Their Industries." Fortune. April 15, 2002.

Appendix III: AAMC White Paper

EMBARGOED UNTIL 3/6/07, 2 P.M. PACFIC TIME

In the Public Interest:
Nine Points to Consider in Licensing University Technology

Licensing approaches, even for comparable technologies, can vary considerably from case to case and from institution to institution based on circumstances particular to each specific invention, business opportunity, licensee and university. In spite of this uniqueness, universities share certain core values that can and should be maintained to the fullest extent possible in all technology transfer agreements.

In the summer of 2006, Stanford University's then Dean of Research Arthur Bienenstock convened a small meeting of research officers, licensing directors and a representative from the Association of American Medical Colleges to brainstorm about important societal, policy, legislative and other issues in university technology transfer. Representatives of the participating institutions, listed below, have tried to capture in this document certain shared perspectives that emerged from that meeting. Recognizing that each license is subject to unique influences that render 'cookie-cutter' solutions insufficient, it is our aim in releasing this paper to encourage our colleagues in the academic technology transfer profession to analyze each licensing opportunity individually in a manner that reflects the business needs and values of their institution, but at the same time, to the extent appropriate, also to bear in mind the concepts articulated herein when crafting agreements with industry. We recognize that many of these points are already being practiced. In the end, we hope to foster thoughtful approaches and encourage creative solutions to complex problems that may arise when universities license technologies in the public interest and for society's benefit.

California Institute of Technology
Cornell University
Harvard University
Massachusetts Institute of Technology
Stanford University
University of California
University of Illinois, Chicago
University of Illinois, Urbana-Champaign
University of Washington
Wisconsin Alumni Research Foundation
Yale University
and
Association of American Medical Colleges (AAMC)

Point 1
Universities should reserve the right to practice licensed inventions and to allow other non-profit and governmental organizations to do so

In the spirit of preserving the ability of all universities to perform research, ensuring that researchers are able to publish the results of their research in dissertations and peer- reviewed journals and that other scholars are able to verify published results without concern for patents, universities should consider reserving rights in all fields of use, even if the invention is licensed exclusively to a commercial entity, for themselves and other non-profit and governmental organizations:

> 1) to practice inventions and to use associated information and data for research and educational purposes, including research sponsored by commercial entities; and
>
> 2) to transfer tangible research materials (e.g., biological materials and chemical compounds) and intangible materials (e.g., computer software, databases and know-how) to others in the non-profit and governmental sectors.

Clear articulation of the scope of reserved rights is critical. Recent examples of such "retained rights" clauses are included in the Appendix for reference.

Point 2
Exclusive licenses should be structured in a manner that encourages technology development and use

When significant investment of time and resources in a technology are needed in order to achieve its broad implementation, an exclusive license often is necessary and appropriate. However, it is important that technology transfer offices be aware of the potential impact that the exclusive license might have on further research, unanticipated uses, future commercialization efforts and markets. Universities need to be mindful of the impact of granting overly broad exclusive rights and should strive to grant just those rights necessary to encourage development of the technology.

Special consideration should be given to the impact of an exclusive license on uses of a technology that may not be appreciated at the time of initial licensing. A license grant that encompasses all fields of use for the life of the licensed patent(s) may have negative consequences if the subject technology is found to have unanticipated utility. This possibility is particularly troublesome if the licensee is not able or willing to develop the technology in fields outside of its core business. Universities are encouraged to use approaches that balance a licensee's legitimate commercial needs against the university's goal (based on its educational and charitable mission and the public interest) of ensuring broad practical application of the fruits of its research programs. There are many alternatives to strict exclusive licensing, several of which are described in the Appendix.

In situations where an exclusive license is warranted, it is important that licensees commit to diligently develop the technology to protect against a licensee that is unable or unwilling to move an innovation forward. In long-term exclusive licenses, diligent development should be well-defined and regularly monitored during the exclusive term of the agreement and should promote the development and broad dissemination of the licensed technology. Ideally, objective, time-limited performance milestones are set,

with termination or non-exclusivity (subject to limited, but reasonable, cure provisions) as the penalty for breach of the diligence obligation. Examples of diligence requirements (also known as performance milestones) are described in the Appendix.

Another means of ensuring diligent development, often used in conjunction with milestones, is to require exclusive licensees to grant sublicenses to third parties to address unmet market or public health needs ("mandatory sublicensing") and/or to diligently commercialize new applications of the licensed rights. Such a requirement could also be implemented through a reserved right of the licensor to grant direct licenses within the scope of the exclusive grant to third parties based on unmet need. In such situations, it is important to ensure that the parties have a common understanding of what constitutes a new application or unmet need for the purpose of implementing such a provision. An example of mandatory sublicensing language is provided in the Appendix.

Absent the need for a significant investment - such as to optimize a technology for wide use - broad, non-exclusive licensing of tools such as genomic and proteomic inventions can help maximize the benefits derived from those technologies, in part by removing obstacles to further innovation. Unlike most research tools or manufacturing methods, diagnostic tests often must go through the regulatory approval process, and so may warrant exclusive licensing when the costs of test development, approval or diffusion require substantial investment of capital. Nevertheless, licensing of diagnostic tests based on broadly applicable genomics or proteomics methods should strive to preserve sufficient flexibility to permit testing for multiple indications (i.e., not an exclusive licensee's single disease of interest) perhaps through multiple field-restricted or non- exclusive licenses. Exclusive licensing of a single gene for a diagnostic may be counterproductive in a multi-gene pathology where only a panel of genes can yield an adequate diagnosis, unless the licensee has access to the other genes of the panel. Such licenses can also be limited in other ways. For example, a university might license a genomics method exclusively for a company to optimize and sell licensed products for diagnostic use. The drafting of the exclusive grant could make it clear that the license is exclusive for the sale, but not use, of such products; in doing so, the university ensures that it is free to license non-exclusively to others the right (or may simply not assert its rights) to use the patented technology, which they may do either using products purchased from the exclusive licensee or those that they make in-house for their own use.

In general, when no alternative testing strategy is available for a given indication, consideration should be given to means of ensuring reasonable access for patients and shielding individual healthcare providers from the risk of suit for patent infringement. As with any medical technology, licenses should not hinder clinical research, professiona education and training, use by public health authorities, independent validation of test results or quality verification and/or control.

Point 3
Strive to minimize the licensing of "future improvements"

Although licensees often seek guaranteed access to future improvements on licensed inventions, the obligation of such future inventions may effectively enslave a faculty member's research program to the company, thereby exerting a chilling effect on their ability to receive corporate and other research funding and to engage in productive collaborations with scientists employed by companies other than the licensee – perhaps even to collaborate with other academic scientists. In particular, if such future rights reach to inventions made elsewhere in the university, researchers who did not benefit from the licensing of the original invention may have their opportunities restricted as well, and may be disadvantaged economically relative to the original inventors if the licensing office has pre-committed their inventions to a licensee.

For these reasons, exclusive licensees should not automatically receive rights to "improvement" or "follow-on" inventions. Instead, as a matter of course, licensed rights should be limited to existing patent applications and patents, and only to those claims in any continuing patent applications that are (i) fully supported by information in an identified, existing patent application or patent and (ii) entitled to the priority date of that application or patent.

In the rare case where a licensee is granted rights to improvement patents, it is critical to limit the scope of the grant so that it does not impact uninvolved researchers and does not extend indefinitely into the future. It is important to further restrict the grant of improvements to inventions that are owned and controlled by the licensor institution - i.e., (i) not made by the inventor at another institution, should they move on or (ii) co-owned with, or controlled by, another party. One refinement to this strategy would be to limit the license to inventions that are dominated by the original licensed patents, as these could not be meaningfully licensed to a third party, at least within the first licensee's exclusive field. As was discussed earlier, appropriate field restrictions enable the licensing not only of the background technology, but also of improvements, to third parties for use outside the initial licensee's core business. In all cases, a license to improvements should be subject to appropriate diligent development requirements.

It should be recognized, however, that not all "improvements" have commercial potential (for example, they may not confer sufficient additional benefit over the existing technology to merit the expense of the development of new or modified products), in which case a licensee might not wish to develop them. In general, it may be best simply not to patent such improvements.

Point 4
Universities should anticipate and help to manage technology transfer related conflicts of interest

Technology transfer offices should be particularly conscious and sensitive about their roles in the identification, review and management of conflicts of interest, both at the investigator and institutional levels. Licensing to a start-up founded by faculty, student or other university inventors raises the potential for conflicts of interest; these conflicts should be properly reviewed and managed by academic and administrative officers and committees outside of the technology transfer office. A technology licensing professional ideally works in an open and collegial manner with those directly responsible for oversight of conflicts of interest so as to ensure that potential conflicts arising from licensing arrangements are reviewed and managed in a way that reflects well on their university and its community. Ideally, the university has an administrative channel and reporting point whereby potential conflicts can be non-punitively reported and discussed, and through which consistent decisions are made in a timely manner.

Point 5
Ensure broad access to research tools

Consistent with the NIH Guidelines on Research Tools, principles set forth by various charitable foundations that sponsor academic research programs and by the mission of the typical university to advance scientific research, universities are expected to make research tools as broadly available as possible. Such an approach is in keeping with the policies of numerous peer-reviewed scientific journals, on which the scientific enterprise depends as much as it does on the receipt of funding: in order to publish research results, scientists must agree to make unique resources (e.g., novel antibodies, cell lines, animal models, chemical compounds) available to others for verification of their published data and conclusions.

Through a blend of field-exclusive and non-exclusive licenses, research tools may be licensed appropriately, depending on the resources needed to develop each particular invention, the licensee's needs and the public good. As suggested with respect to genomics and proteomics method patents in Point 2 above, a university might license a research reagent, kit or device exclusively to a company to optimize and sell licensed products and services for research, diagnostic or other end uses. The drafting of such an exclusive grant should make clear that the license is exclusive for the sale, but not use, of such products and services; in doing so, the university ensures that it is free to license non-exclusively to others the right to use the patented technology, which they may do either using products purchased from the exclusive licensee or those that they make in- house for their own use.

Point 6
Enforcement action should be carefully considered

In considering enforcement of their intellectual property, it is important that universities be mindful of their primary mission to use patents to promote technology development for the benefit of society. All efforts should be made to reach a resolution that benefits both sides and promotes the continuing expansion and adoption of new technologies. Litigation is seldom the preferred option for resolving disputes. However, after serious consideration, if a university still decides to initiate an infringement lawsuit, it should be with a clear, mission-oriented rationale for doing so one that can be clearly articulated both to its internal constituencies and to the public. Ideally, the university's decision to litigate is based on factors that closely track the reasons for which universities obtain and license patents in the first place, as set out elsewhere in this paper. Examples might include:

a. Contractual or ethical obligation to protect the rights of existing licensees enjoy the benefits conferred by their licenses; and
b. Blatant disregard on the part of the infringer for the university's legitimate rights in availing itself of patent protection, as evidenced by refusal on the part of the infringer to negotiate with or otherwise entertain a reasonable offer of license terms.

Under all circumstances, it reflects poorly on universities to be involved in "nuisance suits." Exclusive licensees should be encouraged to approach patent enforcement in a manner that is consistent with the philosophy described in this Point 6.

Point 7
Be mindful of export regulations

University technology transfer offices should have a heightened sensitivity about export laws and regulations and how these bodies of law could affect university licensing practices. Licensing "proprietary information" or "confidential information" can affect the "fundamental research exclusion" (enunciated by the various export regulations) enjoyed by most university research, so the use of appropriate language is particularly important. Diligence in ensuring that technology license transactions comply with federal export control laws helps to safeguard the continued ability of technology transfer offices to serve the public interest.

Point 8
Be mindful of the implications of working with patent aggregators

As is true of patents generally, the majority of university-owned patents are unlicensed. With increasing frequency, university technology transfer offices are approached by parties who wish to acquire rights in

such 'overstock' in order to commercialize it through further licenses. These patent aggregators typically work under one of two models: the 'added value' model and the so-called 'patent troll' model.

Under the added value model, the primary licensee assembles a portfolio of patents related to a particular technology. In doing so, they are able to offer secondary licensees a complete package that affords them freedom to operate under patents perhaps obtained from multiple sources. As universities do not normally have the resources to identify and in-license relevant patents of importance, they cannot offer others all of the rights that may control practice (and, consequently, commercialization) of university inventions. By consolidating rights in patents that cover foundational technologies and later improvements, patent aggregators serve an important translational function in the successful development of new technologies and so exert a positive force toward commercialization. For example, aggregation of patents by venture capital groups regularly results in the establishment of corporate entities that focus on the development of new technologies, including those that arise from university research programs. To ensure that the potential benefits of patent aggregation actually are realized, however, license agreements, both primary and secondary, should contain terms (for example, time-limited diligence requirements) that are consistent with the university's overarching goal of delivering useful products to the public.

In contrast to patent aggregators who add value through technology-appropriate bundling of intellectual property rights, there are also aggregators (the 'patent trolls') who acquire rights that cut broadly across one or more technological fields with no real intention of commercializing the technologies. In the extreme case, this kind of aggregator approaches companies with a large bundle of patent rights with the expectation that they license the entire package on the theory that any company that operates in the relevant field(s) must be infringing at least one of the hundreds, or even thousands, of included patents. Daunted by the prospect of committing the human and financial resources needed to perform due diligence sufficient to establish their freedom to operate under each of the bundled patents, many companies in this situation will conclude that they must pay for a license that they may not need. Unlike the original patent owner, who has created the technology and so is reasonably entitled to some economic benefit in recognition for its innovative contribution, the commercial licensee who advances the technology prior to sublicensing, or the added value aggregator who helps overcome legal barriers to product development, the kind of aggregator described in this paragraph typically extracts payments in the absence of any enhancement to the licensed technology.1 Without delving more deeply into the very real issues of patent misuse and bad-faith dealing by such aggregators, suffice it to say that universities would better serve the public interest by ensuring appropriate use of their technology by requiring their licensees to operate under a business model that encourages commercialization and does not rely primarily on threats of infringement litigation to generate revenue.

Point 9

Consider including provisions that address unmet needs, such as those of neglected patient populations or geographic areas, giving particular attention to improved therapeutics, diagnostics and agricultural technologies for the developing world

Universities have a social compact with society. As educational and research institutions, it is our responsibility to generate and transmit knowledge, both to our students and the wider society. We have a specific and central role in helping to advance knowledge in many fields and to manage the deployment of resulting innovations for the public benefit. In no field is the importance of doing so clearer than it is in medicine.

Around the world millions of people are suffering and dying from preventable or curable diseases. The failure to prevent or treat disease has many causes. We have a responsibility to try to alleviate it, including finding a way to share the fruits of what we learn globally, at sustainable and affordable prices, for the benefit of the world's poor. There is an increased awareness that responsible licensing includes

consideration of the needs of people in developing countries and members of other underserved populations.

The details involved in any agreement provisions attempting to address this issue are complex and will require expert planning and careful negotiation. The application will vary in different contexts. The principle, however, is simple. Universities should strive to construct licensing arrangements in ways that ensure that these underprivileged populations have low- or no-cost access to adequate quantities of these medical innovations.

We recognize that licensing initiatives cannot solve the problem by themselves. Licensing techniques alone, without significant added funding, can, at most, enhance access to medicines for which there is demand in wealthier countries. Diseases that afflict only the global poor have long suffered from lack of investment in research and development: the prospects of profit do not exist to draw commercial development, and public funding for diseases suffered by those who live far away from nations that can afford it is difficult to obtain and sustain. Through thoughtful management and licensing of intellectual property, however, drugs, therapies, and agricultural technologies developed at universities can at least help to alleviate suffering from disease or hunger in historically marginalized population groups.

Summary

As often is the case, guidance as to implementation of practices that will advance the mission of university technology transfer lags behind our collective awareness of both the needs that exist and our obligations to foster an environment in which they can effectively be met. While we may generally agree on the commonality of the above challenges, a multiplicity of approaches are possible to address the dual goals of nurturing future research and using the innovations of university research to provide the broadest possible benefit to the public. The participating universities put forth these considerations in an aspirational sense and we encourage all of our colleagues to stretch the boundaries of conventional technology transfer practice and share with the greater technology transfer community the insights that they gain in doing so.